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# JMIRx Med

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MPA, PhD, CEng, FBCS, EUR ING

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Peer-Review Report

# Peer Review of “Machine Learning–Based Prediction of COVID-19 Mortality With Limited Attributes to Expedite Patient Prognosis and Triage: Retrospective Observational Study”

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Companion article: <https://www.medrxiv.org/content/10.1101/2021.03.21.21253984v2>

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(*JMIRx Med* 2021;2(4):e34082) doi:[10.2196/34082](https://doi.org/10.2196/34082)

**KEYWORDS**

COVID-19; coronavirus; medical informatics; machine learning; artificial intelligence; dimensionality reduction; automation; model development; prediction; hospital; resource management; mortality; prognosis; triage; comorbidities; public data; epidemiology; pre-existing conditions

*This is a peer-review report submitted for the paper “Machine Learning–Based Prediction of COVID-19 Mortality With Limited Attributes to Expedite Patient Prognosis and Triage: Retrospective Observational Study.”*

## Round 1 Review

**General Comments**

The paper [1] uses two standard machine learning algorithms to predict mortality of COVID-19 patients, based on a publicly available data set. The data repository contains over 2,600,000 COVID-19–positive samples, of which only a subset of 212 samples were extracted based on the requirement to have full feature availability. A second set of experiments is performed with 5121 samples where symptom information is not required. The performance of the trained logistic regression and random forest algorithms are compared for the data set with 25 features and a reduced data set containing only 7 features. The result is that the reduced feature set leads to higher specificity, sensitivity, accuracy, and area under the curve. An additional result based on the larger data set of 5121 is that age holds a large predictive value.

Many results on mortality prediction of COVID-19 using a range of standard machine learning and advanced deep learning algorithms on larger data samples have entered the literature by now. Since this manuscript uses simple algorithms on a small data set, the strength of this manuscript is neither in the prediction algorithms nor in the relevance of the use case.

However, an important line of inquiry is the data quality and the extraction of a small subset of features for good predictive power. To strengthen the results in this area, a more detailed exposition of the feature reduction and comparison with other methods is advisable.

**Specific Comments****Major Comments**

1. Mutual information as a method for data reduction is not standard to the extent that a single sentence stating that it was used is sufficient. To aid the reader’s understanding and further reproducibility of the article, it should be detailed exactly how this was used. Were the distributions of variables modeled or binned in the mutual information estimate? Were any priors used in the mutual information estimates? The equations, assumptions, and, if used, software packages should be stated in the *Methods* section along with references if the method is not detailed in full in this article.
2. The 7 features that are left after the dimension reduction should be shown and described. Is this a subset of the original feature set or a linear/nonlinear combination of those features?
3. The larger data set of 5121 patients was selected based on the same data completeness requirements apart from symptoms. It is not clear why models for this larger data set were only trained based on the single feature of age. A comparison of the 5121 patients with all features and the 212 with the same

features plus symptom data is missing but would give a better estimation of how important symptom data is.

4. Error bars for the relevant test metrics are missing. The sensitivity, specificity, accuracy, and area under the curve are based on 3-fold cross-validation for the models with 25 features and 7 features. Since the effect size is small, error bars should be presented, graphically or numerically, to convince the reader.

5. It would strengthen the results of this paper if the relevance of certain features for the prediction of outcomes would be compared to Estiri et al, who have used a similar methodology on the same use case but on a different data set:

Estiri H, Strasser ZH, Klann JG, et al. Predicting COVID-19 mortality with electronic medical records. *NPJ Digit Med.* 2021;4(15). doi:10.1038/s41746-021-00383-x

6. In the spirit of reproducibility, and since the models are not too complicated, parameters after training should be reported.

### **Minor Comments**

7. Since the data repository is continuously updated, the date on which a snapshot was taken should be reported. Ideally, for each experiment, the manuscript should detail exactly which samples were included in training and which were included in testing, because other researchers can directly compare the author's models and possible alternative models on the same data.

8. It is stated that "Receiver Operator Characteristic curves will be plotted for some classifiers..." but the plots are missing.

## **Round 2 Review**

### **General Comments**

The author has addressed all my previous comments and the manuscript is, from my point of view, sound as far as the application and description of the machine learning methods are concerned.

My only minor comment is that Table 2 should have units (I assume mutual information is measured in bits here).

### **Conflicts of Interest**

None declared.

### **Reference**

1. Doyle R. Machine learning-based prediction of COVID-19 mortality with limited attributes to expedite patient prognosis and triage: retrospective observational study. *JMIRx Med* 2021;2(4):e29392 [[FREE Full text](#)] [doi: [10.2196/29392](https://doi.org/10.2196/29392)]

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Peer-Review Report

# Peer Review of “Machine Learning–Based Prediction of COVID-19 Mortality With Limited Attributes to Expedite Patient Prognosis and Triage: Retrospective Observational Study”

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## KEYWORDS

COVID-19; coronavirus; medical informatics; machine learning; artificial intelligence; dimensionality reduction; automation; model development; prediction; hospital; resource management; mortality; prognosis; triage; comorbidities; public data; epidemiology; pre-existing conditions

*This is a peer-review report submitted for the paper “Machine Learning–Based Prediction of COVID-19 Mortality With Limited Attributes to Expedite Patient Prognosis and Triage: Retrospective Observational Study.”*

## Round 1 Review

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### General Comments

This paper [1] shows useful information that would allow better health management in countries with a high incidence of COVID-19 cases. The rationale for the study is clear, but there is little scientific literature to support the information presented.

### Specific Comments

#### Major Comments

1. The introduction of the paper presents only 4 bibliographic references, which is scarce to defend the problem and justification of a study. In the summary, he mentioned at the beginning that human resources in hospitals are scarce, which is an important reality that has not been addressed in the introduction of the paper. I suggest starting by evaluating the problem of hospital saturation, with epidemiological indicators from various studies that can support this information (this will

notably increase the number of references); then, justify the study with the potential benefits of using these types of tools.

2. During the discussion, technical aspects of the statistical models used are evaluated; however, I suggest that a comparison or appreciation can be provided regarding the utility and impact that these results would show in public health.

#### Minor Comments

3. In the Abstract, it is suggested that the general objective of the study be reported. Remember that the summary seeks to capture the reader’s attention and not saturate them with details.

4. In the first line of the introduction of the study, it says “... development of the COVID-19”; it should say “... development of the Coronavirus Disease (COVID-19)”. Remember that the first time an acronym is mentioned, its full name must be written.

5. According to the International Committee of Biomedical Journal Editors, the table description should be at the top of the table. In Tables 1, 2, and 3, the description is below.

6. In order that the tables and figures do not leave doubts to the readers, I suggest that in Table 2, there should be a footnote where it is specified what the author refers to with “AUC.”

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## Conflicts of Interest

None declared.

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**Reference**

1. Doyle R. Machine learning–based prediction of COVID-19 mortality with limited attributes to expedite patient prognosis and triage: retrospective observational study. JMIRx Med 2021;2(4):e29392 [FREE Full text] [doi: [10.2196/29392](https://doi.org/10.2196/29392)]

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# Peer Review of “Influence of Mass Media on Italian Web Users During the COVID-19 Pandemic: Infodemiological Analysis”

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Anonymous

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## KEYWORDS

COVID-19; Google Trends; infodemiology; infoveillance; infodemic; media coverage; mass media influence; mass media; social media

*This is a peer-review report submitted for the paper “Influence of Mass Media on Italian Web Users During the COVID-19 Pandemic: Infodemiological Analysis.”*

## Round 1 Review

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### General Comments

This manuscript [1] explores the very interesting topic of the impact of the COVID-19 infodemic, using Google Trends data. However, there are several points that would need to be addressed for this manuscript to become a contribution to the international literature.

### Specific Comments

#### Major Comments

##### 1. Introduction:

The Introduction is structured like one large paragraph. It should be split. Moreover, the Introduction should be enhanced to include a concise introduction of infodemiology and previous mentions of the term *infodemic*, as well as how the term developed, what other examples in recent history we have, etc. As it is, the Introduction is somewhat poor and not very informative of the wider topic (although it has adequately addressed the Italian infodemic issue).

##### 2. Methods:

The Google Trends methodology for data collection is also very poor and not detailed. This part should be rewritten. The *Statistical Analysis* section consists of very standard tests/correlations, and there is no need to have mathematical expressions/explanations for percentage increase, as an example.

##### 3. Results:

The *Results* section is informative and elaborate, but at points it is too elaborate and also needs to be rewritten in order to not consist of redundant information (the additional information could be moved to an appendix).

##### 4. Discussion:

The *Discussion* section is also not reader friendly and should be restructured, while several parts should be rewritten in order to keep the interest of the reader.

#### Minor Comments

5. Although marginally exceeding the Journal’s 450-word requirement [2], I would suggest that the Abstract be even smaller in size.

6. Try to avoid bullet points, unless absolutely necessary.

7. Cite URLs as standard references at the reference list (see Journal requirements [2]).

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## Conflicts of Interest

None declared.

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## References

1. Rovetta A, Castaldo L. Influence of mass media on Italian web users during the COVID-19 pandemic: infodemiological analysis. JMIRx Med 2021;2(4) [[FREE Full text](#)] [doi: [10.2196/32233](https://doi.org/10.2196/32233)]
  2. Instructions for Authors of JMIR. JMIR Publications. URL: <https://www.jmir.org/content/author-instructions> [accessed 2021-10-14]
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Peer-Review Report

# Peer Review of “Influence of Mass Media on Italian Web Users During the COVID-19 Pandemic: Infodemiological Analysis”

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**KEYWORDS**

COVID-19; Google Trends; infodemiology; infoveillance; infodemic; media coverage; mass media influence; mass media; social media

*This is a peer-review report submitted for the paper “Influence of Mass Media on Italian Web Users During the COVID-19 Pandemic: Infodemiological Analysis.”*

## Round 1 Review

**General Comments**

Thank you for providing me the opportunity of serving as a reviewer for this interesting manuscript [1]. The study aims to estimate the influence of Italian mass media on users' web interests about COVID-19. It is original, well-written, and addresses an important research topic. Despite that, it presented several gaps that can be improved. Below are suggestions/doubts for the authors to consider.

**Specific Comments**

1. The text presents some English errors. I recommend a grammar revision.
2. Introduction: Present a broader view on the subject to justify the study objectives. Moreover, avoid introducing methodological issues in this section.
3. Introduction: Why do people search for health-related information on the internet? How does the pandemic influence this behavior?
4. Introduction: What is the impact of infodemiology studies on public health? Also, what is the importance of infodemiological studies to combat the infodemic?
5. Introduction: What is Google Trends and what are its utility/advantages for infodemiological studies? The following studies may be helpful:

- Higgins TS, Wu AW, Sharma D, Illing EA, Rubel K, Ting JY, Snot Force Alliance. Correlations of online search engine trends with coronavirus disease (COVID-19) incidence: infodemiology study. *JMIR Public Health Surveill* 2020;6(2):e19702. doi: 10.2196/19702. PMID: 32401211
  - Rovetta A, Bhagavathula AS. COVID-19-Related Web Search Behaviors and Infodemic Attitudes in Italy: Infodemiological Study. *JMIR Public Health Surveill* 2020;6(2):e19374. doi: 10.2196/19374. PMID: 32338613
  - Lotto M, Aguirre PEA, Rios D, Machado MAAM, Cruvinel AFP, Cruvinel T. Analysis of the interests of Google users on toothache information. *PLoS One* 2017;12(10):e0186059. doi: 10.1371/journal.pone.0186059. PMID: 29049315
  - Mavragani A, Ochoa G. Google Trends in infodemiology and infoveillance: methodology framework. *JMIR Public Health Surveill* 2019;5(2):e13439. doi:10.2196/13439. PMID:31144671
  - Nuti SV, Wayda B, Ranasinghe I, Wang S, Dreyer RP, Chen SI, Murugiah K. The use of Google Trends in health care research: a systematic review. *PLoS One* 2014;9(10):e109583. doi: 10.1371/journal.pone.0109583. PMID: 25337815
6. Introduction: The third aspect proposed for investigation is not adequate. The authors go beyond the main scope by introducing a “fake news” analysis. The authors did not define what “fake news” is, and the analysis made is too superficial for the proposed outcome. I recommend that this step be better planned and analyzed, being described in a future manuscript.

7. Introduction: Question R4 has already been widely discussed in the literature and can be removed. If necessary, this aspect can be presented in the *Discussion* section.

8. Methods: The data collection is confusing and needs to be better described. Why were these platforms chosen? What are the main media in Italy and which ones have been selected? Describe in detail how data were collected on each platform.

9. Methods: Does analyzing search results on platforms really show the influence of the media? Why was a qualitative study not proposed?

10. Methods: What is the infodemic scale? Present it in detail.

11. Methods: Is the normalization of media data on the same scale as Google Trends correct? Since the absolute Google Trends data is blind, it doesn't seem like a valid comparison to me.

12. Methods: What test was done to assess seasonality?

13. Results: Avoid discussing the results in advance, as in "Evidence supporting causation."

14. Discussion: Only media influence is discussed about Google Trends data. What other factors might influence the findings? Why do people search for information related to COVID-19 during the pandemic?

15. Discussion: Compare the findings with previous literature. Several studies have investigated users' COVID-19-related interests on Google Trends, including in Italy.

16. Discussion: Why are technical terms little used? Where does the Italian population learn about the pandemic? How do eHealth literacy and media literacy influence this process?

17. Discussion: Include a *Practical Implications* subsection.

## Round 2 Review

### General Comments

Thank you for reviewing the manuscript based on my comments. In general, the suggestions were satisfactorily answered, and the quality of the paper has improved considerably.

### Conflicts of Interest

None declared.

### Reference

1. Rovetta A, Castaldo L. Influence of mass media on Italian web users during the COVID-19 pandemic: infodemiological analysis. *JMIRx Med* 2021;2(4) [[FREE Full text](#)] [doi: [10.2196/32233](https://doi.org/10.2196/32233)]

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# Peer Review of “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study”

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Anonymous

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## KEYWORDS

local social network; community health; well-being; digital health; consumer health

*This is a peer-review report submitted for the paper “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study.”*

## Round 1 Review

---

### General Comments

This paper [1] describes a study on a social network intervention to promote well-being in college students using local and community-based activities. The manuscript describes an exploratory feasibility study of the interventions, called Quokka. The authors ran a 6- to 8-week challenge across 4 universities. Three hypotheses were tested.

The paper is well written and will be of interest to JMIR readers; I enjoyed reading it myself and think there is great value in this type of study, particularly now given the many challenges to our mental health due to the COVID-19 pandemic and the move to predominantly online life. I would recommend “probably accept pending some revisions” to clarify some issues in data analysis and presentation.

### Specific Comments

The authors describe the challenges embedded in Quokka, and they present an overview of the program; however, they do not describe the features of the system. A walkthrough of the system would be appropriate to include.

I was confused by the testing of the 3 hypotheses. In the *Results* section, under *Evaluation Outcomes*, the authors first claim “All 3 hypotheses were confirmed”; then, they suggest “we reject the hypothesis that similar proportion of users would participate in local and remote activities during the challenges,” which seems to be H1. Please clarify and also refer to the hypothesis number (eg, H1) when discussing it.

I am not an expert in the approach taken for data analysis. I was hoping to see a better description of the steps taken to analyze the qualitative data to test for significance. I think this is necessary to improve the reliability of the outcomes.

Similarly, I was hoping to see a better description of how the thematic analysis was conducted. What was the approach in coding and forming themes? The themes are described, but we don't get any information about how these themes were identified.

*Limitations* section: I would suggest outlining the limitations of the method and data analysis given that it mainly relied on qualitative data. I do not mean to suggest qualitative data is not valid (quite the opposite); however, the authors have taken the approach to test hypotheses using the qualitative study. So a better engagement with the limitations of their approach would be appropriate.

Ethics: was the study approved by an ethics committee? How was consent obtained? Please specify.

## Round 2 Review

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### General Comments

The revised manuscript provides the details requested previously. The walkthrough of the system that is added is helpful to understand its utility. Details on hypotheses and limitations also address initial concerns around clarity of the manuscript. I am happy with the changes made and recommend accepting the manuscript.

## Specific Comments

### Minor Comments

There were a few errors in writing which I am sure will be easy to address once the authors proofread their manuscript; for instance, they used “patient” instead of “user” in some places.

---

## Conflicts of Interest

None declared.

---

## Reference

1. Shih C, Pudipeddi R, Uthayakumar A, Washington P. A local community-based social network for mental health and well-being (Quokka): exploratory feasibility study. *JMIRx Med* 2021;2(4):e24972 [[FREE Full text](#)] [doi: [10.2196/24972](https://doi.org/10.2196/24972)]
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*Peer Review of “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study”*

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Peer-Review Report

# Peer Review of “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study”

Maria da Graça Campos Pimentel<sup>1</sup>, MSc, PhD, Dr Habil

Departamento de Ciências de Computação, Universidade de São Paulo, São Carlos, SP, Brazil

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(*JMIRx Med* 2021;2(4):e33925) doi:[10.2196/33925](https://doi.org/10.2196/33925)

**KEYWORDS**

local social network; community health; well-being; digital health; consumer health

*This is a peer-review report submitted for the paper “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study.”*

## Round 1 Review

**General Comments**

The authors present a study [1] evaluating the impact of offering college students challenges designed to develop healthy habits. The challenges were offered to students in 4 campuses via a community-based social network. The challenges follow the same structure: volunteers in each campus customize them for their community. The “community-based” research involved partnerships with local mental health resources and services available, local businesses, or school-affiliated groups. The study aimed at evaluating the preferences of the participants relative to three features: (a) local versus remote activities, (b) group versus individual activities, (c) new versus familiar activities.

**Specific Comments****Major Comments**

1. Do the challenges correspond to the “interventional program that makes use of the established success of community-based social programs for behavior change”? Or the “community-based social network”?
2. Given the variety and duration of the challenges and the intervention’s length, were the participants expected to accumulate the “change in habits” over the overall period? And after that?
3. How were the campuses selected?

4. How much of the study could be generalized to different campuses? Please present the “typical” demographics in these campuses (students, staff, and locals) and discuss their impact on the study.

5. How were the volunteers in each campus selected?

6. Are there any data on the demographics of the participants?

7. Please review the text for clarity and precision. In particular:

(a) The hypotheses H1-H3 (presented in the section *Study Design*) do not match the first result reported in the section *Evaluation Outcomes*.

(b) The hypothesis rejected in the study is never presented as a hypothesis (you may want to refer to H1).

(c) Several portions of the text are repetitive.

**Minor Comments**

8. Please revise the style to substitute imprecise terms.

9. Please reconsider employing section headers for the challenges in the section *Challenges Themes*.

## Round 2 Review

**General Comments**

The authors provide answers to reviewers’ questions and present a revised and improved version that tackles their comments. I have a few concerns that I suggest the authors tackle in a new revision, as detailed below.

## Specific Comments

### Major Comments

1. The authors included a related work section after the Introduction. Following the IMRD structure suggested in JMIR's Instructions for Authors document, I suggest that the motivating literature be presented, instead, in the *Introduction* itself.
2. The authors do not compare their contribution with prior work, limiting the potential impact of their approach. I suggest including a *Comparison With Prior Work* section in the *Discussion* section, as suggested in the JMIR's Instructions for Authors document.
3. When comparing your contribution with that of prior work, please specify how you identified the prior work selected for discussion. Please make sure to include recent work.
4. How did you select the work currently discussed in the "Related Section"?

### Minor Comments

5. I suggest modifying the title to make it explicit that "well-being" is related to (mental) health.

## Round 3 Review

### General Comments

The authors responded to reviewers' questions and acted on their suggestions. However, the resulting manuscript still has issues regarding its structure concerning the problems tackled and the work carried out. My main concerns follow.

### Specific Comments

#### Major Comments

1. You propose a system to tackle a problem and then evaluate the system. In my humble opinion, the system itself pertains to the "method" you used to assess whether or not you contributed to the problem. Is this the case? If so, please revise the manuscript structure accordingly.
2. The revised version is annotated, which makes it very hard to follow the resulting manuscript. Accepting all changes exposes (a) contents not aimed at the reviewers, and (b) formatting issues.
3. Please avoid using sections with a single paragraph (as in challenging themes): the result is distracting.

## Conflicts of Interest

None declared.

## Reference

1. Shih C, Pudipeddi R, Uthayakumar A, Washington P. A local community-based social network for mental health and well-being (Quokka): exploratory feasibility study. *JMIRx Med* 2021;2(4):e24972 [FREE Full text] [doi: [10.2196/24972](https://doi.org/10.2196/24972)]

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## Peer-Review Report

# Peer Review of “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study”

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Ziyou Ren<sup>1</sup>, PhD

Center for Research Informatics, University of Chicago, Knapp Center for Biomedical Discovery, Chicago, IL, United States

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### KEYWORDS

local social network; community health; well-being; digital health; consumer health

*This is a peer-review report submitted for the paper “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study.”*

## Round 1 Review

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### General Comments

The authors [1] tried to investigate the effects of a well-being theme (ie, Quokka) through setting challenges in 4 different university campuses. There were 277 participants. The author found the participants preferred local activities to remote, but there was not enough evidence to support other significant differences.

Although the author focused on an interesting topic, most of the analysis was descriptive and lacked depth. For example, the relationship between the major outcomes and well-being was not clear. Is there any measurement for mental health, such as anxiety or depression, after using Quokka? Furthermore, I was confused whether the manuscript is about Quokka, the platform, or is an intervention study using Quokka. I would appreciate if the authors could add more details to the Quokka platform if this is original. Who developed the platform? If the Quokka platform was developed by someone else, please include the reference. The conclusion and generalization of the manuscript is limited. More details can be found in the minor comments below.

### Minor Comments

1. The number of users who completed the final check-in is very different from the number after the first week. Do the authors have an explanation for the low participant rate at the final week? Would the results be any different if the authors considered using the participants at the final week as the evaluation group?
2. Was there an appropriate control group for the study? For example, would there be any survey before using Quokka?
3. Please add the author list and their affiliations to the manuscript.
4. Please provide institutional review board approval from each of the universities.
5. Please indicate when the experiment was conducted. I wonder if the results are affected by the current pandemic.

## Round 2 Review

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### General Comments

This paper is a revised manuscript discussing Quokka and its application in the community. Overall, I feel the quality of manuscript improved significantly after the revision, and my comments are addressed well. I do not have any further comments.

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### Conflicts of Interest

None declared.

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**Reference**

1. Shih C, Pudipeddi R, Uthayakumar A, Washington P. A local community-based social network for mental health and well-being (Quokka): exploratory feasibility study. *JMIRx Med* 2021;2(4):e24972 [[FREE Full text](#)] [doi: [10.2196/24972](https://doi.org/10.2196/24972)]

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Peer-Review Report

# Peer Review of “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study”

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Ashwag Alasmari<sup>1</sup>, PhD

University of Maryland Baltimore County, Baltimore, MD, United States

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## KEYWORDS

local social network; community health; well-being; digital health; consumer health

*This is a peer-review report submitted for the paper “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study.”*

## Round 1 Review

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This research [1] conducted an exploratory study of local community-based interventions and evaluated the intervention’s potential for promotion of local, social, and unfamiliar activities

as they pertain to healthy habits. I like how the authors built the motivation of this research. The introduction is well written and a good list of background information is provided. I am not sure what Quokka is, if it already exists or was just developed for the purpose of the study. I would like to see some background information on this application. I also would appreciate if the authors looked at their findings through the lens of prior work. How similar or different is this research to prior work?

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## Conflicts of Interest

None declared.

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## Reference

1. Shih C, Pudipeddi R, Uthayakumar A, Washington P. A local community-based social network for mental health and well-being (Quokka): exploratory feasibility study. *JMIRx Med* 2021;2(4):e24972 [FREE Full text] [doi: [10.2196/24972](https://doi.org/10.2196/24972)]
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Peer-Review Report

# Peer Review of “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study”

Hamed Mehdizadeh<sup>1</sup>, PhD

Department of Health Information Technology, School of Allied of Medical Sciences, Mazandaran University of Medical Sciences, Mazandaran, Iran

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**KEYWORDS**

local social network; community health; well-being; digital health; consumer health

*This is a peer-review report submitted for the paper “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study.”*

## Round 1 Review

**General Comments**

This article [1] is about the feasibility of using a social network to change behavior in people. This study is interesting and significant in terms of the subject and the work it does, but this article does not have the usual scientific article structure.

**Specific Comments****Major Comments**

1. In the *Methods* section, the authors do not provide any information about how to conduct the study. Important information such as the technical information of the system or application and modules related to the application Quokka are not mentioned.
2. There is no information about how the application works. Also, the method of conducting research is only mentioned in general in the *Abstract*, and in the body of the article, no information is provided in this section.
3. In the *Methods* section, there is no clear information about how to select the statistical population, inclusion and exclusion criteria, study start and end times, etc.
4. The *Methods* section is unstructured and contains too much detail and irrelevant information about the study, which not only does not help the audience to understand more but also confuses the reader.

5. Therefore, it is recommended that the *Methods* section be completely rewritten and structured like other scientific articles.

6. In the *Results* section, although the results are well described in the table, some of this information seems to be added.

7. In the *Discussion* section, there is no information about similar studies.

8. The results obtained in this study have not been compared with previous or similar studies, and the strengths and weaknesses of the study have not been expressed.

## Round 2 Review

First of all, the authors did not answer of any of my comments.

I suggest that the authors read similar papers published in JMIR to better understand how to report their study like a scientific report and write their manuscript based on these papers.

In the *Introduction*, the semantic structure and hierarchy that are needed for a scientific report do not exist.

The *Introduction* should include the problems, existing solutions, and choice of solutions based on logical reasons and references to studies that use it.

In this section, the authors should explain what issue needs to be solved and what can be done to solve this issue (method or tools or...) as well as describe why they chose the selected method for this problem or issue. Then, they should refer to similar studies that have used these methods. In fact, the introduction should answer these questions: What is the problem? What are the ways to solve it? Talk about your choice and the logic behind that.

In the second paragraph, the author says:

“Here, we discuss Quokka's challenge, local...”

This information has nothing to do with this section and should be transferred to the *Results* or *Discussion* section.

The first part of the *Introduction* before *Related Work* only contains one scientific reference, and the rest of the contents are without references. In an introduction, you can't say anything without references.

In the *Introduction*, paragraphs 2, 3, and 4 are not related to this section and must be removed.

At the end of the first paragraph, the author refers to health behavior change; it is necessary to refer to the role of behavior changing theory (BCT) and its application in health interventions. Also, refer to similar studies that have used this approach to change health behaviors.

At the end of paragraph, the author says:

“in contrast with prior works”

Which prior works? You do not say anything about other studies in this field, weaknesses, gaps, or anything else.

In the last paragraph of the *Introduction* or after this section, the aim of the study should be mentioned.

None of the comments that I have mentioned in the previous review have been resolved. My point is that the *Methods* section requires rewriting. This time, I mention the items that must be corrected in more detail, and I hope they will be fixed by the authors.

In the first part of the *Methods*, the information provided has nothing to do with this section.

For example, all content from first paragraph in the *Methods* to the end of *Recruitment* are irrelevant.

In the *Methods*, you should provide information about how you designed the study, like this:

How to design the study?

How do you want to do that?

What is the sampling method?

What were the inclusion/exclusion criteria?

Have people signed consent forms to participate in study?

How was information collected, and what method or instrument has been used?

What is the time period of this study? etc.

In the *Methods*, the author says that the purpose of this program is to change healthy habits, in other words, change behaviors of people.

However, there is no information about the mechanism of behavior change or use of behavior change theories in their intervention.

This is very important in that the intervention aimed to change behavior using behavioral change theories and techniques.

Also, when your main purpose of the design of this program is to change people's behaviors, you should provide information about these techniques and the efficiency of these methods to solve the problem you speak about.

The paper has no *Results* section. The *Methods* section and the results are combined.

In the *Discussion*, the results are interpreted incompletely and are not compared with the results of other studies.

*Limitations and Weaknesses* is unstructured and too long, with unrelated content. Generally, in the “limitations,” the author discusses the weaknesses of the study, including the low number of samples, conducting the study in one center, etc.

The references list, generally, must be rewritten.

I suggest looking at the references list in similar papers published in JMIR so that you can better understand the structure of a scientific article and try to submit your report based on the overall structure of these articles.

I suggest looking at the references list in similar papers published in JMIR and rewrite this section based on the journal format requested.

Reference No. 1, the authors' names must be modified.

Reference No. 2 should also be modified like Reference No 1.

Reference No. 7, after the name of the journal, enter the publication year, not the issue or page number. This problem is seen in most cases, for example:

7. HUNT, JUSTIN, AND DANIEL EISENBERG. “Mental Health Problems and Help-Seeking Behavior Among College Students.” *Journal of Adolescent Health* 46, NO. 1 (2010): 3-10.

Do not write the authors' full name and last name together, for example, in References No. 10, 11, and 13.

If the authors of the study number more than 6 people, you must use “et al.” after the name of the sixth author.

## **Review Round 3:**

### **General Comments**

The revised version addresses the earlier comments and represents an improvement over the prior version.

However, in the References section, there is a minor comment.

### **Minor Comments**

I suggest to the authors to look at the references list in similar papers published in JMIR and rewrite this section based on the journal format requested, like this:

Reference No. 1:

Lake J, Turner MS. Urgent Need for Improved Mental Health Care and a More Collaborative Model of Care. *Perm J*. 2017;21:17-024. doi: 10.7812/TPP/17-024. PMID: 28898197; PMCID: PMC5593510.

Please rewrite all references like this.

---

## Conflicts of Interest

None declared.

---

## Reference

1. Shih C, Pudipeddi R, Uthayakumar A, Washington P. A local community-based social network for mental health and well-being (Quokka): exploratory feasibility study. *JMIRx Med* 2021;2(4):e24972 [FREE Full text] [doi: [10.2196/24972](https://doi.org/10.2196/24972)]
- 

## Abbreviations

**BCT:** behavior changing theory

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*Please cite as:*

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# Peer Review of “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study”

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Anonymous

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## KEYWORDS

local social network; community health; well-being; digital health; consumer health

*This is a peer-review report submitted for the paper “A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study.”*

## Round 1 Review

---

### General Comments

I appreciate the opportunity to review this manuscript [1]. I hope that my feedback will help to strengthen the paper.

This paper has a strong theoretical background and empirical data. Overall, the manuscript is well prepared; however, it requires some major and minor corrections.

### Specific Comments

#### Major Comments

1. The value of this work seems to be significant.

2. The *Results* section should start with a data analysis. If Table 1 and “User Statistics” represent a sample, then the appropriate subheading should be provided.

3. In the *Discussion*, start your discussion with a short summary of what the main finding(s) of this study was/were. This section is too structured but at same time is confusing about the criteria of discussing the findings. I would suggest restructuring the way the data is discussed.

4. The subheadings in the *Methods* section should be related to the subheadings in the *Results* section.

#### Minor Comments

1. Minor technical/language corrections are needed (eg, “There is a strong, well-researched connection between social influence, social media, and health and wellness [2-3]”; “Try 3 different types of exercise this week”).

2. Double-check the style of the references, which should be prepared according to journal requirements (eg, references 22, 23, 28).

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## Conflicts of Interest

None declared.

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## Reference

1. Shih C, Pudipeddi R, Uthayakumar A, Washington P. A local community-based social network for mental health and well-being (Quokka): exploratory feasibility study. *JMIRx Med* 2021;2(4):e24972 [FREE Full text] [doi: [10.2196/24972](https://doi.org/10.2196/24972)]
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# Peer Review of “Offenders With Personality Disorder Who Fail to Progress: A Case-Control Study Using Partial Least Squares Structural Equation Modeling Path Analysis”

Anonymous

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*This is a peer-review report submitted for the paper “Offenders With Personality Disorder Who Fail to Progress: A Case-Control Study Using Partial Least Squares Structural Equation Modeling Path Analysis”.*

## Round 1 Review

### General Comments

This study [1] identified and empirically investigated the causal drivers behind nonprogression of offenders with personality disorder on the UK Offender Personality Disorder pathway. Interestingly, the study found negative attitudes toward treatment to be the leading driver of nonprogression, closely followed by psychopathology. Overall, I found this to be a very interesting and potentially highly impactful paper, with specific practical and applied value. My suggestions for improvement are mostly minor and primarily surround a general neatening-up of the writing and presentation of the manuscript.

### Major Comments

1. The Introduction is interesting to read, easy to follow, and well structured. I think the only thing that it is missing is some more background information on personality disorders. This could involve simply defining personality disorder in a general sense and providing some information surrounding risks associated with them in community populations as well as their prevalence rates in offender populations (with citations). I would probably put this information at the start of the Introduction before going into more specific detail surrounding offenders with personality disorder. Some language/grammatical improvements are also required throughout the introduction.
2. The “Procedure” section in the Methods seems unnecessary as its own section. I would consider incorporating this information in the “Sample” section, potentially changing the heading to “Sample and Procedure.”

3. In the Results section, I would suggest adding the test statistics and *P* values to Table 1, as this would make it very easy to identify where there were key differences.
4. The numbers and interpretation of the results in Table 1 are somewhat difficult to follow. Percentagewise, a higher proportion of the nonprogression group are single compared to the control group, but the chi-square test results indicate that the control group is more likely to be single than the nonprogression group (presumably based on the actual *N*). I think this needs to be clarified/made consistent in the manuscript.
5. I think that it would be informative for the reader for the authors to merge all the supplementary descriptive results tables (Tables S1-S4) into one table and incorporate this into the main text in the Results section (rather than supplemental materials), also adding the test statistics to the tables.
6. The Discussion section was particularly interesting to read. Given the potential clinical impact and practical nature of this study, the only thing I think the Discussion is missing is a section on clinical/practical implications of the study (which was very briefly touched upon in the conclusion). I think that this would really benefit the manuscript and be of interest to readers.

### Minor Comments

1. This is very minor, but the “Engagement With Treatment and Treatment Noncompletion” in the Introduction could probably just be “Engagement With Treatment,” as this covers treatment noncompletion.
2. I would avoid using the term “personality disordered” throughout the manuscript.
3. The semicolons in the first paragraph of the “Engagement With Treatment and Treatment Noncompletion” section should be colons (and in some other parts of the manuscript).
4. Some of the study objectives in the Introduction could be made somewhat more specific/precise (eg, explicitly stating

- “offenders with personality disorder,” rather than just offenders, or offenders that have not progressed on the Offenders Personality Disorder pathway).
5. The capitalization of “N” within tables needs to be made consistent throughout.
  6. When referring to tables in the manuscript, the “t” should be capitalized throughout (eg, “Table 2”).
  7. In the Results section, there may in fact be too much detail regarding the structural model assessment; for example, there is no need to explain what each of the parameters mean/represent.
  8. *P* values should be reported as exact numbers (ie, to 3 decimal points), and *P* values of *P*=.000 should be reported as *P*<.001.
- 

## Reference

1. Mathlin G, Freestone M, Taylor C, Shaw J. Offenders with personality disorder who fail to progress: a case-control study using partial least squares structural equation modeling path analysis. *JMIRx Med* 2021;2(4):e27907 [[FREE Full text](#)]
- 

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Peer-Review Report

# Peer Review of “Offenders With Personality Disorder Who Fail to Progress: A Case-Control Study Using Partial Least Squares Structural Equation Modeling Path Analysis”

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Department of Forensic Psychiatry, Psychiatric Hospital, University of Zurich, Rheinau, Switzerland

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*This is a peer-review report submitted for the paper “Offenders With Personality Disorder Who Fail to Progress: A Case-Control Study Using Partial Least Squares Structural Equation Modeling Path Analysis”.*

## Round 1 Review

**General Comments**

Thank you for the invitation to review “Offenders with Personality Disorder who Fail to Progress: A Case Control Study Using PLS-SEM Path Analysis”. The paper [1] aims at identifying and describing a subgroup of offenders with personality disorders (PDs) that fails to progress in treatment. The method of choice is a structural equation model and allows for modeling and analyzing causal paths of several latent variables and complex interrelations of a range of variables. Outcomes are consistent with the literature that has identified factors associated with nonparticipation in treatment and include a risk assessed as inaccessible to intervention; negative attitudes toward treatment, such as low motivation; and psychopathology. Low treatment motivation was also found to predict problematic institutional behavior. Strengths and limitations are presented and include the critical assessment of the methodological approach and the problem of missing data.

I liked reading your paper and think that it is of great importance to analyze certain subgroups in more detail and with statistical approaches that incorporate latent variables and unravel causal structures.

However, I do not like the fact that many different models are mentioned in the Introduction and that these models are not mentioned further on. These parts could be shortened, and the paper would certainly benefit from this. I found the subdivision of the Introduction into many subunits disruptive as well. There is no common thread to the Introduction. Please try to create a better text flow.

I did like the Methods section and the Discussion, which was balanced and informative for the most part.

**Specific Comments****Major Comments**

1. A distinction between the different PDs would be appropriate, as the risk for offending is not the same for all PDs.
2. Additionally, please give some more information about PDs in general.
3. “The OPD [Offenders Personality Disorder] pathway is informed from the “What Works?” literature [2], the RNR [risk needs responsivity] principles [3] and the Good Lives Model (GLM; [4]. However, the RNR model been criticised for not providing clear guidance for therapists for engaging offenders lacking in treatment readiness [5]. The responsivity principle of the RNR model may not currently be effectively implemented in the OPD pathway and contributing to the problem of offenders being referred but not accepted to numerous OPD services.” Incorporating these resources adds no value in my opinion, since there is no further information about these models.
4. Attitudes towards treatment”: Please specify possible outcomes in the description.
5. A descriptive visual representation of the analysis plan would be helpful.
6. Null hypothesis significance testing (NHST) needs hypotheses. If you use NHST (ie,  $\chi^2$  and t test) in part 1 of the analysis, you need to formulate hypotheses since blind testing always leads to results.
7. No correction (eg, Bonferroni) was made, despite multiple testing. This should be done. If one does not do this, it is fine because the main goal of the study was the model, but this needs to be addressed and reflected upon.
8. Methodology and results flow into each other. Please find a way to separate this better. I would also like to see not

only the inner model described in the methodology but also the outer model (eg, the factors of psychopathology).

- The latent variables create the inner model and the variables were connected using clinical knowledge and theory (Figure 1)."

Please specify "clinical knowledge" and "theory." This is quite speculative. In addition, Figure 1 would benefit from a more specific description.

- "Second, the outer loadings within the SEM [structural equation modeling] model suggest that the single most influential factor was psychopathy or psychopathic disorder, which has long been acknowledged as a limiting factor for treatment and rehabilitation [6]. It could be argued that psychopathic offenders are not best served on a pathway that caters for offenders with personality disorder in the broader sense of the diagnosis as their needs are known to be different [7]."

Do you have a suggestion for these individuals?

- Other limitations are that you specify a model a priori and that so many factors are used for such a complex phenomenon (with a quite limited sample).
- In addition, one must see very critically that psychosis and PS are combined. The fact must be discussed as this is problematic, having a massive influence on therapy and behavior.
- Please consider dividing the Conclusions section into Future Perspectives and Conclusions sections as this seems kind of inconsistent.

### Minor Comments

- Please consider changing the title of the paper by omitting "PLS-SEM [partial least squares structural equation

modeling] Path Analysis," which is too technical in my opinion (or maybe do not use the abbreviation).

- Please divide the sentence in the results section of the Abstract into two sentences and thereby avoiding the semicolon.
- Please avoid the semicolons in the second paragraph and check overall structure of the sentences (and use hyphens if appropriate). Check for missed words, sentence structure, and punctuation in the paper.
- Stay consistent when using abbreviations—do not alternate "PD" and "personality disorder".
- Please define "NHS" (National Health Service) before using the abbreviation.
- I would like to read more about the "screening algorithm" and which PDs this algorithm screens for.
- "However, several of us are clinicians working within the London Pathways Partnership (LPP), a consortium of NHS trusts delivering services within the OPD pathway, are aware of several individuals that no OPD service, in prison or the NHS, is prepared to accept." Reformulate this sentence since it is not comprehensible easily.
- Omit % in the brackets in each row of the tables.
- Although the relationship between problematic custodial behaviour and service refusal was not strong, the results still emphasise that services aiming to support these individuals need be able to receive men with patterns of such behaviour and contain and manage ongoing episodes, without this resulting in treatment termination." Please rephrase this, as it is a quite complicated sentence.

### Conflicts of Interest

None declared.

### References

- Mathlin G, Freestone M, Taylor C, Shaw J. Offenders with personality disorder who fail to progress: a case-control study using partial least squares structural equation modeling path analysis. *JMIRx Med* 2021;2(4):e27907 [[FREE Full text](#)]
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### Abbreviations

**GLM:** Good Lives Model  
**LPP:** London Pathways Partnership  
**NHS:** National Health Service

**NHST:** null hypothesis significance testing  
**OPD:** Offenders Personality Disorder  
**PD:** personality disorder  
**PLS-SEM:** partial least squares structural equation modeling  
**RNR:** risk needs responsivity  
**SEM:** structural equation modeling

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## Peer-Review Report

# Peer Review of “Machine Learning and Medication Adherence: Scoping Review”

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*This is a peer-review report submitted for the paper “Machine Learning and Medication Adherence: Scoping Review”.*

## Round 1 Review

### General Comments

This paper [1] aims to categorize and summarize literature focused on using machine learning for medication compliance activities. There are major concerns associated with this paper.

### Specific Comments

#### Major Comments

1. The aim does not feel like an actual aim. I would suggest saying things like “aim to do a scoping review on... and categorize and summarize...”
2. You should state the design in the methods. In addition, you should state clearly the inclusion and exclusion criteria. As of now, the inclusion and exclusion criteria are too broad to do a robust review.
3. Is it adherence or compliance? The frequent change of terms makes it hard to understand what the authors want to do. They are very different fundamentally.
4. Limitations should be before the Conclusion.
5. The paper lacks Figure 1: the number of articles screened/reviewed.
6. Figure 2 is not right; there are many overlapping diseases in each category.

### Conflicts of Interest

None declared.

### Reference

1. Bohlmann A, Mostafa J, Kumar M. Machine learning and medication adherence: a scoping review. *JMIRx Med* 2021;2(4):e26993 [[FREE Full text](#)]

7. Short forms are not well explained or mentioned in the tables.

Thank you for allowing me to review the paper.

## Round 2 Review

I am appreciative that the authors are willing to do the changes, and the manuscript has improved vastly.

Although this is a scoping review, I would like to find out how the author ensured robustness and reproducibility. As of now, with the study design largely using one author, there is no way to assess if the paper selection is robust or independent. I strongly feel that there is a need for 2 authors to independently select studies, even though it is a scoping review, to give this review some robustness. If not, how different will the results be compared to a narrative review?

I hope to see how the author justifies this step here.

## Round 3 Review

Thanks for revising. Appreciate the effort.

May I suggest shortening the Discussion further? The limitations should be in the second to last paragraph. The last paragraph should be the conclusion of this study. It will be great if the Discussion is shortened to 4-5 paragraphs max.

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Peer-Review Report

# Peer Review of “Machine Learning and Medication Adherence: Scoping Review”

Przemyslaw Kardas<sup>1</sup>, MD

Department of Family Medicine, Medical University of Lodz, Lodz, Poland

**Related Articles:**Companion article: <http://preprints.jmir.org/preprint/26993>Companion article: <https://med.jmirx.org/2021/4/e33962/>Companion article: <https://med.jmirx.org/2021/4/e26993/>*(JMIRx Med 2021;2(4):e33965)* doi:[10.2196/33965](https://doi.org/10.2196/33965)*This is a peer-review report submitted for the paper “Machine Learning and Medication Adherence: Scoping Review”.*

## Round 1 Review

**General Comments**

This paper [1] covers a very interesting area on the use of machine learning for assessment of medication adherence, yet in its current version, it does not add a lot to the field. It is a pity, as it seems that the authors performed their review well. However, the presentation of the results is not acceptable.

**Major Comments**

1. It creates a lot of confusion that the authors use “adherence” instead of “compliance.” In fact, these two are equivalent terms, of which adherence is preferred and compliance is a bit old-fashioned. The authors need to define the major concept they use, and these two need to be carefully checked against available literature and the ABC taxonomy.
2. The Abstract provides no numeric data; even the number of identified publications is missing. Similarly, the conclusions of the Abstract are inconclusive.
3. The authors mentioned previous reviews in this area, yet they did not make it clear what was different about their own work. What exactly was missing in the previous reviews that turned them toward this new exercise?
4. Publication selection for review: What were the criteria used to identify acceptable papers in the full-text review? What was the reason for screening a sample of 20 papers first?
5. “Medication adherence activities” is not a term used in the literature to describe interventions aimed at assessment or modification of medication adherence. Please use another term that is used in the existing literature.
6. The paper is lacking a lot of details; for example, what was the basis for the dichotomization of the source databases into “biomedical” and “computer” in Figure 3?
7. In Tables 1-3, instead of simply providing the number of the reference, it is also advisable to have the first author’s name and the year of the publication.
8. I have a feeling that the studies listed in Table 1, based on self-report and pharmacy claims data, do not “predict” adherence but rather assess it. Please correct me if I am wrong.
9. The paper must be self-explanatory; therefore, abbreviations such as DOT need to be explained. When addressing a general audience, it makes sense to do the same with the abbreviations of algorithms cited within.
10. Numbers, numbers, numbers, please! The Results section reads, for example, “LEAP had the best prediction accuracy of the machine learning methods used”—by how much? Was the difference statistically significant?
11. Being a clinician, I feel that this might be information technology (IT) jargon: “The first of these articles used data collected during hospital stays to generate features” (from Results). However, please make sure that the text is also meaningful for non-IT people.
12. In light of previous publications in the field, the first sentence of the Discussion needs to be rechecked.
13. In the Discussion, the authors say “However, more work needs to be done to better understand the impact of socioeconomic status [on adherence].” In fact, a lot of work has been done in that area, and it would help the paper if authors would broaden their understanding of it.
14. From the Discussion: “Some of these works compared the different types of algorithms to determine which was the most accurate...” Which ones? Please cite!
15. To conclude, it needs to be stressed that the authors should extract a lot more data and conclusions from the material they reviewed—instead of saying “some studies...,” please provide the numbers (eg, “over 40% of studies found the parameter to change by >90%”).

## Round 2 Review

### General Comments

This version of the manuscript is a lot more advanced than the previous one yet still far from the target. Because of the importance and novelty of the topic, it still makes sense to work on making the paper better. Below are my suggestions.

NOTE: I have activated the line numbering in the original manuscript to make my remarks more precise. To make sure that we use the same numbering, the line with the "ABSTRACT" heading was numbered 18.

### Major Comments

1. In the body of text, you refer to the help and advice provided by two librarians and two pharmacists, yet it seems to me that they are not included in the authorship nor thanked in the Acknowledgments. Please take care of solving this.
2. Overall, the interesting work done in this exercise is not followed with a clear description. In fact, it is very hard to learn what exactly the use of machine learning was in the context of medication adherence or the outcomes of this process. These, however, were the major objectives of this paper. In such a case, the conclusion from the Abstract stating that "Machine learning has the potential to greatly improve medication adherence" seems to be unsupported by the data presented.

### Additional Suggestions

- Line 23: The number of identified studies belongs in the Results.
- Line 26 onward: "Verb" is an uncommonly used term in this context; please search the literature to find a more frequently used equivalent.
- Line 29 onward: Using percentiles makes sense when the total number is  $\geq 100$ ; in this case, the number of identified publications was only 43; what justifies fractions and not the percentiles?
- Lines 42-3: The Discussion is missing in the Abstract (what is provided now is not a real discussion of the findings).
- Lines 92-3: The eligibility criteria need to be more detailed; it is unclear now what sort of relationship had to link the included publications with medication adherence, and what was the exclusion criteria?
- Line 134 refers to "predictors"—predictors of what?

- Line 136-7: What do you mean by "The data collected for this study was qualitative and sometimes quantitative"? What does "sometimes" mean in this context?
- Line 165 refers to "13 studies," yet Figure 3 shows only 12 items in that category.
- Tables 1-3 need serious improvement. Putting all the comments together in columns placed to the right makes no sense. No idea why "Some entries were excluded for brevity," especially in cases of short algorithm acronyms. The footnote marked \*\* is not applicable to Table 2.
- Table 1: I would love to see one more column describing what sort of adherence measure the machine learning algorithm was able to predict (eg, "filling the prescription" or "daily drug intake").
- Table 1: How did you identify the "strong predictors"? Has any statistical threshold been applied to this selection?
- Table 2: I would love to see one more column describing what sort of adherence measure the machine learning algorithm was able to identify. For example, there are plenty of studies using smart pill bottles—so what exactly was the role of machine learning in [2] for it to be included in this review and not to include other studies?
- Table 3: Same as above, plus which aspect of adherence was improved—the one that was tested; the other one?
- Line 210, 213: Correct "99 DOTS" to "99DOTS."
- Line 221, 222: "The next paper used face recognition software and computer vision to monitor medication adherence"—which aspect of medication adherence are you considering here?
- Line 241-2: "These assessments were then used to create predictors"—predictors of what? I guess not of medication adherence, if you say that medication adherence was a...predictor!
- Line 247-50: Usually, limitations are provided at the end of the Discussion.
- Line 285-6 states: "Approximately 87% of these studies used either logistic regression, artificial neural networks, support vector machines, or random forest algorithms." Why is this not visible in Table 1?
- Lines 282 and 342 still use the term "compliance" instead of "adherence."
- Lines 288-291: You provide comparisons of the accuracy of diverse algorithms yet without any statistical significance values. That sort of simple comparison is not inconclusive

### Conflicts of Interest

None declared.

### References

1. Bohlmann A, Mostafa J, Kumar M. Machine learning and medication adherence: scoping review. *JMIRx Med* 2021;2(4):e26993 [[FREE Full text](#)]
2. Aldeer M, Alaziz M, Ortiz J, Howard RE, Martin RP. A sensing-based framework for medication compliance monitoring. In: Proceedings of the 1st ACM International Workshop on Device-Free Human Sensing. 2019 Presented at: DFHS'19; November 10, 2019; New York, NY p. 52-56. [doi: [10.1145/3360773.3360886](https://doi.org/10.1145/3360773.3360886)]

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**Abbreviations**

**IT:** information technology

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Peer-Review Report

# Peer Review of “Comparison Between Male and Female Survivors of Sexual Abuse and Assault in Relation to Age at Admission to Therapy, Age of Onset, and Age at Last Sexual Assault: Retrospective Observational Study”

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## KEYWORDS

sexual abuse; sexual assault; age of onset; sex; gender; age; therapy; abuse; assault; mental health; victim; childhood; children; gender disparity; violence

*This is a peer-review report submitted for the paper “Comparison Between Male and Female Survivors of Sexual Abuse and Assault in Relation to Age at Admission to Therapy, Age of Onset, and Age at Last Sexual Assault: Retrospective Observational Study.”*

## Round 1 Review

### General Comments

This multicenter study [1] explores differences between male and female victims who were sexually abused or assaulted and sought therapy. The differences are investigated with regard to the age of the first and last assault as well as the age at which the victims entered therapy. Although there is a high imbalance between the female (2901) and male (401) groups, the author provides the data distributions, detailed statistical metrics, and explanations of the studied cohorts that allow the reader to have a good understanding of the investigated cohorts.

### Specific Comments

Overall, it is a well-written and clear paper. The author makes an extensive introduction and provides a detailed description of the study results. The quality of the paper could be improved by considering the following aspects:

### Major Comments

1. The sections *Limitations* and *Conclusions* are given in bullet format. This formatting should be converted to a paragraph-like formatting. Additionally, the *Limitations* section should be placed before the *Conclusions* section and not after, as it is now.

2. In the *Discussion* section, more text is needed regarding the comparison of the current study with previous studies.

3. When a linear relationship is reported in the paper (Figure 5), it is better for it to be accompanied by a statistical metric, such as the Spearman correlation.

### Minor Comments

1. There are few typos in the paper.

a. *Introduction* section (second paragraph, first sentence)—please correct the year. Obviously, it is not 2104.

b. Other minor typos; for example, please replace the phrase “first the sexual assault” with “the first sexual assault” (second paragraph before the end of the *Introduction*) as well as “Cleary” with “Clearly.”

2. Suggestion for the author: In future studies that deal with highly imbalanced data sets, the author could consider using bootstrapping methods. For example, in the current study, the number of victims in the males group was 401 and that in the females group was 2901. If we assume that we study the differences in the two groups with regard to the age of the first assault, we could do the following: In the male group, we compute the mean value of the age of the first assault using all 401 victims. In the females group, we randomly take a subcohort of 401 victims multiple times (eg, 1000). In every random selection, we compute the mean value of the age of assault; hence, at the end, for the female group, we will have a distribution of 1000 values. Afterward, from the distribution of these 1000 values, we can compute confidence intervals,

medians, etc. In this way, the number between the female and male group is the same, and therefore the results between the two groups are more comparable.

---

### Conflicts of Interest

None declared.

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### Reference

1. AL-Asadi AM. Comparison between male and female survivors of sexual abuse and assault in relation to age at admission to therapy, age of onset, and age at last sexual assault: retrospective observational study. JMIRx Med 2021;2(4):e23713 [FREE Full text] [doi: [10.2196/23713](https://doi.org/10.2196/23713)]

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Peer-Review Report

## Peer Review of “Medical Brain Drain from Southeastern Europe: Using Digital Demography to Forecast Health Worker Emigration”

Niamh Humphries<sup>1</sup>, PhD

Royal College of Physicians of Ireland, Dublin, Ireland

**Related Articles:**Companion article: <https://preprints.jmir.org/preprint/30831>Companion article: <https://med.jmirx.org/2021/4/e34077>Companion article: <https://med.jmirx.org/2021/4/e30831>*(JMIRx Med 2021;2(4):e34078)* doi:[10.2196/34078](https://doi.org/10.2196/34078)**KEYWORDS**

digital demography; Google Trends; the emigration of doctors and nurses; medical brain drain; Croatia; demography; brain drain; emigration; doctors; nurses; health care workers; health professionals; health systems; jobs; Germany; personnel; migration; workforce; medical professionals

*This is a peer-review report submitted for the paper “Medical Brain Drain From Southeastern Europe: Using Digital Demography to Forecast Health Worker Emigration.”*

**Round 1 Review****General Comments**

Thank you for the opportunity to review this paper [1]. I think it is potentially a very interesting paper, but it needs more work to bring it to publishable standards.

**Specific Comments**

## 1. Data

- Have digital traces been used as an indicator of migration before? If so, please cite.
- I have concerns that some of the Google terms used indicate wider emigration rather than health worker migration.
- If you want to refer to the wider emigration from Croatia to Germany/Austria (either via digital traces or via secondary data), you need to be clear that this is not health care worker (HW) migration you're referring to. I've compared HW migration with migration more generally in a recent paper [2].
- As an indication of health migration or HW migration intent, you should only focus on the doctor/nurse-specific information.
- It would greatly strengthen your paper if you had stronger secondary/official data on the migration of nurses/doctors from Croatia/Bosnia and Herzegovina (B&H)/Serbia to Germany/Austria.
- Can you get data on the number of Croatian/Bosnian/Serbian-trained nurses/doctors who

have joined a nursing/medical register in Germany/Austria?

- Can you get data on the number of Bosnian/Serbian citizens who have obtained visas to work in Germany/Austria?
  - This data would greatly strengthen your argument that digital traces can provide an early indicator of HW migration.
2. Paper structure
- The Introduction jumps around between source and destination countries. I would suggest that the paper discusses source countries and destination countries separately.
  - Also, I think it's important to separate out push from pull factors and to be specific about the impact on each of the source countries; for instance, as an EU member state, Croatian doctors and nurses can freely migrate and work in Germany/Austria, but doctors/nurses from Serbia or B&H would need visas to work there, right?
  - The pandemic as a push factor is really interesting and an important issue to raise.
  - Why use the term *Western Balkan* if it does not include Croatia? Better to use the countries that you're talking about (ie, Croatia, Bosnia and Herzegovina, and Serbia).
3. Engaging with the wider literature
- I think that the World Health Organization (WHO) Global Code on the International Recruitment of Health Personnel (2010), which is mentioned on page 11, should be more central to the paper, especially in relation to the concept of sustainability and the need

- for high-income countries to train and retain sufficient HWs to meet needs (article 5.4).
- Perhaps the paper also needs to mention the WHO 2006 list or the WHO 2020 safeguard list, which lists countries with critical health care shortages. Your paper makes an interesting contribution in highlighting that these issues are also relevant in European countries (see [3]).
  - In relation to Europe, the paper should connect back to the European Observatory books on HW migration from 2014/2015, which highlighted health worker migration from new EU member states to older EU member states [4].
  - In the Introduction, the paper should also connect with the wider literature on brain drain/health worker migration.
3. Measuring health worker mobility is a challenge for most countries (not just Croatia, Bosnia, and Serbia), which is why registration and/or visa data from the destination country is often used as a measure of health worker emigration.
  4. On page 4, you say that 65,288 nurses emigrated, and I think you're saying that there are more Croatian/Bosnian nurses in Germany than in Croatia and Bosnia; are you? Perhaps tighten up this sentence as it's a strong statement.
  5. On page 7, the paragraph beginning *in Austria* is unclear. Rewrite these sentences.
  6. In Table 3, perhaps mark the stock data versus the flow data (ie, differentiate between the overall number of nurses in Germany [stock] vs the number of nurses entering Germany [flow]).
  7. On page 11, the section beginning *what could the European Union do to address the problem*, I think this should be moved out of the Introduction and into the Discussion.
  8. I think you could bring one or two issues out in the Discussion that you've mentioned in the text already but could make more of:
    - The issue of the European Union drawing health workers from EU countries (Croatia) and nearby countries (Bosnia, Serbia) is an important issue to raise in the Discussion, as it is a clash between free movement (EU free movement) and the right to health care/need to ensure a health workforce in all regions (as per the WHO Global Code and/or the UN Sustainable Development Goals).
    - I think that this method is a really interesting way of generating timely data on health worker migration. During the pandemic, the *normal* ways of data collection are simply too slow (particularly when EU countries are fast tracking health workers into the European Union). Your method is a really good way of generating timely insights into *intent to migrate* among health workers. As you mention in your paper, this should be useful for policy makers (but obviously only if they respond/react to the data). And then the next question for policy makers is how can they retain health workers during a pandemic? Increased salaries? Improved working conditions? Which links nicely to the section on what the European Union can do.

## Round 2 Review

### General Comments

Thank you for the revised manuscript; it is a much stronger paper, and the potential of digital demography in forecasting HW migration is now much clearer.

### Specific Comments

1. Perhaps the title should read: Medical Brain Drain From Southeastern Europe: Using Digital Demography to Forecast Health Worker Emigration.
2. You need to be consistent in the terms used throughout the paper (title/abstract/main text). At present the following terms are used to refer to the same places:
  - Western Balkans and Croatia
  - Southeastern Europe
  - B&H
  - I'd suggest using one term that includes Croatia and/or refer to the individual countries and use it throughout the paper.
  - B&H is misspelled once in the Abstract.
  - In displaying numbers/percentages use either decimals (60.09% or 60,09%) or commas in figures, not both.
  - Throughout the paper, perhaps use *a shortage of* in place of *a lack of*.

### Conflicts of Interest

None declared.

### References

1. Jurić T. Medical brain drain from southeastern Europe: using digital demography to forecast health worker emigration. *JMIRx Med* 2021;2(4):e30831 [FREE Full text] [doi: [10.2196/30831](https://doi.org/10.2196/30831)]
2. Humphries N, Connell J, Negin J, Buchan J. Tracking the leavers: towards a better understanding of doctor migration from Ireland to Australia 2008–2018. *Hum Resour Health* 2019;17(1):36 [FREE Full text] [doi: [10.1186/s12960-019-0365-5](https://doi.org/10.1186/s12960-019-0365-5)] [PMC: [31138211](https://pubmed.ncbi.nlm.nih.gov/31138211/)]
3. Health workforce support and safeguards list, 2020. World Health Organization. URL: <https://cdn.who.int/media/docs/default-source/health-workforce/hwf-support-and-safeguards-list8jan.pdf> [accessed 2021-10-20]
4. Health professional mobility and health systems. World Health Organization. URL: [https://www.euro.who.int/\\_data/assets/pdf\\_file/0017/152324/Health-Professional-Mobility-Health-Systems.pdf](https://www.euro.who.int/_data/assets/pdf_file/0017/152324/Health-Professional-Mobility-Health-Systems.pdf) [accessed 2021-10-20]

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**Abbreviations****B&H:** Bosnia and Herzegovina**HW:** health care worker**WHO:** World Health Organization

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Peer-Review Report

# Peer Review of “Medical Brain Drain From Southeastern Europe: Using Digital Demography to Forecast Health Worker Emigration”

Monika Komušanac<sup>1</sup>, PhD

Department for Demography and Croatian Emigration, Faculty of Croatian Studies, University of Zagreb, Zagreb, Croatia

**Related Articles:**

Companion article: <https://preprints.jmir.org/preprint/30831>

Companion article: <https://med.jmirx.org/2021/4/e34077/>

Companion article: <https://med.jmirx.org/2021/4/e30831/>

(*JMIRx Med* 2021;2(4):e34079) doi:[10.2196/34079](https://doi.org/10.2196/34079)

**KEYWORDS**

digital demography; Google Trends; the emigration of doctors and nurses; medical brain drain; Croatia; demography; brain drain; emigration; doctors; nurses; health care workers; health professionals; health systems; jobs; Germany; personnel; migration; workforce; medical professionals

*This is a peer-review report submitted for the paper “Medical Brain Drain From Southeastern Europe: Using Digital Demography to Forecast Health Worker Emigration.”*

## Round 1 Review

**General Comments**

This paper [1] represents an important contribution to the development of digital demographic methods and digital tools that can monitor and analyze demographic processes, especially migration as a highly dynamic component of population movement. This is extremely important in the management and planning of population development, especially in those populations that, as the examples of countries (subject areas) mentioned in the text, are struggling with intensive and increased emigration of young people. Given the lack of such studies, I consider this paper very important for developing new methods in demography and therefore suggest that you publish this paper because it represents an excellent starting point for further research and validation of digital traces that enrich the classical demographic methodological system and alleviate existing methodological limitations in the monitoring migration process.

This paper examines negative demographic processes and differences in the health system of countries of origin and destination with the example of the Google Trends tools combined with standard demographic analysis and official statistics to confirm the outflow of medical workers from the Western Balkans and Croatia to Germany and Austria.

The main goal of the work is to be satisfied and that is to determine the correlation between the official data and auxiliary data collected by the Google Trends tool. The results showed a high level of interdependence of trends shown by official

statistics and analysis of Google Trends data by searching for relevant terms and keywords. The author pointed out the basic methodological limitations and advantages of using digital methods and tools with the intention to point out how the advanced digital age provides us a number of digital traces that can be used for observing demographic processes, especially migrations in the future.

**Major Comments**

1. The lack of demographic potential in the health system is current and interesting, and the topic is actually a case report of the Western Balkans and Croatia through new approaches and tools of digital tracing and monitoring of migration processes. The author introduced readers to the demographic situation in the countries of origin to create a basis for understanding the processes that preceded the emigration of health workers based on a review of previous research and relevant authors.
2. The value of the paper is that the author, in addition to appropriate, standard, and common methods in demographic analysis, also used the method of tracking digital traces that is perhaps more common in other social sciences. He thus made an important step forward in methodological terms and focused on new approaches that will, in accordance with advanced and dynamic information technology, be more and more present and will provide us an important source of information and knowledge. Therefore, the development of digital methods in demography in the methodological sense is an expected necessity and an aid to the study of demographic processes and phenomena.
3. The results and the main findings of the paper are clear and unambiguous, and confirm the hypotheses, they are supported by data and graphical attachments, and they

- confirm the basic goal of the paper. The selected conclusions confirmed the importance of the new approaches and the connection that exists between the analysis of Google Trends and official data on the emigration of health workers to Germany and Austria using classical demographic methods.
4. The writing style is simple, clear, and understandable to the reader, and the issues are addressed clearly, concisely, and meaningfully. The research was conducted in accordance with ethical standards and the GDPR, and the data used by the Google Trends tool are anonymous and aggregate, and no one's personal rights have been violated.
  5. The paper shows a disproportion between the cited references and those in the bibliography; some references were mentioned in the text but are not listed in the bibliography and vice versa, some listed in the bibliography are not cited anywhere so the author is invited to revise bibliographic references and harmonize the text and the list of references.

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## Conflicts of Interest

None declared.

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## Reference

1. Jurić T. Medical brain drain from southeastern Europe: using digital demography to forecast health worker emigration. *JMIRx Med* 2021;2(4):e30831 [[FREE Full text](#)] [doi: [10.2196/30831](https://doi.org/10.2196/30831)]

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# Peer Review of “Influence of the COVID-19 Lockdown on the Physical and Psychosocial Well-being and Work Productivity of Remote Workers: Cross-sectional Correlational Study”

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Anonymous

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## Related Articles:

Companion article: <https://psyarxiv.com/dnuk3/>

Companion article: <https://med.jmirx.org/2021/4/e34609/>

Companion article: <https://med.jmirx.org/2021/4/e30708/>

(*JMIRx Med* 2021;2(4):e34607) doi:[10.2196/34607](https://doi.org/10.2196/34607)

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*This is a peer-review report submitted for the paper “Influence of the COVID-19 Lockdown on the Physical and Psychosocial Well-being and Work Productivity of Remote Workers: Cross-sectional Correlational Study”.*

**Editorial Note:** We acknowledge that the reviewer may have engaged in citation manipulation by encouraging the authors to cite the reviewer’s own work. Citation manipulation refers to “excessive citation of an author’s research by the author (ie, self-citation by authors) as a means solely of increasing the number of citations of the author’s work” [1]. JMIR follows the COPE/OASPA/WAME “Principles of Transparency and Best Practice in Scholarly Publishing,” and citation manipulation violates principle 6 [2].

## Review Round 1

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### General Comments

This paper [3] is about the impact of the COVID-19 pandemic on workers.

### Major Comments

1. The authors stated, “The COVID-19 pandemic has had catastrophic effects on global economies, with significant

- reductions in commercial and business activities projected, as well as increasing un- and under-employment with associated loss of income.” Please discuss the following study on how COVID-19 lockdown affects occupation: Dang AK, Le XTT, Le HT, Tran BX, Do TTT, Phan HTB, Nguyen TT, Pham QT, Ta NTK, Nguyen QT, Duong QV, Hoang MT, Pham HQ, Nguyen TH, Vu LG, Latkin CA, Ho CSH, Ho RCM. Evidence of COVID-19 impacts on occupations during the first Vietnamese national lockdown. *Ann Glob Health*. 2020;86(1):112. doi:10.5334/aogh.2976
2. This study mainly talked about how workers cope. Under the *Discussion* section, please refer to the following study that mentions the approach adopted by the workplace to help workers to cope during the pandemic: Tan W, Hao F, McIntyre RS, Jiang L, Jiang X, Zhang L, Zhao X, Zou Y, Hu Y, Luo X, Zhang Z, Lai A, Ho R, Tran B, Ho C, Tam W. Is returning to work during the COVID-19 pandemic stressful? A study on immediate mental health status and psychoneuroimmunity prevention measures of Chinese workforce. *Brain Behav Immun*. 2020;87:84-92. doi:10.1016/j.bbi.2020.04.055

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  3. Tronco HYA, Parente F, Faghy MA, Roscoe CMP, Maratos FA. Influence of the COVID-19 lockdown on the physical and psychosocial well-being and work productivity of remote workers: cross-sectional correlational study. *JMIRx Med* 2021 [FREE Full text] [doi: [10.2196/30708](https://doi.org/10.2196/30708)]
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Peer-Review Report

# Peer Review of “Influence of the COVID-19 Lockdown on the Physical and Psychosocial Well-being and Work Productivity of Remote Workers: Cross-sectional Correlational Study”

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Laura Taraboanta<sup>1</sup>, MS

Click Therapeutics, New York, NY, United States

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## Related Articles:

Companion article: <https://psyarxiv.com/dnuk3/>

Companion article: <https://med.jmirx.org/2021/4/e34609/>

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(*JMIRx Med* 2021;2(4):e34608) doi:[10.2196/34608](https://doi.org/10.2196/34608)

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*This is a peer-review report submitted for the paper “Influence of the COVID-19 Lockdown on the Physical and Psychosocial Well-being and Work Productivity of Remote Workers: Cross-sectional Correlational Study”.*

COVID-19 pandemic on remote workers in the UK and help facilitate broader conversations on how to continue to track physical and psychological metrics as restrictions are easing. Additionally, the paper offers recommendations on how employers and government policy and guidelines can best support overall well-being and productivity by looking at the data and seeing where the unmet needs are. A follow-up study would be interesting with the same participants, tracking them over the span of 1 year to 18 months and assessing the same metrics to look for any change in the scores (improvements, further decline, etc).

## Round 1 Review:

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### General Comments

No major comments to add. The overall design, analysis, and conclusion [1] present a critical view into the impact of the

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### Conflicts of Interest

None declared.

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### Reference

1. Tronco HYA, Parente F, Faghy MA, Roscoe CMP, Maratos FA. Influence of the COVID-19 lockdown on the physical and psychosocial well-being and work productivity of remote workers: cross-sectional correlational study. *JMIRx Med* 2021 [[FREE Full text](#)] [doi: [10.2196/30708](https://doi.org/10.2196/30708)]
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Peer-Review Report

# Peer Review of “Information Technology Ambidexterity, Digital Dynamic Capability, and Knowledge Processes as Enablers of Patient Agility: Empirical Study”

Ibrahim Taiwo Adeleke<sup>1</sup>, MSc

Health Records, Federal Medical Centre, Bida, Nigeria

**Related Articles:**

Companion article: <https://www.medrxiv.org/content/10.1101/2021.07.20.21260841v1>

Companion article: <https://preprints.jmir.org/preprint/32336>

Companion article: <https://med.jmirx.org/2021/4/e34106/>

Companion article: <https://med.jmirx.org/2021/4/e32336/>

(*JMIRx Med* 2021;2(4):e34107) doi:[10.2196/34107](https://doi.org/10.2196/34107)

**KEYWORDS**

IT ambidexterity; dynamic capabilities; digital dynamic capability; knowledge processes; patient agility; hospitals; information sciences; information technology; digital health; health care; digital transformation; research models

*This is a peer-review report submitted for the paper “Information Technology Ambidexterity, Digital Dynamic Capability, and Knowledge Processes as Enablers of Patient Agility: Empirical Study”*

## Round 1 Review

**Specific Comments****Major Comments**

1. Methods
  - a. Describe the study [1] settings
  - b. Move the highlighted (in the reviewed manuscript) content under Data Collection Procedures to a new subsection under subsection heading Study Population (see comments in the reviewed manuscript)
  - c. The highlighted content should be under a new subsection heading Study Design
  - d. Provide content on another two subsection headings:
    - i. Sampling Techniques
    - ii. Sample Size
  - e. Separate content under Data Collection Procedure into two new subsection headings
    - i. Data Collection Tool and Procedure
    - ii. Data Analysis and Management
  - f. Move Table 1 to Analyses & Results section
  - g. Provide content under two new subsection headings:
    - i. Inclusion and Exclusion Criteria
    - ii. Ethics Considerations

**Minor Comments**

1. Abstract
  - a. Do not begin a sentence with abbreviation of figure
  - b. Use past tense under Methods (eg, consider ‘used’ in lieu of ‘uses’)
  - c. See comments in the reviewed manuscript
2. Introduction
  - a. Use physicians in lieu of doctors
  - b. Use health care providers not other medical professionals
  - c. Keep in-text citation to the end of sentence
  - d. Add health information management professionals among the key stakeholders
  - e. Consider reducing the whole of section 2 (Theoretical Background) to 1-2 paragraphs and keep it within the Introduction section just before your study objective. This is to reduce readers’ boredom.
  - f. Compress the content under research models and hypotheses
3. Results
  - a. Make your findings more visible here
  - b. Make your writing more readable to known and unknown readers
4. Discussion
  - a. Plausible and insightful discussion but not a reflection of the content under the Results. Make the Results section more readable and meaningful to your audience.
5. Figure

- a. Use Fig not Figure
6. Acknowledgement
  - a. It is scientifically necessary that you acknowledge the numerous (n=107) participants, who are the major stakeholders in your research.
7. Reference
  - a. List at least 3 authors before et al
  - b. Follow the Referencing Style consistently
8. Others
  - a. Use participants not respondents

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### Conflicts of Interest

None declared.

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### Reference

1. van de Wetering R, Versendaal J. Information technology ambidexterity, digital dynamic capability, and knowledge processes as enablers of patient agility: empirical study. *JMIRx Med* 2021;2(4):e32336 [[FREE Full text](#)] [doi: [10.2196/32336](https://doi.org/10.2196/32336)]

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Peer-Review Report

# Peer Review of “Information Technology Ambidexterity, Digital Dynamic Capability, and Knowledge Processes as Enablers of Patient Agility: Empirical Study”

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Joseph Walsh<sup>1</sup>, MSc

School of Health Information Science, University of Victoria, Victoria, BC, Canada

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## Related Articles:

Companion article: <https://www.medrxiv.org/content/10.1101/2021.07.20.21260841v1>

Companion article: <https://preprints.jmir.org/preprint/32336>

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(*JMIRx Med* 2021;2(4):e34110) doi:[10.2196/34110](https://doi.org/10.2196/34110)

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## KEYWORDS

IT ambidexterity; dynamic capabilities; digital dynamic capability; knowledge processes; patient agility; hospitals; Information sciences; Information technology; digital health; healthcare; digital transformation; research models

*This is a peer review of “Information Technology Ambidexterity, Digital Dynamic Capability, and Knowledge Processes as Enablers of Patient Agility: Empirical Study”*

technology ambidexterity. The paper is well cited, uses appropriate methods, and discusses the concepts and findings in a clear and thorough manner. The paper should appeal to a broad audience. It is a good example of the underrepresented information and communications technology–centered literature in health care.

## Round 1 Review

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### General Comments

Thank you for the opportunity to review this paper [1] on the lesser known topic of information and communications

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### Conflicts of Interest

None declared.

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### Reference

1. van de Wetering R, Versendaal J. Information technology ambidexterity, digital dynamic capability, and knowledge processes as enablers of patient agility: empirical study. *JMIRx Med* 2021;2(4):e32336 [FREE Full text] [doi: [10.2196/32336](https://doi.org/10.2196/32336)]
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*Walsh J*

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Peer-Review Report

# Peer Review of “Information Technology Ambidexterity, Digital Dynamic Capability, and Knowledge Processes as Enablers of Patient Agility: Empirical Study”

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Laura Taraboanta<sup>1</sup>, MS

Click Therapeutics, New York, NY, United States

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## Related Articles:

Companion article: <https://www.medrxiv.org/content/10.1101/2021.07.20.21260841v1>

Companion article: <https://preprints.jmir.org/preprint/32336>

Companion article: <https://med.jmirx.org/2021/4/e34106/>

Companion article: <https://med.jmirx.org/2021/4/e32336/>

(*JMIRx Med* 2021;2(4):e34113) doi:[10.2196/34113](https://doi.org/10.2196/34113)

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IT ambidexterity; dynamic capabilities; digital dynamic capability; knowledge processes; patient agility; hospitals; information sciences; information technology; digital health; health care; digital transformation; research models

*This is a peer review of “Information Technology Ambidexterity, Digital Dynamic Capability, and Knowledge Processes as Enablers of Patient Agility: Empirical Study”*

## Round 1 Review

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### General Comments

Well thought out study design [1] with specific hypotheses and methods of analysis spelled out. Interesting conclusions drawn out that would be fruitful for further discussion and analysis to replicate on a broader sample of hospital systems outside of the current reviewed sites.

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## Conflicts of Interest

None declared.

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## Reference

1. van de Wetering R, Versendaal J. Information technology ambidexterity, digital dynamic capability, and knowledge processes as enablers of patient agility: empirical study. *JMIRx Med* 2021;2(4):e32336 [[FREE Full text](#)] [doi: [10.2196/32336](https://doi.org/10.2196/32336)]
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Peer-Review Report

# Peer Review of “COVID-19 Outcomes and Genomic Characterization of SARS-CoV-2 Isolated From Veterans in New England States: Retrospective Analysis”

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Mathew Mbwogge, MEPA, MSc

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**Related Articles:**

Companion article: <https://www.medrxiv.org/content/10.1101/2021.04.27.21256222v3>

Companion article: <https://preprints.jmir.org/preprint/31503>

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(*JMIRx Med* 2021;2(4):e35516) doi:[10.2196/35516](https://doi.org/10.2196/35516)

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**KEYWORDS**

infectious disease; COVID-19; epidemiology; veteran; outcome; sequencing; genetics; virus; United States; impact; testing; severity; mortality; cohort

*This is a peer-review report submitted for the paper “COVID-19 Outcomes and Genomic Characterization of SARS-CoV-2 Isolated From Veterans in New England States: Retrospective Analysis.”*

## Round 1 Review

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**General Comments**

The sudden menace imposed by the COVID-19 pandemic has led to the proliferation of studies on the epidemiology of viral genomics, specifically to understand disease risk factors, characteristics, and prognosis of those with COVID-19 [1-3]. Between 20% to 40% of COVID-19 admissions are reported to require intensive care [4], and have a fatality rate of 35% to 50% [5]. Many factors have been reported to either account for or to be associated with the clinical characteristics and prognosis of patients with COVID-19 [6-8]. Given that the aforementioned body of knowledge among veterans in New England is currently limited, the authors of the paper titled “COVID-19 Outcomes and Genomic Characterization of SARS-CoV-2 Isolated From Veterans in New England States” [9] investigated the patient characteristics, comorbidities, and disease predictors in a cohort of 426 veterans hospitalized for COVID-19. They found using a multivariate regression that age was the most significant predictor of being hospitalized, the severity of disease, and mortality; being non-White was more associated with being hospitalized; and those in need of oxygen upon admission were more likely to die.

Even though widely reported, genomic epidemiology remains a rapidly growing domain in virology [10]. Besides, the diversity of the four coronavirus genera (alpha, beta, gamma, and delta)

[11] and the emergence and spreading of the B.1.1.7 variant from the United Kingdom, B.1.1.28 from Brazil, and B.1.351 from South Africa [12] warrant constant new data and knowledge translation. To this effect, this paper addresses a major area of concern and interest to the readership of the journal. The authors are clear in their title, which still needs to fully comply with the journal guidelines. The Abstract follows the guidelines and presents an overview of the study. Being an area that has received tremendous interest since the start of the COVID-19 pandemic, there was an overriding need for this study to be put in context. The paper’s introduction does well, ends with the study aim, and is brief at highlighting the main concern but deserves more attention. The general structure of the paper needs improvement to comply with the journal guidelines. The data collection methods, albeit needing clarification, seem reasonable with appropriate analysis, thereby giving value to the results. The discussion of the paper has been well articulated, and the conclusion ties with the research objective. The English used is simple and in plain language for easy comprehension.

Although congratulating the authors for a good attempt and concise paper, the paper will benefit from more value if the following specific comments are given consideration.

**Specific Comments**

1. The general structure of the paper needs to conform to the journal guidelines.
2. The paper deserves to be put in context to be more appealing.
3. The introduction appears too restrictive and could be made more robust.

4. The methods and reported results warrant the use of appropriate guidelines.
5. All tables and figures need to be formatted following the guidelines.
6. Your references need slight improvement, in line with the guidelines.

To elucidate the aforementioned specific comments, kindly refer to the major and minor comments.

### **Major Comments**

1. Kindly format your title following the guidelines [13]. Your title should normally end with a study design after a semicolon.
2. The methods subsection of the Abstract needs to summarize the study design; total sample, setting, and recruitment; mean age and gender differences; end points measured; data collection procedure; and data analysis. You may want to change the subtitle from “Study Design” to “Methods.”
3. Kindly use the following template to give your paper an overall structure that complies with the journal guidelines [14].
4. Given the high amount of reported literature in this field, I suggest putting your study in context [1]. Kindly search the Cochrane and Pubmed databases to:
  - 1) Summarize the evidence already reported on the topic
  - 2) Report why this study was necessary and the value added to the existing literature
  - 3) The implication of all available evidence (including that from this study)
  5. It will be good to structure your Introduction into Background, Study Rationale, and Study Aim.
  6. Kindly structure your Methods section and report it as follows:
    - 1) Specific objectives
    - 2) Study design with justification (kindly make clear if this was a retrospective or prospective cohort study)
    - 3) Study setting
    - 4) Sample size calculations
    - 5) Participant recruitment (with inclusion and exclusion criteria)
    - 6) Sample/data collection
    - 7) Sample handling procedure and quality control
    - 8) Outcome measures (indicate whether these were continuous, binary, or categorical).
    - 9) Whole genome sequencing and phylogenetic analysis
    - 10) Data analysis (with justification for the approach used)
    - 11) Ethical considerations
  7. It is not clear whether this was a retrospective study since patients were still hospitalized at the time of this study. In 6.2 above, kindly be precise about the type of cohort study you undertook.

8. As part of your participant recruitment, indicate attempts made to reduce bias.
9. In 6.6 above, give details of those that collected samples and how that was done. If this was done by your research team, ensure to report the protocol used to collect samples. Organize your data collection into:
  - 1) Hospitalization data
  - 2) Peak disease severity data
  - 3) Mortality data
  - 4) Genome sequencing data
10. In 6.7 above, kindly clarify how samples were handled (including storage). If this was not done by the research team and was only reported, kindly indicate as such. If samples were not collected by you, provide details on how you had access to samples.
11. In 6.9 above, it is important to report the protocol/guidelines you used in genome sequencing. You may want to justify your procedure using these WHO guidelines [15] as well as substantiating your procedure with a visual display/flow of how the sequencing works.
12. As part of your statistical analysis, could you please justify your use of nonparametric tests? Kindly report the normality tests that were performed and the figures.
13. It might be worth arranging your data analysis first into univariate analysis and multivariate analysis, and then into hospitalization, peak disease severity, mortality, and genome sequencing.
14. In your data analysis, kindly report how you moved from univariate to multivariate analysis or how you selected variables for your multivariate model.
15. It is very important to indicate the guidelines used to report your review results. As part of your ethical considerations, indicate the guidelines you used to report your results. You may want to use these depending on which best suits your study method [16,17].
16. Your Results section should be reported in line with the Methods section starting with the participant characteristics. You might want to report your results as follows:
  - 1) Participant characteristics
  - 2) Predictors of hospitalization
  - 3) Predictors of peak disease severity
  - 4) Predictors of mortality
  - 5) Genome sequencing and phylogenetics
17. Kindly move your Supplemental Table 1 to Participant Characteristics in the Results section.
18. Kindly move Supplemental Figure 1 and Supplemental Figure 2 to the Predictors of Hospitalization and Predictors of Mortality subsections of the Results section, respectively.

19. Note that the whole of your manuscript must be in portrait. You may want to highlight your Table 1 then click on “fit to window” on the automatic adjustment tab of Microsoft Word and move it together with Figure 1 to the Genomic Sequencing subsection of your Results section.

20. In the presentation of the results of your logistic regression, it will be good to state how the following assumptions were met:

- 1) Binary outcome
- 2) Linearity
- 3) Outliers
- 4) Multicollinearity

21. As part of the reported results of your regression, I suggest providing an explanation on your model’s goodness of fit by plotting and reporting the area under the receiver operating characteristic curve.

22. Kindly follow the guidelines to structure your Discussion section as follows:

- 1) Principal findings (summary)
- 2) Comparison with prior studies
- 3) Study limitations

23. Include a subsection “Author Contribution” after the Acknowledgments section to state the contribution of each author included in this paper.

24. Include a subsection “Conflicts of Interest” after “Author Contributions” to declare any conflict of interest.

25. Kindly list all Multimedia Appendices before the References section. For instance, your supplemental Table 2 will be labeled in the body of the manuscript as follows:

- Multimedia Appendix 1: Genomic lineage

26. Create a section “Abbreviations” after your references to list and expand all abbreviations in the text.

### **Minor Comments**

27. You may want to include just the corresponding author on the manuscript and add all other authors in the metadata section of the online manuscript management system.

28. Kindly format your tables following the journal guidelines [18].

29. Kindly number your tables in the body of the text in order of appearance (Table 1, 2, 3, etc).

30. You need to report any *P* values based on the guidelines (eg,  $P=.05$  or  $P<.001$ ).

31. Review all your figures and their captions to ensure they are in line with the guidelines [19]. Apart from being uploaded as multimedia appendices, all figures must appear in the body of the text where they are first mentioned. The caption of each figure must appear at the bottom of the figure.

32. In your Discussion section, it will be appropriate to organize the “Comparison With Prior Studies” into subtitles as follows:

- 1) Predictors of hospitalization
- 2) Predictors of peak disease severity
- 3) Predictors of mortality
- 4) Genomic sequencing

33. I suggest starting your conclusion with a statement on the study objectives followed by a summary of findings, then lessons learned from your findings, and finally suggested direction of future research.

34. You need to delete your “Supplemental Table 2. Lineages of genomes” from the manuscript and upload it as a Multimedia Appendix in the online manuscript submission system. All multimedia appendices must be referenced in the body of your paper. Kindly have a look at other papers published in JMIRx Med.

35. Kindly make Acknowledgments, Funding, and Conflicts of Interest subsections.

36. Your references need to be formatted following the journal guidelines. Set your reference manager to the American Medical Association (AMA) citation style and make sure to include a PubMed ID at the end of each reference. You can search the PubMed IDs of articles at <https://pubmed.ncbi.nlm.nih.gov/>. It is also possible to copy your citation directly from the PubMed site provided it has been set to the AMA style (see references to this report for examples).

For articles without PMIDs, kindly include a DOI and ensure you verify your DOIs using <https://www.doi.org/> to make sure they work.

37. For referenced websites, ensure to make as much effort as possible to get and reference the PDF version of the article (ie, in the absence of a PMID and DOI).

## **Round 2 Review**

### **General Comments**

The authors of the paper titled “COVID-19 Outcomes and Genomic Characterization of SARS-CoV-2 Isolated From Veterans in New England States: A Retrospective Analysis” have addressed all concerns raised close to full satisfaction. The paper is in much better shape now; however, there still are a few concerns worth noting. Kindly refer to the minor comments.

### **Specific Comments**

#### **Minor Comments**

1. Under “Study Design,” the second and third sentences should be moved to the “Study Setting” and the last sentence moved to “Ethical Considerations.” The justification for the study design initially recommended was to cite any studies on the topic that have used similar methods (if possible).

2. Tables 1 and 2 still need to be formatted according to the guidelines.

3. I still see the captions of figures appearing above the figures, contrary to the guidelines.
4. Kindly maintain the heading “Multimedia Appendix: Lineages of genomes” in the manuscript but remove the table and upload it in the online manuscript management system.
5. Ensure that all reported percentages in your manuscript are accompanied with the absolute values on which they were calculated, for instance, 25% (5/20) or (25%, 5/20).

## Conflicts of Interest

None declared.

## References

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## Abbreviations

**AMA:** American Medical Association

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Peer-Review Report

# Peer Review of “COVID-19 Outcomes and Genomic Characterization of SARS-CoV-2 Isolated From Veterans in New England States: Retrospective Analysis”

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(*JMIRx Med* 2021;2(4):e35517) doi:[10.2196/35517](https://doi.org/10.2196/35517)

**KEYWORDS**

infectious disease; COVID-19; epidemiology; veteran; outcome; sequencing; genetics; virus; United States; impact; testing; severity; mortality; cohort

*This is a peer-review report submitted for the paper “COVID-19 Outcomes and Genomic Characterization of SARS-CoV-2 Isolated From Veterans in New England States: Retrospective Analysis.”*

## Round 1 Review

**General Comments**

The authors presented a study [1] about the clinical and genomic characterization of COVID-19 from a veteran group. I have some questions for the authors.

1. Line 85: Authors wrote, “we recorded hospitalization status, mortality, and oxygen (O<sub>2</sub>)-requirement within 24 hours of admission.” Here, can authors clarify if they recorded each single patient’s clinical information within 24 hours of admission or they collected them from chart review? In addition, for O<sub>2</sub>, the 2 should be subscript.

2. Lines 105 and 106: The disease name should be capitalized.

3. Line 113: Authors did not provide a transition between the univariate regression and multivariate regression. Univariate analysis was simply mentioned in the first sentence without any explanation or discussion. Authors should indicate the reason why they conducted multivariate analysis (eg, univariate was not specific enough). Additionally, in general, the factors should have the first letter capitalized, for example, Age, Non-White Race.

4. Line 129: Authors wrote, “our study found that in an older cohort of veterans.” Here, older cohort could cause some confusion to some readers. When one reads the paper a few years later, he or she probably cannot understand what the older cohort is related to. Authors can add a time frame to it.

5. Line 131: Similar to point 4, authors should add the Centers for Disease Control and Prevention (CDC) report date.

6. Line 133: Authors wrote, “veterans are a unique cohort because of advanced age on average, and more comorbidities. Understanding clinical factors that impact outcomes in veterans will help clinicians risk-stratify patients with similar demographic profiles.” Many veterans could be young in some Veterans Affairs (VA) medical centers. It may be right to general veteran populations, but authors need to cite references to support this claim.

7. Line 137: Authors wrote, “in our study, age was a significant predictor for all of our outcomes and was a confounder for other variables.” Most scientific papers are written from the third point of view. Therefore, it is not common to state the study outcomes as “our outcome.” Authors should use a better phrase, such as in line 151: “This may explain the outcomes in our study.”

8. Line 138: Authors wrote, “interestingly, LTC status predicted all three of our outcomes on univariate analysis, but not on multivariate analyses. Earlier in the COVID-19 pandemic, residents of nursing homes had higher rates of infection as well as severe illness and mortality [2].” There is no transition between these two sentences. The first few sentences in the paragraph discussed age as a predictor. However, the sentence “earlier in the COVID-19 pandemic...” did not show an immediate connection with the age issue. Maybe the authors would like to express that nursing homes have older patients. If this is the case, the authors need to provide some connection or background information here.

9. Line 140: Authors wrote that “our study shows that among veterans in LTC facility, disease outcomes were not impacted by their residence status.” Here, authors should provide some discussion or reasons for their findings.

10. Line 148: Authors wrote, “our study supports data from previous reports that non-White patients are at increased risk of hospitalization but have similar peak severity and mortality outcomes [3-6].” Are these non-White patients in the United States or in other countries? This could change the dynamic and purpose of citing the reference. Please clarify.

11. Line 156: Authors concluded that, for patients with dementia, they could have a high risk of death because of biological factors. Another possibility is the lack of self-report ability in patients with dementia. As a result, they probably do not understand their body’s changes, which could delay the needed care.

12. For the Discussion section, authors may add subtitles to different issues they would like to discuss. The current writing may be a little bit confusing to some readers.

13. In the Discussion, the authors mentioned multivariate analysis of many potential risk factors as their strength. It is true that the multivariate model is a powerful tool, but it is not necessarily fit for the COVID-19 situation very well. Authors need to cite references about other cases of using the multivariate model for COVID-19 outcome analysis.

14. Figures and supplemental tables: Authors should include more details in the titles. Simply writing “genomes” or “hospitalization” in the title is not standard in scientific papers.

15. Figure 1: Authors should provide a better maximum likelihood tree. The current figure has many branches stacked to each other, barely providing any helpful information to readers.

## Round 2 Review

The authors presented an updated manuscript after taking the reviewers’ suggestions. I have a few minor comments.

1. Authors added reference [7] but did not indicate or cite it in the paper. I guess it should be listed here: “which has been frequently used in COVID-19 literature [8-11].”

2. Authors wrote, “this study included all veterans who tested positive for COVID-19 from April 8, 2020, to September 16, 2020 at one of the six New England VA hospitals.” Previously authors wrote, “Connecticut had been entrusted with testing for SARS-CoV-2 for all six VA healthcare centers.” Does this mean the patients enrolled in this study are from one of six VA hospitals, or they are from all six hospitals?

3. Authors wrote, “the CDC provides a list of chronic medical conditions (May 2021) that predispose individuals to severe illness from SARS-CoV-2 infection [12], but >75% of United States adults fall under a high-risk category [13].” In general, if the word “but” is in the sentence, readers will pay attention to the words following “but,” which means the first part may not be important or critical. Authors can kindly use another connection word.

4. In the Abstract, the authors wrote “Multiple SARS-CoV-2 lineages were distributed in patients in New England early in the COVID-19 era, mostly related to viruses from New York with D614G mutation.” Can the authors kindly clarify if it is New York State or New York City?

## Conflicts of Interest

None declared.

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## Abbreviations

**CDC:** Centers for Disease Control and Prevention

**VA:** Veterans Affairs

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Authors' Response to Peer Reviews

# Author's Response to Peer Reviews of "Machine Learning–Based Prediction of COVID-19 Mortality With Limited Attributes to Expedite Patient Prognosis and Triage: Retrospective Observational Study"

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**KEYWORDS**

COVID-19; coronavirus; medical informatics; machine learning; artificial intelligence; dimensionality reduction; automation; model development; prediction; hospital; resource management; mortality; prognosis; triage; comorbidities; public data; epidemiology; pre-existing conditions

*This is the author's response to peer-review reports for "Machine Learning–Based Prediction of COVID-19 Mortality With Limited Attributes to Expedite Patient Prognosis and Triage: Retrospective Observational Study."*

## Round 1 Review

**Reviewer DD**

More detail is provided in the responses to individual comments [1], but for general context, to increase originality, the revised manuscript [2] now focuses more heavily on the impact of feature reduction on model performance rather than model performance as a standalone finding. The original reduction method, mutual information, is complemented by chi-square reduction, and comparisons between the impact of each were

made, highlighting the need for different reduction methods to be tested as part of model tuning. Additional points were added to the *Discussion* stating that comparable models drawing from much richer feature sets performed comparably to our reduced ones and that large amounts of explanatory power can be captured by even a single variable, with the ultimate goal of reducing the number of variables, and consequently the tests and imaging, needed before models can be used in a hospital setting.

1. Mutual information was used due to the mixture of categorical and continuous variables, with a large presence of the former. A general equation for mutual information, which is the criterion used for feature selection, was provided. Variables were not binned but rather modelled through a k-nearest neighbors estimation approach; this was mentioned in the study, and the

relevant source paper was cited for further detail. Software packages used (methods from Python's sklearn library) were mentioned explicitly in the methodology.

2. Features are a subset/extraction of the original feature set, not a transformation/combination. A section was added to the *Results* section detailing the 7 most salient features selected via mutual information.

3. This would be a productive comparison; however, the reason it was not performed is due to data limitations. As outlined in the original paper, the 5121-patient data set has an extremely small proportion of patients affected by pre-existing conditions, meaning that keeping those features and training a 5121 patient model on age + comorbidities and comparing it to the full 212-patient data set would really simply be a comparison of the impact of age in the 5121-patient model against the full features in the 212-patient model, given that co-morbidity data is largely absent (and vastly underrepresented) in the 5121-patient data set. However, from other helpful revision comments, a feature importance table using mutual information was provided in the *Results* section; it shows that with the exception of fever, symptoms do not seem to play a high-importance role in prediction and do not feature in the top 7 explanatory variables.

Additionally, to further facilitate comparisons between data sets and feature reductions, only the 212-patient data set was retained in the study.

4. 95% confidence intervals were added to the result tables for all sensitivity, specificity, accuracy, and area under the curve (AUC) findings.

5. A paragraph has been added to the *Discussion* section briefly comparing the 7 features extracted in our study using mutual information to the most salient features from the proposed paper, finding substantial overlap, particularly with fever and pneumonia as high-value features.

6. The parameters used were reported in the *Results* section.

7. The date on which the data were accessed was added to the relevant data section in the methodology. Detailing the exact

breakdown of samples in training and testing over multiple iterations of sample splitting and dimensionality reduction seems excessive, especially considering that the sample is small and retrievable and the methodology (3-fold cross-validation coupled with simple classifiers) is easily reproducible.

8. This was poor wording on the study's end; it was intended to state that receiver operating characteristic (ROC) curves will be produced in order to obtain numerical AUC estimates, but the ROC plots were never meant to be graphically reported in the study. The original sentence was removed from the paper to avoid confusion.

### Reviewer EB

1. Noted; the suggestion [3] has been implemented. An in-depth review of existing equipment, public spending, and staff shortage limitations prior to the COVID-19 pandemic was provided with examples from around the world, with additional indicators of strain following the pandemic, as well as studies directly linking shortage of resources to worse patient outcomes, therefore justifying the need for better resource management. The primary management tool proposed in the study is the introduction of predictive modelling for better triage, providing potential benefits to "pre-allocation or local hospital transfer of life saving equipment, quantifying the need for further diagnostics or early treatment and directing limited staff attention and resources toward highest risk patients." All condensed points in this response can be found in expanded form in the introduction of the study.

2. In the new *Discussion* section, a paragraph has been added regarding the real-world use cases of the models explored in the study.

3. Noted; a more streamlined and direct objective has been included in the new Abstract.

4. Noted; this has now been rectified.

5. Noted; this has now been rectified.

6. This refers to the Area Under the Curve, and a footnote has now been added.

### References

1. Boie SD. Peer review of "Machine learning-based prediction of COVID-19 mortality with limited attributes to expedite patient prognosis and triage: retrospective observational study". *JMIRx Med* 2021;2(4):e34082 [FREE Full text] [doi: [10.2196/34082](https://doi.org/10.2196/34082)]
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3. Moquillaza Alcántara VH. Peer review of "Machine learning-based prediction of COVID-19 mortality with limited attributes to expedite patient prognosis and triage: retrospective observational study". *JMIRx Med* 2021;2(4):e34083 [FREE Full text] [doi: [10.2196/34083](https://doi.org/10.2196/34083)]

### Abbreviations

**AUC:** area under the curve

**ROC:** receiver operating characteristic

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Authors' Response to Peer Reviews

# Authors' Response to Peer Reviews of "Influence of Mass Media on Italian Web Users During the COVID-19 Pandemic: Infodemiological Analysis"

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**KEYWORDS**

COVID-19; Google Trends; infodemiology; infoveillance; infodemic; media coverage; mass media influence; mass media; social media

*This is the authors' response to peer-review reports for "Influence of Mass Media on Italian Web Users During the COVID-19 Pandemic: Infodemiological Analysis."*

## Round 1 Review

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**Reviewer E**

1. Dear Reviewer [1], thanks for the warning. The text [2] has been double-checked. If there are any further inaccuracies, the manuscript will be sent to a proofreading service.
2. Dear Reviewer, the *Introduction* section has been rewritten and enriched following your instructions. Thank you so much for the valuable advice. Changed text is highlighted in blue in the new file.
3. Dear Reviewer, thank you for raising this important issue. The answer given was the following: "The internet represents a fast, user-friendly means to seek health-related information.

Especially during a pandemic or any major health crisis, the need for quality web information is more pressing than ever: fear, anxiety, stress, and confusion due to the overabundance of often conflicting or dramatic news increases the consultation of web sources to seek remedies or reassurance."

4. Dear Reviewer, once again, thanks for the valuable comment. The answer to this question is too long to be reported here. However, we created the *Countermeasures to the Infodemic* subsection to discuss this point.
5. Dear Reviewer, thanks for the help and references provided. The use of Google Trends has been addressed in the subsection *Countermeasures to the Infodemic*.
6. Dear Reviewer, we agree that this subsection is too limited to fully represent the influence of the infodemic information reported by the mass media on users. However, we think it is important to point out that infodemic videos and articles have led to a great media clamor and a very high number of views.



Indeed, these have been shared by the main information channels in Italy, thus reaching a vast audience. Since conspiracy theorists are subject to confirmation bias [3], absolute visibility is as relevant as relative visibility. For this reason, we think it important that a peer-reviewed source denounces this dangerous phenomenon. In this regard, we changed the name of the research question from “What was the role of the Italian mass media in the COVID-19 infodemic?” to “Among the contents proposed by mass media channels, what was the interest aroused by the infodemic news?” As for the definition of infodemic news, we drew on the infodemic scale (which has now been appropriately explained in the *Methods* section).

7. Dear Reviewer, thank you for noting this. We agree with you. We have removed R4 from the manuscript. To mention the matter, we wrote: “Alongside this, our analysis can provide further evidence on the reliability of Google Trends for studies other than infodemiological ones.”

8. Dear Reviewer, we again agree and thank you. We rewrote the section specifying the procedure in detail and why each source was chosen for analysis. Thank you very much for raising this essential inconsistency.

9. Dear Reviewer, this paper aims not only to understand if there is an influence of the media on web searches but also to quantify it. The correlational analysis shows strong evidence in favor of a marked and statistically significant influence both in the adoption of keywords and monikers and search trends. These results can help understand the overriding need to provide quality information (especially during health emergencies) and the relevance of the media in the diffusion of the latter.

10. Dear Reviewer, thank you for noting this. The following explanation was provided in the manuscript: “We exploited the infodemic scale (I-scale) to assess the infodemicity of the terms examined: each moniker was assigned 1 to 2 points per category (ie, generic, misinformative, discriminatory, deviant, other specificities), ranging from 0 to 10. Based on the sum of the I-scale scores, the infodemic monikers were classified as follows: not infodemic (0), slightly infodemic (1), moderately infodemic (2-4), highly infodemic (5-8), and extremely infodemic (9-10). Further details on the use of the I-scale are given in reference 10.”

11. Dear Reviewer, we agree with the difference you highlighted between the types of data. In this regard, we considered that the correlational analysis (unlike the regression) is not influenced by absolute values but only by trends, which are not affected by normalization. This paper relates relative web interest (relative search volume) to newspaper headlines but not the exact number of web searches. This was specified in the *Limitations* section. However, since it is known from other papers that the number of searches on COVID-19 has always been high [4], even relative trends provide valuable information.

Similar analyzes have been made, for example, between RSV and COVID-19 cases (eg, [5]).

12. Dear Reviewer, thank you for the question. As we have now added in the paper, “To evaluate time-series seasonalities, we used a graphical check and the ‘Time Series Analysis’ tool of the XLSTAT package. In particular, we have divided the signal into the trend, seasonal, and random components. Finally, we calculated the autocorrelogram plot.”

13. Dear Reviewer, we did as requested. Thanks.

14. Dear Reviewer, thank you very much for raising this interesting point. The *Discussion* section has been rewritten to include these topics.

15. Thank you so much for the valuable comment. The *Discussion* section has been redesigned and divided into the following parts: *Principal Findings*, *Comparison With Recent Literature*, *Practical Implications*, *Limitations*, and *Conclusions*.

16. Once again, thank you so much for highlighting this essential aspect. The new *Discussion* section addresses these points based on what is found in this paper and on previous literature.

17. Done. We thank you very much for your help in improving our manuscript.

### Anonymous

1. Dear Reviewer [6], we appreciate your constructive criticism. The *Introduction* section has been rewritten and enriched following your suggestions. Thank you very much.

2. Dear Reviewer, we fully agree with your comment and thank you. The *Data Collection* section is now explained in more detail. Furthermore, we have added Google Trends among the sources, specifying the geographic region (Italy, national data), the type of data analyzed (web searches), and the category (all categories). Keywords and search periods are shown in Table 1. In addition, we have removed unnecessary information from the statistical analysis as required (we have just left the legend).

3. Dear Reviewer, thank you very much for your valuable suggestion. We have significantly lightened the *Results* section by including more data in the supplementary file and removing redundant information. Furthermore, we simplified the correlational analysis by introducing a cross-correlation summary result.

4. Dear Reviewer, the section has been completely rewritten. Thank you for raising this relevant issue.

5. Dear Reviewer, thanks for the helpful information. We have arranged the Abstract as requested.

6. Dear Reviewer, we have removed the vast majority of bullet points. Thanks for your help.

7. Dear Reviewer, we did as requested. We thank you very much for your help in improving our paper.

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1. Lotto M. Peer review of "Influence of mass media on Italian web users during the COVID-19 pandemic: infodemiological analysis". JMIRx Med 2021;2(4) [[FREE Full text](#)] [doi: [10.2196/34137](https://doi.org/10.2196/34137)]
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Authors' Response to Peer Reviews

# Authors' Response to Peer Reviews of "A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study"

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**KEYWORDS**

local social network; community health; well-being; digital health; consumer health

*This is the authors' response to peer-review reports for "A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study."*

## Round 1 Review

We would like to thank the Editor and Reviewers for excellent comments that have vastly improved the quality of our manuscript [1]. Below, we provide a point-by-point response to reviewers, and we address all points made by all reviewers.

**Anonymous Reviewer [2]**

1. We thank the anonymous reviewer for pointing out this omission. We have added an entire subsection to the *Methods* section, titled *Quokka System*, which explicitly describes the components of the Quokka system in more detail.
2. We apologize for this confusion, and we should have been more careful when originally reporting our results. We meant to convey that we reject the NULL hypothesis that similar proportions of users would participate in local and remote

activities during the challenges. Our alternate hypothesis, that users prefer local over remote activities, was therefore confirmed. We have clarified this language throughout the manuscript and have explicitly referred to the hypotheses as H1, H2, and H3.

3. We thank the anonymous reviewer for finding this lack of clarity. We have added a new section to the *Methods*, called *Statistical Tests*, which provides details about how we tested for significance. In particular, we added: “To perform statistical testing for H1-H3, we conducted a binomial proportion test, where we used the proportion of local (H1), social (H2), and new (H3) self-reported activities per week. The null hypothesis is that the proportion is 0.5 (equal number of local and remote, social and individual, as well as new and familiar activities). The goal was to determine if the increased rates of local, social, and new self-reported activities was statistically significant. We calculated a Clopper-Pearson Binomial proportion confidence interval for one test, a method which leverages the cumulative probabilities of the binomial distribution.”

4. We have clarified these points throughout the manuscript. We chose the local versus social, remote versus in-person, and familiar versus new categories because these were the unique aspects of Quokka that we wanted to test. Other health and wellness digital health tools do not focus on the social, in-person, and novel experience aspects of well-being, and we wanted to ensure that Quokka would feasibly promote increased activity of these kinds. In order to code these categories from participant questionnaire responses, we hired 3 independent raters recruited on Upwork, a popular web-based freelancing platform that connects workers to job providers. To reach the final category, a majority-rules consensus was taken for the categorical labels provided by raters. In cases where all 3 raters disagreed, the authors provided the final rating. Protected user data were anonymized when provided to Upwork workers. We have updated the manuscript with these details.

5. We have added a new section to our manuscript, called *Limitations: Study Design*, which highlights the limitation of the analysis consisting of quantitative analysis of coded qualitative data.

6. Because this research was conducted outside of our capacity as students at a University, and our startup company does not have an ethics review committee, no formal University ethics review was sought for this study. However, all users provided informed consent for participation. In particular, all participants consented on signup to a Privacy Policy and a Terms and Conditions that walked through how their data would be used. We ensured that all user data were anonymized during our analyses, and we do not reveal any protected health information or any other identifiable information in the manuscript. We believe that we fulfill JMIR’s requirements for ethics approval [3]. We have added to the manuscript that the research was conducted in accordance with the Declaration of Helsinki.

We are happy to work with the Editor to ensure that this manuscript can fulfill the ethics review requirements on JMIR. Please let us know if there are any additional steps we should take to address this concern.

## Reviewer J

1. We thank Reviewer J [4] for pointing out this lack of clarity. The challenges were part of the interventional program that makes use of the established success of community-based social programs for behavior change, in particular through a new community-based social network, Quokka, which was the embodiment of the interventional paradigm we were exploring the feasibility of. We have updated the manuscript to reflect this more clearly.

2. The program focused on one habit per week, although participants were encouraged to stick to whichever habits they found most effective both through the duration of the program and afterwards. A final survey was sent to participants at the end of each program to collect input and feedback from participants. Respondents cited which habits they had continued and were planning to continue from then on, although this was not further assessed after the program completion.

3. We reached out to over 15 US colleges and universities and met with several administrative health services and student health club staff in order to discuss the possibility of running a program on their campuses. Since this was an early pilot, we chose a small subset of schools to coordinate programs based on their overall interest and availability in dedicating time and effort towards participating. We have clarified this point in the manuscript.

4. We believe that the confirmation of the feasibility of Quokka to promote local, social, and novel experiences can be generalized to other universities, particularly given the differences in student body size and demographics between the schools.

Typical demographics of college students in the United States follow an approximately equal split of women and men (with women holding a slight majority). The vast majority of these students are between 18 and 24 years old (87.5% in 2017, when this study took place). By ethnicity, the undergraduate college student population in 2017 was approximately 53% non-Hispanic White, 21% Hispanic, 15% Black, 8% Asian, and 3% non-Hispanic “Other” [5].

For the four universities included in this study, the typical demographics of their undergraduate college students followed a similar pattern to the national statistics: approximately equal split between women/men, primarily between 18 and 24 years old, and predominantly identifying as non-Hispanic White with varying distributions of students identifying as Hispanic, Black, Asian, or “Other.”

We have included this information in the manuscript.

5. We reached out to administrative health services and student health clubs on each campus, meeting with prospective candidates who would be interested in volunteering. Typically, one student health club or group per campus would become the designated “host” while working with other school resources and groups to customize their programs. We have added this information to the manuscript.

6. Typical demographics of college students in the United States follow an approximately equal split of women and men (with

women holding a slight majority). The vast majority of these students are between 18 and 24 years old (87.5% in 2017, when this study took place). By ethnicity, the undergraduate college student population in 2017 was approximately 53% non-Hispanic White, 21% Hispanic, 15% Black, 8% Asian, and 3% non-Hispanic “Other” [5].

For the four universities included in this study, the typical demographics of their undergraduate college students followed a similar pattern to the national statistics: approximately equal split between women/men, primarily between 18 and 24 years old, and predominantly identifying as non-Hispanic White with varying distributions of students identifying as Hispanic, Black, Asian, or “Other.”

We have included this information in the manuscript.

7. We thank Reviewer J for identifying these areas for improvement. We have clarified all of these issues throughout the manuscript, and we refer to explicit hypotheses throughout.

8. We have reviewed the manuscript with an eye towards substituting imprecise terms throughout the manuscript.

9. We have now added section headers for the challenges list in the *Challenges Themes* section.

### Reviewer K

1. We agree with this point [6], and we concur that an ideal study would have included outcome measures relating to well-being. Because such an analysis was missing, we have limited the scope of this manuscript to be an “exploratory feasibility study” with the aim of evaluating the Quokka system’s potential for promotion of local, social, and unfamiliar activities as they pertain to healthy habits. A larger, more controlled study with outcome measure tracking will be required to claim anything beyond an exploratory feasibility study.

2. The Quokka Challenge was designed as a new program in the fall academic quarter/semester of 2017 to promote healthier habits in the university setting. The program design and implementation were influenced by prior research in the field, although it was uniquely created for the university setting. This manuscript highlights Quokka’s first pilot programs, evaluating its framework’s potential for increasing participation in healthy habits.

3. The Quokka platform was designed by a team of engineers, including the authors of this manuscript, who designed every aspect of the platform and challenge. Additional names are listed in the manuscript’s *Acknowledgments* section.

4. We do not have an explanation for the low retention, other than that our program had higher retention than the average well-being digital application [7]. We have included in the manuscript a citation to this study about the user retention of digital wellbeing apps.

5. We did not employ a control group for this study. We agree that this is a limitation which prevents us from describing the presented study as anything beyond an “exploratory feasibility study.” We have emphasized throughout the manuscript that the presented study is only exploratory in nature, and we have emphasized in the *Limitations* that we do not know whether

Quokka increases social, local, or new activities. We only know that when participating in the Quokka challenge, users are more likely to conduct social, local, or new activities than individual, remote, or familiar activities, by a large and statistically significant margin.

6. We thank Reviewer K for pointing out this omission, which we have corrected in the manuscript.

7. Because this research was conducted outside of our capacity as students at a University, and our startup company does not have an ethics review committee, no formal University ethics review was sought for this study. However, all users provided informed consent for participation. In particular, all participants consented on sign up to a Privacy Policy and a Terms and Conditions which walked through how their data would be used. We ensured that all user data were anonymized during our analyses, and we do not reveal any protected health information or any other identifiable information in the manuscript. We believe that we fulfill JMIR’s requirements for ethics approval as outlined here [3]. We have added to the manuscript that the research was conducted in accordance with the Declaration of Helsinki.

We are happy to work with the Editor to ensure that this manuscript can fulfill JMIR’s ethics review requirements. Please let us know if there are any additional steps we should take to address this concern.

8. The program was conducted during the fall academic quarter/semester of 2017, and this detail has been added to the manuscript introduction.

### Reviewer L

1. We thank Reviewer L [8] for bringing up this point. The Quokka Challenge was designed as a new program in the fall academic quarter/semester of 2017 to promote healthier habits in the university setting. The program design and implementation were influenced by prior research in the field, although it was uniquely created for the university setting. This manuscript now highlights Quokka’s first pilot programs, evaluating its framework’s potential for increasing participation in healthy habits. We have added this information to the manuscript.

2. We thank Reviewer L for pointing out this omission in the manuscript. We have created an explicit *Related Work* subsection in the *Introduction* which discusses the present study in the context of prior works.

## Round 2 Review

### Anonymous Reviewer [2]

1. We appreciate this response from the anonymous reviewer, and we have extensively proofread our manuscript to minimize any writing errors. We have replaced all instances of “patient” with “user.”

### Reviewer J

1. We thank Reviewer J for this suggestion, and we have removed the *Related Work* section and integrated this material into the *Introduction* section.

2. We thank Reviewer J for pointing us to the JMIR Instructions for Authors, which we have read and more carefully adhered to in the currently submitted revision, including adding a *Comparison With Prior Work* subsection in the *Discussion* section.

3. We have identified prior studies discussed here and in the *Introduction*; we searched for “digital mental health intervention local community”, “digital mental health intervention online community”, “mental health social network”, and “digital mental health intervention local social network” on Google Scholar as well as the Journal of Medical Internet Research website. We have added this information to the manuscript.

4. We have selected the work currently in the *Related Work* section in the same way we identified works in the *Comparison With Prior Work* section, as described above. We have clarified this methodology in the manuscript.

5. We have updated the title to be “Exploratory Feasibility Study of Quokka: A Local Community-Based Social Network for Mental Health and Wellbeing.” This title now reflects the major mental health component of this work.

### Reviewer K

1. We greatly thank Reviewer K for the kind review.

### Reviewer M

1. We sincerely apologize for our omission of Reviewer M’s comments [9]. This was completely unintentional on our end and was due to a copying error. We are embarrassed by this mistake and we have ensured that all reviewer comments are properly addressed for this revision round. We thank Reviewer M and the Editor for allowing us to address these issues here.

2. We have checked similar papers published in JMIR and we believe that the updated manuscript adheres to the journal style.

3. We thank Reviewer M for pointing out these missing details in the *Introduction*. We have added a new introductory paragraph that motivates the problem that Quokka attempts to address, namely, the large mental health burden globally. We also discuss the current solutions to mental health care in the second paragraph, including the limitations of these approaches and why a guided yet remote digital health intervention could address these issues.

4. We agree, and we have moved this section down to the *Discussion* section.

5. We agree that this formatting was not ideal. To address this concern, we have incorporated the old *Related Work* section into the *Introduction* section, which now provides several references in the *Introduction* providing motivation for the work. In addition, we have significantly bolstered the citations when describing the motivation for Quokka and the current solutions which exist today.

6. We have moved these paragraphs to other sections of the paper and we have restructured the *Introduction* as requested by Reviewer M.

7. We thank Reviewer M for informing us about behavior changing theory (BCT) literature. We have added a section

about BCT and prior related studies in the *Introduction* section (the fourth paragraph in the revised manuscript).

8. We thank Reviewer M for pointing out this omission. We have added a list of manuscripts and clarified that the prior work we are comparing against, and in fact all prior work in this space does not leverage both local health opportunities and community-based programming to drive behavior change in a single social network.

9. We have added an explicit description of the aim of this study in the second to last paragraph of the *Introduction* section.

10. We sincerely apologize for our omission of Reviewer M’s comments. This was completely unintentional on our end and was due to a copying error. We are embarrassed by this mistake and we have ensured that all reviewer comments are properly addressed for this revision round. We thank Reviewer M and the Editor for allowing us to address these issues here.

11. We have separated what was previously the *Methods* section into two sections. The first section, called *The Quokka Platform and Challenge*, describes the Quokka system and program, and the *Methods* section now starts with the *Recruitment* subsection.

12. We thank Reviewer M for pointing out our lack of clarity regarding the exact study design and the purpose of the study. We note that the primary goal of this study was not to provide a controlled trial or to claim that Quokka is an intervention. Our goal was to test the feasibility of such a system by verifying that study participants engage in the behaviors suggested by Quokka for the duration of the program. We have clarified in the manuscript all questions asked by Reviewer M. In particular:

We designed the study as a feasibility study with three central hypotheses: (1) users will spend more time on local over remote activities, (2) users will spend more time on novel over familiar experiences, and (3) users will spend more time on social over individual challenges.

We acquired users through several recruitment strategies (eg, emails, posters) at four separate universities.

We did not include any exclusion criteria besides being a student at one of the four target universities.

All users signed a Terms of Service and Privacy Policy providing study consent. All user data is fully anonymized.

Data were collected by a weekly check-in which consisted of a weekly email reminder to fill in a survey form embedded on the Quokka website. All responses were free-form, and we categorized the responses after the study. Details are provided in the *Methods* section.

The study took place during the fall quarter/semester of 2017 at the respective universities.

13. We appreciate this response, and we have added a paragraph (fourth paragraph in the *Introduction*) discussing the theories of behavior change that Quokka is based on. Theories of behavior change suggest that intervention effectiveness may be increased through the incorporation of social and cultural factors that also influence behavior [10,11,12]. These theories targeting the lifestyle focus on learning and decision-making to drive

action and reflection, but understanding other factors such as individual beliefs, motivations, and the environment, are important for continued maintenance of health as well [13,14]. Examples of behavior change theories that examine these additional factors as applied to health outcomes include the health belief model (ie, behavior change is posited on barriers, benefits, self-efficacy, and threat) and the theory of planned behavior (ie, actions are driven by behavioral intent, subjective norms, and perceived behavioral control) [14,15,16]. Several of these have been in the university setting, which is especially pertinent given the Quokka setting. Quokka builds upon prior works by incorporating social, cultural, and local environmental elements into its framework and examining the effects of these community factors on individual action and reflection. Furthermore, Quokka utilizes several digital intervention techniques (including option-based, attribute-based, and goal-based techniques) that build upon these theories to drive further habit formation and maintenance [11].

14. We have ensured that the paper has a clear and distinct *Results* section. This *Results* section include the following subsections: *User Statistics* (quantitative), *Evaluation Outcomes* (quantitative), *Participation Due to Localized Social Influence*

(qualitative), *Shared Experiences* (qualitative), *Local Community-Supported Resources* (qualitative), and *User Reflection* (qualitative).

15. We thank Reviewer M for pointing out this omission. We have added an explicit section comparing against prior work and have clarified that the prior work we are comparing against, and in fact all prior work in this space, does not leverage both local health opportunities and community-based programming to drive behavior change in a single social network.

16. We have ensured that the *Limitations* sections are succinct and discuss the points brought up by Reviewer M.

17. We thank Reviewer M for finding this error in the reference format. We have updated the references according to the provided suggestions and have ensured that our reference format matches that of papers previously published in JMIR.

18. We thank Reviewer M for finding this error in the reference format. We have updated the references according to the provided suggestions.

19. We thank Reviewer M for pointing this out. We have included "et al" for all papers with more than 6 people.

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## Abbreviations

**BCT:** behavior changing theory

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Authors' Response to Peer Reviews

# Authors' Responses to Peer Review of “Offenders With Personality Disorder Who Fail to Progress: A Case-Control Study Using Partial Least Squares Structural Equation Modeling Path Analysis”

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*This is the authors' response to peer-review reports for the paper “Offenders With Personality Disorder Who Fail to Progress: A Case-Control Study Using Partial Least Squares Structural Equation Modeling Path Analysis”.*

## Round 1 Review

**Overview of Changes**

Several changes have been made to the manuscript [1] in response to the comments provided by both reviewers. These include additional information about personality disorder (PD) being included in the Introduction to further contextualize the population of interest in this paper. Information about the risk needs responsivity (RNR) model and readiness for treatment has been removed from the Introduction. Further details have been provided in the Methods section, and a visualization of the data analysis plan has been included as a second figure. Within the Discussion section, a new subsection focusing on the clinical and practical implications has been added. General

sentence restructuring and grammatical errors have been amended throughout.

**Individual Responses****Anonymous****Major Comments**

1. The Introduction is interesting to read, easy to follow, and well structured. I think the only thing that it is missing is some more background information on PDs. This could involve simply defining PD in a general sense and providing some information surrounding risks associated with them in community populations as well as their prevalence rates in offender populations (with citations). I would probably put this information at the start of the introduction, before going into more specific detail surrounding offenders with PD. Some language/grammatical improvements are also required throughout the introduction.

*Response:* This has been addressed in the revised manuscript; two new paragraphs have been included at the start of the Introduction. Language and grammatical improvements have been made; although this was from a general read through and if there are any specific sentences that need rewriting, please identify them for further revisions.

- The “Procedure” section in the Methods seems unnecessary as its own section. I would consider incorporating this information in the “Sample” section, potentially changing the heading to “Sample and Procedure.”

*Response:* This has been addressed in the revised manuscript; the Procedure section has been combined with the Sample section.

- In the Results section, I would suggest adding the test statistics and *P* values to Table 1, as this would make it very easy to identify where there were key differences.

*Response:* This has been addressed in the manuscript, two new columns have been added to Table 1 to provide test statistics and *P* values. As there are two different types of test statistics used in the table (*t* test and chi-square), a footnote at the end of the table has been provided to explain this.

- The numbers and interpretation of the results in Table 1 are somewhat difficult to follow. Percentagewise, a higher proportion of the nonprogression group is single compared to the control group, but the chi-square test results indicate that the control group is more likely to be single than the nonprogression group (presumably based on the actual *N*). I think this needs to be clarified/made consistent in the manuscript.

*Response:* This has been addressed in the manuscript; only the percentages are now reported in Table 1 to make it easier to interpret. The supporting text has also been revised as there were correctly identified inconsistencies here that are now correct.

- I think that it would be informative for the reader for the authors to merge all the supplementary descriptive results tables (Tables S1-S4) into one table and incorporate this into the main text in the Results section (rather than supplemental materials), also adding the test statistics to the tables.

*Response:* Test statistics and *P* values have been added to the supplementary tables; however, we do not think merging the tables and entering them into the main text would be a good use of the reader’s time. This is summary information about the sample and did not inform the subsequent model.

- The Discussion section was particularly interesting to read. Given the potential clinical impact and practical nature of this study; the only thing I think the Discussion is missing is a section on clinical/practical implications of the study (which was very briefly touched upon in the Conclusion). I think that this would really benefit the manuscript and be of interest to readers.

*Response:* A section considering the clinical and practical implications of the study findings is now included prior to the Conclusion in the Discussion section.

## Minor Comments

- This is very minor, but the “Engagement With Treatment and Treatment Noncompletion” in the Introduction could probably just be “Engagement With Treatment,” as this covers treatment noncompletion.

*Response:* This has been addressed in the revised manuscript.

- I would avoid using the term “personality disordered” throughout the manuscript.

*Response:* This has been addressed throughout the revised manuscript and adapted to “offenders with personality disorder” instead. A search for the phrase has ensured any occurrence of the phrase is now removed.

- The semicolons in the first paragraph of the “Engagement With Treatment and Treatment Noncompletion” section should be colons (and in some other parts of the manuscript).

*Response:* This has been addressed throughout the revised manuscript.

- Some of the study objectives in the Introduction could be made somewhat more specific/precise (eg, explicitly stating “offenders with PD,” rather than just offenders, or offenders that have not progressed on the Offender Personality Disorder [OPD] pathway).

*Response:* This has been addressed in the study objectives, specifically the first objective has been rephrased.

- The capitalization of “*N*” within tables needs to be made consistent throughout.

*Response:* This has been addressed throughout the manuscript and in all tables.

- When referring to tables in the manuscript, the “*t*” should be capitalized throughout (eg, “Table 2”).

*Response:* This has been addressed in the revised manuscript; all references to tables are now capitalized.

- In the Results section, there may in fact be too much detail regarding the structural model assessment—for example, there is no need to explain what each of the parameters mean/represent.

*Response:* This has been addressed in the revised manuscript; details on the standardized root mean square residual, acceptable loadings, and average variance extracted has been removed.

- P* values should be reported as exact numbers (ie, to 3 decimal points), and *P* values of *P*=.000 should be reported as *P*<.001.

*Response:* As per the guidance provided by JMIR [3], the *P* values are expressed to two digits and three digits for *P*>.001.

## Reviewer CJ [4]

### Major Comments

However, I do not like the fact that many different models are mentioned in the Introduction and that these models are not mentioned further on. These parts could be shortened, and the paper would certainly benefit from this. I found the subdivision of the Introduction into many subunits disruptive as well. There is no common thread to the Introduction. Please try to create a better text flow.

*Response:* The section on the RNR and readiness for treatment has been removed with more contextualized information on PD provided instead. We hope this has helped with the text flow and reduced the number of subsections in the Introduction.

1. A distinction between the different PDs would be appropriate, as the risk for offending is not the same for all PDs.

*Response:* This has been addressed in the revised manuscript at the start of the Introduction; differing PD types are discussed and defined.

2. Additionally, please give some more information about PDs in general.

*Response:* This has been addressed in the revised manuscript at the start of the Introduction.

3. “The OPD pathway is informed from the “What Works?” literature [5], the RNR principles [6] and the Good Lives Model (GLM; [7]. However, the RNR model been criticised for not providing clear guidance for therapists for engaging offenders lacking in treatment readiness [8]. The responsivity principle of the RNR model may not currently be effectively implemented in the OPD pathway and contributing to the problem of offenders being referred but not accepted to numerous OPD services.” Incorporating these resources adds no value in my opinion since there is no further information about these models.

*Response:* This has been addressed in the revised manuscript, and this section has been removed from the Introduction.

4. “Attitudes towards treatment”: Please specify possible outcomes in the description.

*Response:* Additional information about the possible outcomes that were measured in attitudes toward treatment is provided in the revised manuscript.

5. A descriptive visual representation of the analysis plan would be helpful.

*Response:* This has been developed and provided as Figure 2 in the manuscript.

6. Null hypothesis significance testing (NHST) needs hypotheses. If you use NHST (ie,  $\chi^2$  and  $t$  test) in part 1 of the analysis, you need to formulate hypotheses since blind testing always leads to results.

*Response:* The purpose of this analysis was to explore possible sources of sampling bias in the case-control matching procedure; therefore, it was by definition exploratory and inductive, and to suggest this was driven by hypotheses would be inaccurate. We would draw the editor’s attention to highly cited case-control work elsewhere (eg, [9]) as an indication of how this analysis is typically presented, noting that there is no reference to hypothesis testing.

7. No correction (such as Bonferroni) was made, despite multiple testing. This should be done. If one does not do this, it is fine because the main goal of the study was the model, but this needs to be addressed and reflected upon.

*Response:* A sentence regarding a significance threshold has been provided at the start of the Results section to address this.

8. Methodology and results flow into each other. Please find a way to separate this better. I would also like to see not only the inner model described in the methodology but also the outer model (eg, the factors of psychopathology).

*Response:* The comment regarding the methodology and results is too vague, and it is not clear what was wanted here, and therefore, no amendments have been made. The outer model has now been added to the supplementary materials and can be used to sense check—it is referred to in this way in the revised manuscript.

9. “The latent variables create the inner model and the variables were connected using clinical knowledge and theory (Figure 1).”

Please specify “clinical knowledge” and “theory.” This is quite speculative. In addition, Figure 1 would benefit from a more specific description.

*Response:* Further detail here has been added to expand upon the clinical knowledge and theory used. The Introduction to the paper is also regarded as the theory used.

10. “Second, the outer loadings within the SEM [structural equation modeling] model suggest that the single most influential factor was psychopathy or psychopathic disorder, which has long been acknowledged as a limiting factor for treatment and rehabilitation [10]. It could be argued that psychopathic offenders are not best served on a pathway that caters for offenders with personality disorder in the broader sense of the diagnosis as their needs are known to be different [11].”

Do you have a suggestion for these individuals?

*Response:* Additional information has been added to the manuscript regarding this that suggests a sustained focus on engagement and prosocial lifestyle changes, rather than on maladaptive personality traits.

11. Other limitations are that you specify a model a priori and that so many factors are used for such a complex phenomenon (with a quite limited sample).

*Response:* It was not clear what was wanted here, so no amendments in the revised manuscript have been made in relation to this.

12. In addition, one must see very critically that psychosis and PS are combined. The fact must be discussed as this is problematic, having a massive influence on therapy and behavior.

*Response:* It is not clear what “PS” is referring to.

13. Please consider dividing the Conclusions section into Future Perspectives and Conclusions sections, as this seems kind of inconsistent.

*Response:* A section on clinical and practical implications has been added into the Discussion; the final paragraph has been moved above the Conclusions and called Future Perspectives, and then the Conclusions section summarizes the paper.

#### Minor Comments

1. Please consider changing the title of the paper by omitting “PLS-SEM [partial least squares structural equation modeling] Path Analysis,” which is too technical in my opinion (or maybe do not use the abbreviation).

- Response:* We are happy to change the title of the paper if the editor feels it is necessary.
2. Please divide the sentence in the Results section of the Abstract into two sentences and thereby avoiding the semicolon.  
*Response:* Having two sentences does not make sense, but the sentence has been restructured.
  3. Please avoid the semicolons in the second paragraph and check the overall structure of the sentences (and use hyphens if appropriate). Check for missed words, sentence structure, and punctuation in the paper.  
*Response:* This has been addressed throughout the revised manuscript.
  4. Stay consistent when using abbreviations—do not alternate “PD” and “personality disorder.”  
*Response:* This has been addressed throughout the revised manuscript; all should now appear as personality disorder (abbreviation only in the short running title).
  5. Please define “NHS” (National Health Service) before using the abbreviation.  
*Response:* This has been addressed in the revised manuscript.
  6. I would like to read more about the “screening algorithm” and which PDs this algorithm screens for.  
*Response:* Further information about the screening algorithm has been provided in the Methods section.
  7. “However, several of us are clinicians working within the London Pathways Partnership (LPP), a consortium of NHS trusts delivering services within the OPD pathway, are aware of several individuals that no OPD service, in prison or the NHS, is prepared to accept.” Reformulate this sentence since it is not easily comprehensible.  
*Response:* This sentence has been rephrased in the revised manuscript.
  8. Omit % in the brackets in each row of the tables.  
*Response:* All % in the brackets have been removed from the tables.
  9. “Although the relationship between problematic custodial behaviour and service refusal was not strong, the results still emphasise that services aiming to support these individuals need be able to receive men with patterns of such behaviour and contain and manage ongoing episodes, without this resulting in treatment termination.” Please rephrase this, as it is a quite complicated sentence.  
*Response:* This sentence has been rephrased in the revised manuscript.

## References

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## Abbreviations

- GLM:** Good Lives Model  
**LPP:** London Pathways Partnership  
**NHS:** National Health Service  
**NHST:** null hypothesis significance testing

**OPD:** Offenders Personality Disorder  
**PD:** personality disorder  
**PLS-SEM:** partial least squares structural equation modeling  
**RNR:** risk needs responsivity  
**SEM:** structural equation modeling

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Authors' Response to Peer Reviews

# Authors' Responses to Peer Review of “Machine Learning and Medication Adherence: Scoping Review”

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*This is the authors' response to peer-review reports for the paper “Machine Learning and Medication Adherence: Scoping Review”.*

## Round 1 Review

**Reviewer F [1]****General Comments**

This paper [2] covers a very interesting area on the use of machine learning for assessment of medication adherence, yet in its current version, it does not add a lot to the field. It is a pity, as it seems that the authors performed their review well. However, the presentation of the results is not acceptable.

**Major Comments**

1. It creates a lot of confusion that the authors use “adherence” instead of “compliance.” In fact, these two are equivalent terms, of which adherence is preferred and compliance is a bit old-fashioned. The authors need to define the major concept they use, and these two need to be carefully checked against available literature and the ABC taxonomy.  
*Response:* Definition explained under the updated Methods Eligibility Criteria section.

This taxonomy defines medication adherence as “The process by which patients take their medications as prescribed, composed of initiation, implementation and discontinuation” [3].

2. The Abstract provides no numeric data; even the number of identified publications is missing. Similarly, the conclusions of the Abstract are inconclusive.  
*Response:* This point is addressed mostly in the updated Abstract and the updated Discussion/Conclusions section.
3. The authors mentioned previous reviews in this area, yet they did not make it clear what was different about their own work. What exactly was missing in the previous reviews that turned them toward this new exercise?  
*Response:* This is addressed under Introduction, paragraphs three and four.
4. Publication selection for review: What were the criteria used to identify acceptable papers in the full-text review? What was the reason for screening a sample of 20 papers first?  
*Response:* Updated the eligibility criteria and selection of sources of evidence sections to address this issue.
5. “Medication adherence activities” is not a term used in the literature to describe interventions aimed at assessment or modification of medication adherence. Please use another term that is used in the existing literature.

- Response:* I have determined that the creation of a new term is not necessary to explain my ideas in this part of the paper. I have changed medication adherence activities to verbs related to medication adherence. In this way, I can explain my idea without introducing new terminology that is potentially confusing for the reader. The changes are located in the analysis of natural categories paragraph and throughout the manuscript.
6. The paper is lacking a lot of details; for example, what was the basis for the dichotomization of the source databases into “biomedical” and “computer” in Figure 3?  
*Response:* This part of the analysis has been removed to reduce confusion and to allow more room for a figure depicting the article review process (Figure 1).
  7. In Tables 1-3, instead of simply providing the number of the reference, it is also advisable to have the first author’s name and the year of the publication.  
*Response:* I added the date of publication for all three tables. I have decided against adding the author’s name because I do not know what it would add to the publication, and it was not a part of the original data charting document. Additionally, the tables barely fit neatly on the page as is, making it very difficult to add any additional information.
  8. I have a feeling that the studies listed in Table 1, based on self-report and pharmacy claims data, do not “predict” adherence but rather assess it. Please correct me if I am wrong.  
*Response:* All of the studies listed in Table 1 use machine learning to actually predict medication adherence in the future. These predictions are made according to past patient information (age, sex, socioeconomic status, etc) and their level of medication adherence. Claims data from the past can be used in combination with personal information to build models that predict if a specific patient will be adherent to their medication in the future.
  9. The paper must be self-explanatory; therefore, abbreviations such as DOT need to be explained. When addressing a general audience, it makes sense to do the same with the abbreviations of algorithms cited within.  
*Response:* The paper has been reviewed to either eliminate or explain all abbreviations. However, some algorithms look like abbreviations but that is simply the name of the algorithm, so this may still be somewhat confusing. For example, J48 is the full name of an algorithm and is not an abbreviation.
  10. Numbers, numbers, numbers, please! The Results section reads, for example, “LEAP had the best prediction accuracy of the machine learning methods used”—by how much? Was the difference statistically significant?  
*Response:* I went through the paper and greatly increased the number of numbers and citations. This is particularly evident in the updated Abstract and the updated Discussion/Conclusions section. When different algorithms were used, I stated the prediction accuracy, as this was the most frequently reported metric. Most of the papers that I state the main results of did not specifically say if results were statistically significant or not so this was not added to the paper.
  11. Being a clinician, I feel that this might be information technology (IT) jargon: “The first of these articles used data collected during hospital stays to generate features” (from Results). However, please make sure that the text is also meaningful for non-IT people.  
*Response:* Feature and features are IT jargon. Features are variables selected from a data set for further analysis using machine learning techniques. I have changed all mentions of feature or features to predictor or predictors since this is a synonym that provides more insight for non-IT people.
  12. In light of previous publications in the field, the first sentence of the Discussion needs to be rechecked.  
*Response:* To my knowledge, this is the first scoping review to focus broadly on using machine learning for medication adherence activities. There are other reviews in this field, but they are typically much more narrowly focused, probably because they are systematic reviews and not scoping reviews.
  13. In the Discussion, the authors say “However, more work needs to be done to better understand the impact of socioeconomic status [on adherence].” In fact, a lot of work has been done in that area, and it would help the paper if authors would broaden their understanding of it.  
*Response:* I am not trying to say that there has not been a lot of work examining the impact of socioeconomic status on adherence. I am explaining that machine learning algorithms are not currently leveraging this information enough. This point has been clarified in the Discussion/Conclusions section, paragraph three.
  14. From the Discussion: “Some of these works compared the different types of algorithms to determine which was the most accurate...” Which ones? Please cite!  
*Response:* I see why this is confusing after reading your comment. The studies comparing algorithms are listed in the tables with a reference number, but it does not specify if the multiple algorithms listed indicate a comparison or if different algorithms in combination make a single prediction. This point has been clarified in the Discussion/Conclusions section.
  15. To conclude, it needs to be stressed that the authors should extract a lot more data and conclusions from the material they reviewed—instead of saying “some studies...,” please provide the numbers (eg, “over 40% of studies found the parameter to change by >90%”).  
*Response:* This point has been addressed in the updated Abstract and the updated Discussion/Conclusions section.

#### Reviewer BQ [4]

##### General Comments

This paper aims to categorize and summarize literature focused on using machine learning for medication compliance activities. There are major concerns associated with this paper.

##### Major Comments

1. The aim does not feel like an actual aim. I would suggest saying things like “aim to do a scoping review on... and categorize and summarize...”  
*Response:* The Introduction paragraphs three and four have been updated to address this point.

- You should state the design in the Methods. In addition, you should state clearly the inclusion and exclusion criteria. As of now, the inclusion and exclusion criteria are too broad to do a robust review.

*Response:* This is a scoping review, so the inclusion criteria are supposed to be more broad than a systematic review. I have added more detail in the eligibility criteria and selection of sources of evidence sections to address this issue.

- Is it adherence or compliance? The frequent change of terms makes it hard to understand what the authors want to do. They are very different fundamentally.

*Response:* Medication adherence is used throughout the manuscript to reduce confusion.

- Limitations should be before the Conclusion.

*Response:* The Limitations section was moved before the Discussion/Conclusions section.

- They lack Figure 1: the number of articles screened/reviewed.

*Response:* Figure 1 in the appendix was moved into the paper and explains the screening/review process in detail.

- Figure 2 is not right; there are many overlapping diseases in each category.

*Response:* Figure 2 was updated by grouping diseases instead of listing them separately.

- Short forms are not well explained or mentioned in the tables.

*Response:* Explanations have been added to explain short forms in the table. The explanations are mentioned throughout the manuscript when the abbreviated term first appears.

## Round 2 Review

### Reviewer F

#### Major Comments

- In the body of text, you refer to the help and advice provided by two librarians and two pharmacists, yet it seems to me that they are not included in the authorship nor thanked in the Acknowledgments. Please take care of solving this.

*Response:* In the Search Query section, I have added the names of the librarians that helped with query creation.

- Overall, the interesting work done in this exercise is not followed with a clear description. In fact, it is very hard to learn what exactly the use of machine learning was in the context of medication adherence or the outcomes of this process. These, however, were the major objectives of this paper. In such a case, the conclusion from the Abstract stating that “Machine learning has the potential to greatly improve medication adherence” seems to be unsupported by the data presented.

*Response:* I agree with this comment and have extensively reworked the Discussion and Conclusion sections to address this issue. Additionally, a column has been added to Tables 1-3 to provide the main outcome metric for each study. This addition of the outcome metric and further explanation of how the systems work have allowed me to provide more context on the current status of these systems and some

insight into their future potential. I also extensively reworked the Abstract to address this point.

#### Additional Suggestions

- Line 23: The number of identified studies belongs in the Results.

*Response:* The explanation of how studies were selected is located in the Selection of Sources of Evidence section per the recommendation of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) scoping review guidelines. I added a brief mention of the number of selected studies in the Results of Individual Sources of Evidence section as well.

- Line 26 onward: “Verb” is an uncommonly used term in this context; please search the literature to find a more frequently used equivalent.

*Response:* After talking this point over with the coauthors (MK and JM), we have decided to change the terms to either action or actions. We have determined that these terms are the most easily understood within this context.

- Line 29 onward: Using percentiles makes sense when the total number is  $\geq 100$ ; in this case, the number of identified publications was only 43; what justifies fractions and not the percentiles?

*Response:* Percentages were changed to fractions or individual numbers where appropriate throughout the Results sections.

- Lines 42-3: The Discussion is missing in the Abstract (what is provided now is not a real discussion of the findings).

*Response:* The Discussion has been extensively reworked to address this issue.

- Lines 92-3: The eligibility criteria need to be more detailed; it is unclear now what sort of relationship had to link the included publications with medication adherence, and what was the exclusion criteria?

*Response:* More detail has been added to the following sections to address this comment: Eligibility Criteria, Search Query, and Selection of Sources of Evidence.

- Line 134 refers to “predictors”—predictors of what?

*Response:* These are predictors of medication adherence. Medication adherence has been added here to clear up this confusion.

- Line 136-7: What do you mean by “The data collected for this study was qualitative and sometimes quantitative”? What does “sometimes” mean in this context?

*Response:* After discussion with one of the coauthors (MK), this sentence has been removed. He concluded correctly that I was simply talking about numerical and text data, which does not need to be mentioned specifically.

- Line 165 refers to “13 studies,” yet Figure 3 shows only 12 items in that category.

*Response:* I have corrected the number from 13 to 12 in the text.

- Tables 1-3 need serious improvement. Putting all the comments together in columns placed to the right makes no sense. No idea why “Some entries were excluded for brevity,” especially in cases of short algorithm acronyms. The footnote marked \*\* is not applicable to Table 2.



*Response:* For Table 1, the merged cells were removed to provide more specific detail from each study. The summarized findings are still presented later in the writing, so it does not need to be expressed twice. All algorithms were included in Table 1 to address this comment, and the \*\* footnote was removed from Tables 1 and 2.

- Table 1: I would love to see one more column describing what sort of adherence measure the machine learning algorithm was able to predict (eg, “filling the prescription” or “daily drug intake”).

*Response:* Removed the limitations column and replaced it with the adherence metric predicted column. The information in the Limitations section is stated later in writing, so it seemed redundant. I also agree that the adherence metric predict column provides readers with more insight about the individual studies in Table 1.

- Table 1: How did you identify the “strong predictors”? Has any statistical threshold been applied to this selection?

*Response:* Strong predictors were identified in the individual studies, and this process varies depending on the methods used in each study. Typically, the strongest predictors are chosen by adding and or removing variables from the prediction algorithm until the highest prediction accuracy was achieved. However, this has to be balanced against overfitting, which is when the algorithm is trained too closely to the test data and performs very poorly when tested using a new data set. Often algorithms become overfit when too many predictor variables are included. Certain algorithms can also provide a strength metric for every variable allowing easy comparison of the strength of each predictor. Some studies did mention the statistical significance of specific predictors, but this was not common. I have added a footnote to Table 1 that states that predictor strength was based on individual study results to clarify that this study did not determine the strength of different predictors.

- Table 2: I would love to see one more column describing what sort of adherence measure the machine learning algorithm was able to identify. For example, there are plenty of studies using smart pill bottles—so what exactly was the role of machine learning in [5] for it to be included in this review and not to include other studies?

*Response:* For Table 2, the limitations column was removed and replaced with a new column describing how medication adherence was being monitored in each study. These studies were often very fundamental, so often they are being conducted to determine if the technology can differentiate between medication-taking actions or other unrelated behaviors. This new column is titled data analyzed using machine learning to determine adherence. For [5], they are using movement sensors in addition to the traditional cap sensor used in many adherence studies in the past. This is a potential stepping-stone toward monitoring medication adherence with devices that people wear in their everyday lives like a smartwatch. The movement sensors are providing movement data similar to a smartwatch but also provide cap sensor data, which is more reliable at this time for determining medication ingestion. This information can be used together to determine when the movement data

alone is actually able to accurately report medication ingestion.

- Table 3: Same as above, plus which aspect of adherence was improved—the one that was tested; the other one?

*Response:* I agree that the title of the table is confusing and have changed it to summary of studies that monitor and attempt to improve medication adherence. These studies all introduce some type of intervention to hopefully improve medication adherence but did not necessarily accomplish their goal. Like Table 2, I have removed the limitations column and replaced it with a column titled data analyzed using machine learning to determine adherence. I believe that this new column provides a lot of useful information that makes understanding the purpose of each study much easier.

- Line 210, 213: Correct “99 DOTS” to “99DOTS.”

*Response:* I have corrected to 99DOTS.

- Line 221, 222: “The next paper used face recognition software and computer vision to monitor medication adherence”—which aspect of medication adherence are you considering here?

*Response:* I have added more detail to this part of the paper to make it more clear. This study used machine learning to monitor medication adherence for clinical trials and to predict which patients were not likely to be adherent over the duration of the study. This system also provided reminders to patients to help maintain or improve their adherence.

- Line 241-2: “These assessments were then used to create predictors”—predictors of what? I guess not of medication adherence, if you say that medication adherence was a...predictor!

*Response:* One of the strongest predictors of future medication adherence in this study was medication adherence of the same patient in the past. I have added the words past and future to make this distinction more clear.

- Line 247-50: Usually, limitations are provided at the end of the Discussion.

*Response:* I agree with this point and have moved the Limitations after the Discussion and Conclusions.

- Line 285-6 states: “Approximately 87% of these studies used either logistic regression, artificial neural networks, support vector machines, or random forest algorithms.” Why is this not visible in Table 1?

*Response:* This is portrayed in Table 1 but not in the form of a summarized percentage. If you add up the number of studies that are using at least one of these algorithms and then divide this by the total number of studies in this group, you get 87%. It would be difficult to put this on the table in a way that is easily understandable, which is why I stated it in the text.

- Lines 282 and 342 still use the term “compliance” instead of “adherence.”

*Response:* I have corrected these terms from compliance to adherence.

- Lines 288-291: You provide comparisons of the accuracy of diverse algorithms yet without any statistical significance values. That sort of simple comparison is not inconclusive.

*Response:* In the Discussion and Conclusions section, I acknowledge that no meaningful conclusions can be drawn from these comparisons. I only included this part in the paper because someone that I presented my work to previously asked if any of the studies compared the accuracy of different algorithms. Some of the studies did do this, so I thought I should briefly mention it to show that not much work has been accomplished yet on this front.

### Reviewer BQ

I am appreciative that the author was willing to do the changes, and the manuscript has improved.

Although this is a scoping review, I would like to find out how the author ensured robustness and reproducibility. As of now,

with the study design largely using one author, there is no way to assess if the paper selection is robust or independent. I strongly feel that there is a need for 2 authors to independently select studies, even though it is a scoping review, to give this review some robustness. If not, how different will the results be compared to a narrative review?

*Response:* This study was created using the insight of multiple people and I have added a lot of detail to better illustrate their role in creating this work throughout the Methods section. Additionally, I have added another coauthor that independently repeated the title/abstract and full-text reviews. They also evaluated the grouping of studies to increase the robustness of the review.

### References

1. Kardas P. Peer review of "Machine Learning and Medication Adherence: Scoping Review". JMIRx Med 2021;2(4):e33965 [FREE Full text]
2. Bohlmann A, Mostafa J, Kumar M. Machine learning and medication adherence: scoping review. JMIRx Med 2021;2(4):e26993 [FREE Full text]
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### Abbreviations

**IT:** information technology

**PRISMA:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses

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Authors' Response to Peer Reviews

# Author's Response to Peer Reviews of "Comparison Between Male and Female Survivors of Sexual Abuse and Assault in Relation to Age at Admission to Therapy, Age of Onset, and Age at Last Sexual Assault: Retrospective Observational Study"

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**KEYWORDS**

sexual abuse; sexual assault; age of onset; sex; gender; age; therapy; abuse; assault; mental health; victim; childhood; children; gender disparity; violence

*This is the author's response to peer-review reports for "Comparison Between Male and Female Survivors of Sexual Abuse and Assault in Relation to Age at Admission to Therapy, Age of Onset, and Age at Last Sexual Assault: Retrospective Observational Study."*

## Round 1 Review

**Major Comments**

1. Corrected [1]. The sections have been switched around [2] and the bullet format was changed to paragraphs.
2. More texts and references to previous studies were added where applicable.

3. A statistical metric (Pearson  $r$ ) was reported where a linear relationship was mentioned.

**Minor Comments**

1. Both are corrected.
2. I shall consider bootstrapping methods in future submissions where applicable.

Finally, a comment to the editor: I used Mendeley's AMA 11th edition style.

Thank you so much for the reviewer's work and your diligence.

**References**

1. Laiou P. Peer review of “Comparison between male and female survivors of sexual abuse and assault in relation to age at admission to therapy, age of onset, and age at last sexual assault: retrospective observational study”. JMIRx Med 2021;2(4):e34623 [[FREE Full text](#)] [doi: [10.2196/34623](https://doi.org/10.2196/34623)]
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Authors' Response to Peer Reviews

# Author's Responses to Peer Reviews of "Medical Brain Drain From Southeastern Europe: Using Digital Demography to Forecast Health Worker Emigration"

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**KEYWORDS**

digital demography; Google Trends; the emigration of doctors and nurses; medical brain drain; Croatia; demography; brain drain; emigration; doctors; nurses; health care workers; health professionals; health systems; jobs; Germany; personnel; migration; workforce; medical professionals

*This is the author's response to peer-review reports for "Medical Brain Drain From Southeastern Europe: Using Digital Demography to Forecast Health Worker Emigration."*

## Round 1 Review

**General**

The paper [1] is shortened.

I deleted the parts:

- Section Consequences of Emigration on the Ageing Population of Croatia, Serbia, and Bosnia and Herzegovina (B&H)
- Data on students for Serbia and B&H
- Tables 1 and 5
- I deleted 3000 words and added 3200 new words according to suggestions of reviewers
- Inserted data on visas for Serbia and B&H
- Modified graphs: new tests

The Abstract is structured.

References are cleaned up.

More scholarly references are cited: more pertinent/related articles published in JMIR journals and elsewhere in the past 2 to 3 years.

New references added:

- Britnell M. Human: Solving the Global Workforce Crisis in Healthcare. Oxford, England: Oxford University Press 2019:19-20.
- Mara I. Doctors on the move: mobility patterns in the EU. Wiiw Monthly Report 2019;7-8:16-22.
- Tackling brain drain requires joint efforts to improve the quality of life in all EU regions. European Committee of the Regions. URL: <https://cor.europa.eu/en/news/Pages/tackling-brain-drain.aspx> [accessed 2021-07-17]
- Recent trends in international migration of doctors, nurses and medical students. OECD iLibrary. 2019. URL: <https://doi.org/10.1787/5571ef48-en> [accessed 2021-04-04]

- Stonawski M, Sabourin P, Bélanger A, Loichinger E, Marois G, Ghio D, et al. Demographic Scenarios for the EU: Migration, Population and Education. Luxembourg: Publications Office of the European Union; 2019:6398.
- Knez R, Martić Biocina S, Starčević B, Moravek D, Musović M, Sarajlić Vuković I, et al. Migration of Croatian physicians in the global context. *Medicina Fluminensis* 2020 Jun 01;56(2):88-96. [doi: 10.21860/medflum2020\_237296]

### Reviewer A [2]

- I have now elaborated on the part related to digital traces used as an indicator of migration before.

“I have concerns that some of the Google terms used indicate wider emigration rather than health worker migration.”

I harmonized the text so that it does not talk about migrations in general but only about migrations of medical staff. In this regard, I had to make new calculations and graphs:

- Figure 5. Correlation between Google search index for query “posao u Njemačkoj + medicinska sestra” (work in Germany + nurses) in Croatia and the Organisation for Economic Co-operation and Development (OECD) statistics for emigrated nurses from Croatia to Germany (annual inflow)
- Graph 5 shows that the increase in Google search for the query “posao u Njemačkoj + medicinska sestra” (work in Germany + nurses) correlates with the increase of emigrated nurses to Germany. In the following, we show that the verification can also be performed in the opposite (ie, from Croatia in German), which again gives reliable estimates.
- Figure 6. Correlation between Google Search index for query “Arbeit in Deutschland + Arzt” (work in Germany + doctor) in German in Croatia and the OECD statistics for emigrated doctors from Croatia to Germany. This example shows that in the case of emigration of doctors, the increase in the Google search query “Arbeit in Deutschland + Arzt” (work in Germany + doctor) is in correlation with the increase of emigrated doctors to Germany.
- Figure 7. Correlation between Google Search index for query “Arbeit in Deutschland + Arzt” (work in Germany + doctor) in B&H and the OECD statistics for emigrated doctors from B&H to Germany (annual inflow).
- In the case of B&H, we calculated the annual inflow of Bosnian doctors to Germany and compared these data with the Google Trends (GT) index. As in the case of Croatia, there is a positive correlation.
- Figure 8. Correlation between Google Search index for query “Arbeit in Deutschland + Arzt” (work in Germany + doctor) in Serbia and the OECD statistics for emigrated doctors from Serbia to Germany.
- Also, in the case of Serbia, the increase in Google search for the query “posao u Nemačkoj + Doktor” (work in Germany + doctor) is correlated with the increase of emigrated doctors to Germany. There is a positive linear association between the Google index and data from official statistics (OECD).
- All tested migration-related search queries that show an indication about HWs’ (HWs) emigration planning shows

a positive linear association between Google index and data from official statistics (OECD): Serbia:  $R^2=0.3381$ ; B&H:  $R^2=0.2722$ ; Croatia:  $R^2=0.4515$ . The increase in Google Search is correlated with the increase in the number of emigrated HWs from Croatia, Serbia, and B&H. The decrease in Google Search is correlated with the decrease in the emigration of HW.

- Reference added: Humphries N, Connell J, Negin J, Buchan J. Tracking the leavers: towards a better understanding of doctor migration from Ireland to Australia 2008-2018. *Hum Resour Health* 2019 May 28;17(1):36 [doi: 10.1186/s12960-019-0365-5] [Medline: 31138211]

“It would greatly strengthen your paper if you had stronger secondary/official data on the migration of nurses/doctors from Croatia/B&H/Serbia to Germany/Austria.”

I funded the data and entered it into the text.

“Can you get data on the number of Bosnian/Serbian citizens who have obtained visas to work in Germany/Austria?”

I funded the data and entered it into the text:

Table 3. Doctors in Germany from Serbia, Croatia and B&H, OECD, 2021.

- Year: 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017, 2018, 2019
- B&H: 118, 150, 165, 202, 236, 270, 327, 397, 470, 505
- Annual inflow: 32, 15, 37, 34, 34, 57, 70, 73, 35
- Serbia: 246, 292, 381, 501, 648, 826, 1026, 1236, 1364, 1504
- Annual inflow: 46, 89, 120, 147, 178, 300, 210, 128, 140
- Croatia: 137, 158, 175, 196, 254, 295, 341, 380, 412, 428
- Annual inflow: 21, 16, 21, 63, 57, 48, 46, 42, 26

“The Introduction jumps around between source and destination countries. I would suggest that the paper discusses source countries and destination countries separately.”

I did so and better structured the whole paper.

“The pandemic as a push factor is really interesting and an important issue to raise.”

Thanks for the suggestion. I emphasized that part.

“Why use the term Western Balkan if it does not include Croatia? Better to use the countries that you’re talking about (ie, Croatia, Bosnia and Herzegovina, and Serbia).”

This term is important because research on this topic is generally neglected. In this paper, I focus not only on these countries but also on the wider area of Southeast Europe.

“I think that the World Health Organization (WHO) Global Code on the International Recruitment of Health Personnel (2010), which is mentioned on page 11, should be more central to the paper.”

Thanks for the suggestion. I emphasized that part.

“Perhaps the paper also needs to mention the WHO 2006 list or the WHO 2020 safeguard list, which lists countries with critical health care shortages.”

Thanks for the suggestion. I emphasized that part.

“In relation to Europe, the paper should connect back to the European Observatory books on HW migration.”

Thank you. I did so.

“In the Introduction, the paper should also connect with the wider literature on brain drain/health worker migration.”

Thank you. I did so.

### Reviewer E [3]

“The paper shows a disproportion between the cited references and those in the bibliography.”

Now everything is aligned.

## Round 2 Review

### Reviewer A

1. Perhaps the title should read: Medical Brain Drain From Southeastern Europe: Using Digital Demography to Forecast Health Worker Emigration.

I agree.

2. You need to be consistent in the terms used throughout the paper (title/abstract/main text).

The new term is “Croatia and the Western Balkans (WB).”

“In displaying numbers/percentages use either decimals (60.09% or 60,09%) or commas in figures, not both.”

Ok.

3. Measuring health worker mobility is a challenge for most countries (not just Croatia, Bosnia, and Serbia), which is why registration and/or visa data from the destination country is often used as a measure of health worker emigration.

I emphasized this.

4. On page 4, you say that 65,288 nurses emigrated, and I think you’re saying that there are more Croatian/Bosnian nurses in Germany than in Croatia and Bosnia; are you? Perhaps tighten up this sentence as it’s a strong statement.

When we put these data on 65,288 emigrated HW from this region in context, we can see that this is a higher number than the total number of nurses in Croatia and B&H together. Without such intense emigration in the last 10 years, the regions of Croatia and the WB would have 50% more health workforce today. It is necessary to emphasize that this staff is crucial in the fight against a pandemic.

5. On page 7, the paragraph beginning in Austria is unclear. Rewrite these sentences.

Corrected

6. In Table 3, perhaps mark the stock data versus the flow data (ie, differentiate between the overall number of nurses in Germany [stock] vs the number of nurses entering Germany [flow]).

Corrected:

Table 3. Doctors in Germany from Serbia, Croatia, and B&H, OECD, 2021.

- Year: 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017, 2018, 2019
- Overall number of doctors from B&H in Germany: 118, 150, 165, 202, 236, 270, 327, 397, 470, 505
- Annual inflow from B&H: 32, 15, 37, 34, 34, 57, 70, 73, 35
- Overall number of doctors from Serbia in Germany: 246, 292, 381, 501, 648, 826, 1026, 1236, 1364, 1504
- Annual inflow from Serbia: 46, 89, 120, 147, 178, 300, 210, 128, 140
- Overall number of doctors from Croatia in Germany: 137, 158, 175, 196, 254, 295, 341, 380, 412, 428
- Annual inflow from Croatia: 21, 16, 21, 63, 57, 48, 46, 42, 26

7. On page 11, the section beginning what could the European Union do to address the problem, I think this should be moved out of the Introduction and into the Discussion.

I did so.

8. I think you could bring one or two issues out in the Discussion that you’ve mentioned in the text already but could make more of:

- The issue of the European Union drawing health workers from EU countries (Croatia) and nearby countries (Bosnia, Serbia) is an important issue to raise in the Discussion, as it is a clash between free movement (EU free movement) and the right to health care/need to ensure a health workforce in all regions (as per the WHO Global Code and/or the UN Sustainable Development Goals).
- I think that this method is a really interesting way of generating timely data on health worker migration. During the pandemic, the *normal* ways of data collection are simply too slow (particularly when EU countries are fast tracking health workers into the European Union). Your method is a really good way of generating timely insights into *intent to migrate* among health workers. As you mention in your paper, this should be useful for policy makers (but obviously only if they respond/react to the data). And then the next question for policy makers is how can they retain health workers during a pandemic? Increased salaries? Improved working conditions? Which links nicely to the section on what the European Union can do.

New Discussion added:

From 2010 to 2020 from the regions of Croatia and the WB emigrated 65,288 HW. Without such intense emigration in the last 10 years, the regions of Croatia and the WB would have 50% more health workforce today. It is necessary to emphasize that this staff is crucial in the fight against a pandemic.

During the pandemic, the “normal” ways of data collection are simply too slow (particularly when EU countries are fast tracking health workers into the European Union). The presented method here showed a way of generating timely insights into intent to migrate among health workers. All tested migration-related search queries that show an indication about

HWs' emigration planning shows a positive linear association between Google index and data from official statistics (OECD): Serbia:  $R^2=0.3381$ ; B&H:  $R^2=0.2722$ ; Croatia:  $R^2=0.4515$ . The increase in Google search is correlated with the increase in the number of emigrated HW from Croatia, Serbia, and B&H. The decrease in Google search is correlated with the decrease in the emigration of HW.

The presented method contributes in a way that proves the feasibility of predicting further migrations from Croatia, Serbia, and B&H in this specific case of HWs to Germany and Austria, which allows reliable forecasts for the future. This procedure also presents a new methodological approach to how data obtained through GT can be standardized for comparison with official databases.

The insights are particularly relevant for national and EU policy makers and can help design appropriate strategies to retain HWs. The method can enable state agencies and the government to prepare and better respond to the shortage of HW in the future and protect the functioning of the health system. Regarding the WHO report about countries with critical health workforce shortages, this paper highlights that these issues are also relevant in European countries and that the list should be updated to include the countries B&H, Serbia, and Croatia. In addition, it is emphasized that the concept of sustainability of health care systems in the European Union is unsustainable if high-income countries do not train and retain sufficient health workers to meet the need.

While this mobility is beneficial for receiving states and contributes to a well-functioning monetary union, it negatively affects the sending countries, resulting in a *brain drain* and an erosion of public finances [4]. The issue of the European Union drawing HW from the EU periphery (Croatia) and nearby countries (B&H, Serbia) clearly shows a clash between the EU free movement and the right to health care and a need to ensure a health workforce in all European regions (as per the WHO Global Code and the UN Sustainable Development Goals).

This method could be useful for policy makers, but only if they respond and react to the data. Important question for policy makers is how they can retain health workers during a pandemic. Increased salaries and improved working conditions is certainly a good way. What precisely could the European Union do to address this problem? One approach would be to strengthen fiscal transfers to the member states and countries of the European periphery that are most affected by the harmful effects of freedom of movement [5]. However, fiscal transfers can never fully compensate for the loss of population. For example, financial compensation cannot fully compensate the departure of a nurse who left a Croatian hospital and now works in Germany—until a Croatian hospital finds a replacement. Otherwise, the specific hospital will still lack a nurse, which is reflected in Croatia's general quality of health care. That is why we proposed a compensation solution so that Germany funds centers of excellence for the education of nurses in Croatia and the WB, provided that they remain to work in their homeland for 5 years after completing their education. In this context, it is undoubtedly to welcome the appeal of the WHO that calls on high-income countries to strive for self-sufficiency through educating, retaining, and sustaining enough doctors and nurses to staff their health care systems [6].

In a situation where there is only freedom of movement of workers but not a common pension and health care system in the European Union, or a guaranteed minimum wage, nothing significant will change at the EU level. This means that the EU framework remains a structure in which the wealthy members will continue to become richer and the poor members increasingly poorer, which also applies to the whole European periphery. Moreover, with the onset of the pandemic, the situation worsened.

Without systemic regulation of this issue at the EU level, such trends of the emigration of HWs will threaten the national health system's capacity to respond to the needs of an ageing population and possible new waves of the pandemic.

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## Abbreviations

**B&H:** Bosnia and Herzegovina  
**GT:** Google Trends  
**HW:** health care worker



**OECD:** Organisation for Economic Co-operation and Development

**WB:** Western Balkans

**WHO:** World Health Organization

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Authors' Response to Peer Reviews

# Authors' Responses to Peer Review of “Influence of the COVID-19 Lockdown on the Physical and Psychosocial Well-being and Work Productivity of Remote Workers: Cross-sectional Correlational Study”

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*This is the authors' response to peer-review reports for the paper “Influence of the COVID-19 Lockdown on the Physical and Psychosocial Well-being and Work Productivity of Remote Workers: Cross-sectional Correlational Study”.*

## Round 1 Review

**Anonymous**

We are thankful to the reviewer [1] for the helpful suggestions regarding background literature. The first study is now mentioned in the first paragraph of the *Introduction* [2], in the context of income loss as a result of lockdown restrictions. The second study is now discussed in the first paragraph of the *Implications* section, in the context of a return to office-based work and contingencies that employers can implement to improve the psychophysical well-being of their workers.

**Reviewer AB**

1. We are grateful to the reviewer [3] for the positive review of our manuscript.
2. We agree! Indeed, there is some scope within our project to track down a few of our respondents to assess changes in their psychophysical well-being and work productivity since their first survey response, particularly now that the United Kingdom appears set to begin lifting most lockdown restrictions and to rescind the recommendation that people work from home where possible. We will consider the possibility and produce a follow-up study should this prove feasible (eg, sufficient sample size).

**Further Amendments**

In addition to addressing the reviewers' comments, we have taken heed of the editorial recommendations and implemented the following changes:

- Ensured the structured abstract has the recommended section headings.
- Ensured the major headings follow the IMRD schema.
- Ensured the major headings and subheadings follow the Microsoft Word style guidelines.
- Amended Table 3 as per the caption to ensure a good portrait fit.
- Changed all in-text citations from a superscript format to an [n] format.

We believe these changes have resulted in an improved revised manuscript, and we hope you will find they have been addressed satisfactorily.

We look forward to receiving an outcome regarding the publication of our manuscript in JMIRx Med.

## References

1. Anonymous. Peer review of "Influence of the COVID-19 Lockdown on the Physical and Psychosocial Well-being and Work Productivity of Remote Workers: Cross-sectional Correlational Study". JMIRx Med 2021 [[FREE Full text](#)] [doi: [10.2196/34607](https://doi.org/10.2196/34607)]
2. Tronco HYA, Parente F, Faghy MA, Roscoe CMP, Maratos FA. Influence of the COVID-19 lockdown on the physical and psychosocial well-being and work productivity of remote workers: cross-sectional correlational study. JMIRx Med 2021 [[FREE Full text](#)] [doi: [10.2196/30708](https://doi.org/10.2196/30708)]
3. Taraboanta L. Peer review of "Influence of the COVID-19 Lockdown on the Physical and Psychosocial Well-being and Work Productivity of Remote Workers: Cross-sectional Correlational Study". JMIRx 2021 [[FREE Full text](#)] [doi: [10.2196/34608](https://doi.org/10.2196/34608)]

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Authors' Response to Peer Reviews

# Authors' Response to Peer Reviews of "Information Technology Ambidexterity, Digital Dynamic Capability, and Knowledge Processes as Enablers of Patient Agility: Empirical Study"

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(*JMIRx Med* 2021;2(4):e34106) doi:[10.2196/34106](https://doi.org/10.2196/34106)

**KEYWORDS**

IT ambidexterity; dynamic capabilities; digital dynamic capability; knowledge processes; patient agility; hospitals; information sciences; information technology; digital health; health care; digital transformation; research models

*This is the authors' response to peer-review reports for "Information Technology Ambidexterity, Digital Dynamic Capability, and Knowledge Processes as Enablers of Patient Agility: Empirical Study"*

## Round 1 Review

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Comments and Responses by the Authors [1]

**Reviewer AE**

1. Methods
  - a. Describe the study [1] settings
  - b. Move the highlighted (in the reviewed manuscript) content under Data Collection Procedures to a new subsection under subsection heading Study Population (see comments in the reviewed manuscript)
  - c. The highlighted content should be under a new subsection heading Study Design
  - d. Provide content on another two subsection headings:
    - i. Sampling Techniques
    - ii. Sample Size
  - e. Separate content under Data Collection Procedure into two new subsection headings
    - i. Data Collection Tool and Procedure
    - ii. Data Analysis and Management
  - f. Move Table 1 to Analyses & Results section
  - g. Provide content under two new subsection headings:
    - i. Inclusion and Exclusion Criteria
    - ii. Ethics Considerations

Authors: The sections mentioned in this review [2] are essential, and therefore, we added them to the article's Methods section. Concerning Ethics Consideration, respondents were allowed to complete the survey anonymously, and we did not log anything in the survey system that could trace respondents. Also, reusable personal data was not requested, and the survey did not include questions about personal or sensitive topics. Furthermore, before starting the survey, the respondents had to sign a consent form. This approach is in line with the General Data Protection Regulation. Finally, respondents were given the option to leave their email addresses to receive a research report. These email addresses were removed from the data set after this report was sent.

Inclusion and exclusion criteria were combined with sample size, as we described how we got the final sample and why we included respondents (and why not).

### Minor Comments

1. Abstract
  - a. Do not begin a sentence with abbreviation of figure
  - b. Use past tense under Methods (eg, consider 'used' in lieu of 'uses')
  - c. See comments in the reviewed manuscript
2. Introduction
  - a. Use physicians in lieu of doctors
  - b. Use health care providers not other medical professionals
  - c. Keep in-text citation to the end of sentence
  - d. Add health information management professionals among the key stakeholders
  - e. Consider reducing the whole of section 2 (Theoretical Background) to 1-2 paragraphs and keep it within the Introduction section just before your study objective. This is to reduce readers' boredom.
  - f. Compress the content under research models and hypotheses
3. Results
  - a. Make your findings more visible here
  - b. Make your writing more readable to known and unknown readers
4. Discussion

- a. Plausible and insightful discussion but not a reflection of the content under the Results. Make the Results section more readable and meaningful to your audience.
5. Figure
  - a. Use Fig not Figure
6. Acknowledgement
  - a. It is scientifically necessary that you acknowledge the numerous (n=107) participants, who are the major stakeholders in your research.
7. Reference
  - a. List at least 3 authors before et al
  - b. Follow the Referencing Style consistently
8. Others
  - a. Use participants not respondents

Authors: We adjusted this accordingly.

### Reviewer AO

#### General Comments

Thank you for the opportunity to review this paper on the lesser known topic of information and communications technology ambidexterity. The paper is well cited, uses appropriate methods, and discusses the concepts and findings in a clear and thorough manner. The paper should appeal to a broad audience. It is a good example of the underrepresented information and communications technology-centered literature in health care.

Authors: We would like to thank this reviewer for these kind words [3]. We hope that we can make a great contribution to this journal and the field.

### Reviewer BQ

#### General Comments

Well thought out study design with specific hypotheses and methods of analysis spelled out. Interesting conclusions drawn out that would be fruitful for further discussion and analysis to replicate on a broader sample of hospital systems outside of the current reviewed sites.

Authors: We would also like to thank this reviewer for these kind words [4]. We agree that there could be a very interesting follow-up study.

### References

1. van de Wetering R, Versendaal J. Information technology ambidexterity, digital dynamic capability, and knowledge processes as enablers of patient agility: empirical study. *JMIRx Med* 2021;2(4):e32336 [FREE Full text] [doi: [10.2196/32336](https://doi.org/10.2196/32336)]
2. Adeleke IT. Peer review of "Information technology ambidexterity, digital dynamic capability, and knowledge processes as enablers of patient agility: empirical study". *JMIRx Med* 2021;2(4):e34107 [FREE Full text] [doi: [10.2196/34107](https://doi.org/10.2196/34107)]
3. Walsh J. Peer review of "Information technology ambidexterity, digital dynamic capability, and knowledge processes as enablers of patient agility: empirical study". *JMIRx Med* 2021;2(4):e34110 [FREE Full text] [doi: [10.2196/34110](https://doi.org/10.2196/34110)]
4. Taraboanta L. Peer review of "Information technology ambidexterity, digital dynamic capability, and knowledge processes as enablers of patient agility: empirical study". *JMIRx Med* 2021;2(4):e34113 [FREE Full text] [doi: [10.2196/34113](https://doi.org/10.2196/34113)]

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Authors' Response to Peer Reviews

# Authors' Response to Peer Reviews of “COVID-19 Outcomes and Genomic Characterization of SARS-CoV-2 Isolated From Veterans in New England States: Retrospective Analysis”

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**KEYWORDS**

infectious disease; COVID-19; epidemiology; veteran; outcome; sequencing; genetics; virus; United States; impact; testing; severity; mortality; cohort

*This is the authors' response to peer-review reports for “COVID-19 Outcomes and Genomic Characterization of SARS-CoV-2 Isolated From Veterans in New England States: Retrospective Analysis.”*

## Round 1 Review

**Reviewer W [1]****General Comments**

The sudden menace imposed by the COVID-19 pandemic has led to the proliferation of studies on the epidemiology of viral

genomics, specifically to understand disease risk factors, characteristics, and prognosis of those with COVID-19 [2-4]. Between 20% to 40% of COVID-19 admissions are reported to require intensive care [5], and have a fatality rate of 35% to 50% [6]. Many factors have been reported to either account for or to be associated with the clinical characteristics and prognosis of patients with COVID-19 [7-9]. Given that the aforementioned body of knowledge among veterans in New England is currently limited, the authors of the paper titled “COVID-19 Outcomes and Genomic Characterization of SARS-CoV-2 Isolated From Veterans in New England States” [10] investigated the patient

characteristics, comorbidities, and disease predictors in a cohort of 426 veterans hospitalized for COVID-19. They found using a multivariate regression that age was the most significant predictor of being hospitalized, the severity of disease, and mortality; being non-White was more associated with being hospitalized; and those in need of oxygen upon admission were more likely to die.

Even though widely reported, genomic epidemiology remains a rapidly growing domain in virology [11]. Besides, the diversity of the four coronavirus genera (alpha, beta, gamma, and delta) [12] and the emergence and spreading of the B.1.1.7 variant from the United Kingdom, B.1.1.28 from Brazil, and B.1.351 from South Africa [13] warrant constant new data and knowledge translation. To this effect, this paper addresses a major area of concern and interest to the readership of the journal. The authors are clear in their title, which still needs to fully comply with the journal guidelines. The Abstract follows the guidelines and presents an overview of the study. Being an area that has received tremendous interest since the start of the COVID-19 pandemic, there was an overriding need for this study to be put in context. The paper's introduction does well, ends with the study aim, and is brief at highlighting the main concern but deserves more attention. The general structure of the paper needs improvement to comply with the journal guidelines. The data collection methods, albeit needing clarification, seem reasonable with appropriate analysis, thereby giving value to the results. The discussion of the paper has been well articulated, and the conclusion ties with the research objective. The English used is simple and in plain language for easy comprehension.

Although congratulating the authors for a good attempt and concise paper, the paper will benefit from more value if the following specific comments are given consideration.

Response: We thank the reviewer for the careful review of this paper and the summary. Their feedback has certainly improved this manuscript. Our response to each comment is in the following sections.

### **Specific Comments**

1. The general structure of the paper needs to conform to the journal guidelines.

Response: We have reformatted the paper to conform to journal guidelines.

2. The paper deserves to be put in context to be more appealing.

Response: We have added more context throughout the paper to achieve this. The main areas where this is reflected now are in the Study Rationale subsection (Introduction) and throughout the Results and Discussion sections.

3. The introduction appears too restrictive and could be made more robust.

Response: We thank the reviewer for this suggestion. This has been done now.

4. The methods and reported results warrant the use of appropriate guidelines.

Response: This has been done now.

5. All tables and figures need to be formatted following the guidelines.

Response: This has been done now.

6. Your references need slight improvement, in line with the guidelines.

Response: We have reformatted based on journal guidelines and have also added relevant references based on reviewer suggestions.

To elucidate the aforementioned specific comments, kindly refer to the major and minor comments.

### **Major Comments**

1. Kindly format your title following the guidelines [14]. Your title should normally end with a study design after a semicolon.

Response: We have edited our title to be: "COVID-19 Outcomes and Genomic Characterization of SARS-CoV-2 Isolated From Veterans in New England States: A Retrospective Analysis."

2. The methods subsection of the Abstract needs to summarize the study design; total sample, setting, and recruitment; mean age and gender differences; end points measured; data collection procedure; and data analysis. You may want to change the subtitle from "Study Design" to "Methods."

Response: Thank you. We have modified the Abstract to provide age and gender differences in the target population as well as the actual subject population. Subsections have been added to the Abstract as suggested.

3. Kindly use the following template to give your paper an overall structure that complies with the journal guidelines [15].

Response: We have formatted our manuscript according to the template provided.

4. Given the high amount of reported literature in this field, I suggest putting your study in context [2]. Kindly search the Cochrane and Pubmed databases to:

- 1) Summarize the evidence already reported on the topic
- 2) Report why this study was necessary and the value added to the existing literature
- 3) The implication of all available evidence (including that from this study)

Response: We thank the reviewer for this comment. It has certainly made our Introduction section stronger. We have added references and language on the implication and relevance of evidence in this area of work in the field of COVID-19. Please see our full introduction for the additions and modifications, pages 2-3, lines 60-98.

5. It will be good to structure your Introduction into Background, Study Rationale, and Study Aim.

Response: We have added these subheadings to our Introduction section.



6. Kindly structure your Methods section and report it as follows:

- 1) Specific objectives
- 2) Study design with justification (kindly make clear if this was a retrospective or prospective cohort study)
- 3) Study setting
- 4) Sample size calculations
- 5) Participant recruitment (with inclusion and exclusion criteria)
- 6) Sample/data collection
- 7) Sample handling procedure and quality control
- 8) Outcome measures (indicate whether these were continuous, binary, or categorical).
- 9) Whole genome sequencing (WGS) and phylogenetic analysis
- 10) Data analysis (with justification for the approach used)
- 11) Ethical considerations

Response: We have structured the Methods section with all these subheadings. Specific comments about methods will be addressed in the following points.

7. It is not clear whether this was a retrospective study since patients were still hospitalized at the time of this study. In 6.2 above, kindly be precise about the type of cohort study you undertook.

Response: This was a retrospective study, which we have now stated clearly in our Methods section, page 6, line 106: “We conducted a retrospective chart review to gather the demographic and clinical variables.”

For further clarification of our methods, we included the following in our Methods section, page 7, lines 131-134: “All data collection was retrospective after a diagnosis of COVID-19 had been confirmed. If chart review occurred while a veteran was hospitalized, the chart was again reviewed retrospectively after discharge from hospital.”

8. As part of your participant recruitment, indicate attempts made to reduce bias.

Response: This was a retrospective study, so we did not recruit participants. As indicated in our Methods section, we included all veterans who were diagnosed with COVID-19 in this era with accessible medical records.

9. In 6.6 above, give details of those that collected samples and how that was done. If this was done by your research team, ensure to report the protocol used to collect samples. Organize your data collection into:

- 1) Hospitalization data
- 2) Peak disease severity data
- 3) Mortality data
- 4) Genome sequencing data

Response: This has been defined clearly now in the Methods section and the subsections Data Collection, Sample Collection, Whole Genome Sequencing, and Outcome Measures.

10. In 6.7 above, kindly clarify how samples were handled (including storage). If this was not done by the research team and was only reported, kindly indicate as such. If samples were not collected by you, provide details on how you had access to samples.

Response: This has been clarified now in the subsection Sample Collection and Handling, page 7, lines 136-144: “Sample collection and handling: Handling of nasopharyngeal specimens or isolated virus was carried out by the VACHS clinical laboratory as part of clinical care, following standardized CLIA guidelines. Our viral repository was populated by the positive test results of all New England veterans. VACHS laboratory handled specimens, isolated the SARS-CoV-2 RNA, and shipped it for whole genome sequencing (WGS) to non-VA laboratory. We obtained the details of platform used to diagnose, the cycle threshold, and the date of test from the laboratory. Sequencing of viral genome was conducted at the non-VA laboratory by our co-authors as follows.”

11. In 6.9 above, it is important to report the protocol/guidelines you used in genome sequencing. You may want to justify your procedure using these WHO guidelines [16] as well as substantiating your procedure with a visual display/flow of how the sequencing works.

Response: We thank the reviewer for this comment and would like to provide clarification. The genome sequencing method and the alignment approach are defined clearly in the subsection on WGS. Assignment of lineages was with Pangolin as described. Citations have been provided for reference. Any further granular detail on this method would be out of the scope of this paper.

12. As part of your statistical analysis, could you please justify your use of nonparametric tests? Kindly report the normality tests that were performed and the figures.

Response: We used logistic regressions to model the outcomes of hospitalization and mortality, and ordinal logistic regression to model peak disease severity because the outcomes were categorical and ordinal, respectively. Logistic and ordinal logistic regressions do not require an assumption of normality. We have edited our paper to make this clearer, page 8, lines 168 and 169: “We used STATA v16 (College Station, TX) for logistic regressions to predict our hospitalization and mortality, and ordinal logistic regression to predict peak disease severity.”

13. It might be worth arranging your data analysis first into univariate analysis and multivariate analysis, and then into hospitalization, peak disease severity, mortality, and genome sequencing.

Response: We have rephrased our Methods section to make the structure of analysis more clear, pages 8 and 9, lines 168-172: “We used STATA v16 (College Station, TX) for logistic regressions to predict our hospitalization and mortality, and ordinal logistic regression to predict peak disease severity. We first conducted a univariate analysis, then used significant

variables from the univariate analysis ( $P < 0.05$ ) to use in a multivariate model for each of our outcomes to assess the impact of several variables at once, which has been frequently used in COVID-19 literature. Genomic characteristics were reported descriptively.”

14. In your data analysis, kindly report how you moved from univariate to multivariate analysis or how you selected variables for your multivariate model.

Response: We agree with the reviewer that more clarification is necessary, so we have described our methods in more detail, Page 8 and 9, lines 169-172: “We first conducted a univariate analysis, then used significant variables from the univariate analysis ( $P < 0.05$ ) to use in a multivariate model for each of our outcomes to assess the impact of several variables at once, which has been frequently used in COVID-19 literature.”

15. It is very important to indicate the guidelines used to report your review results. As part of your ethical considerations, indicate the guidelines you used to report your results. You may want to use these depending on which best suits your study method [17,18].

Response: We thank the reviewer. We have cited the Record statement for this. Our report follows those guidelines, page 9, lines 181 and 182: “RECORD statement guidelines were used to maintain transparency in the reporting of this work.”

16. Your Results section should be reported in line with the Methods section starting with the participant characteristics. You might want to report your results as follows:

- 1) Participant characteristics
- 2) Predictors of hospitalization
- 3) Predictors of peak disease severity
- 4) Predictors of mortality
- 5) Genome sequencing and phylogenetics

Response: We thank the reviewer for the comments, and we have organized the Results section into three headings to make it more clear for the reader: (1) Participant Characteristics; (2) Rates and Predictors of Hospitalization, Peak Severity, and Mortality; and (3) Genomic Characteristics

17. Kindly move your Supplemental Table 1 to Participant Characteristics in the Results section.

Response: We have moved Supplemental Table 1 to the Results section on page 10 and have renamed it Table 1.

18. Kindly move Supplemental Figure 1 and Supplemental Figure 2 to the Predictors of Hospitalization and Predictors of Mortality subsections of the Results section, respectively.

Response: We have moved Supplemental Figures 1 and 2 to the Results section on pages 13 and 14, and renamed them Figure 1 and Figure 2.

19. Note that the whole of your manuscript must be in portrait. You may want to highlight your Table 1 then click on “fit to window” on the automatic adjustment tab of Microsoft Word

and move it together with Figure 1 to the Genomic Sequencing subsection of your Results section.

Response: We thank the reviewer for this comment, and we have adjusted Table 1 so that it fits within a portrait page.

20. In the presentation of the results of your logistic regression, it will be good to state how the following assumptions were met:

- 1) Binary outcome
- 2) Linearity
- 3) Outliers
- 4) Multicollinearity

Response: We thank the reviewer for the comment and have included the following sentence in the Methods section, page 9, lines 173 and 174: “Assumptions for logistic regressions (binary outcome, linearity, no outliers, and multicollinearity) were tested and met, with maximum variance inflation factors of 2.”

21. As part of the reported results of your regression, I suggest proving an explanation on your model’s goodness of fit by plotting and reporting the area under the receiver operating characteristic (ROC) curve.

Response: We agree with the reviewer, and we have provided the area under the ROC curve (the C-statistic) for our multivariate models in the text of the Results section, page 11, lines 207-213: “In multivariate regression, significant predictors of hospitalization (C-statistic: 0.75) were age (OR: 1.05, 95% CI: 1.03, 1.08) and non-White race (OR: 2.39, 95% CI: 1.13, 5.01) (Table 3). Peak severity (C-statistic: 0.70) also varied by age (OR: 1.07, 95% CI: 1.03, 1.11) and O2 requirement on admission (OR: 45.7, 95% CI: 18.79, 111). Mortality (C-statistic: 0.87) was predicted by age (OR: 1.06, 1.01, 1.11), dementia (OR:3.44, 95% CI: 1.07, 11.1), and O2 requirement on admission (OR: 6.74, 95% CI: 1.74, 26.1).”

22. Kindly follow the guidelines to structure your Discussion section as follows:

- 1) Principal findings (summary)
- 2) Comparison with prior studies
- 3) Study limitations

Response: We have structured the Discussion section in this format and have added subheadings with the exact wording.

23. Include a subsection “Author Contribution” after the Acknowledgments section to state the contribution of each author included in this paper.

Response: We have included author contributions on page 19, lines 348-354: “Author contributions: The authors confirm contribution to the manuscript as follows: ML and SG participated in the conception, design, data collection, analysis and interpretation of results, and manuscript preparation. YHS and MR participated in the data collection, analysis and interpretation of results, and manuscript preparation. MEP and NDG participated in the conduction, analysis and interpretation

of whole genome sequencing, and in manuscript preparation. DC participated in the data collection, analysis and interpretation of results. CBFV, JRF and TA participated in the conduction and analysis of whole genome sequencing.”

24. Include a subsection “Conflicts of Interest” after “Author Contributions” to declare any conflict of interest.

Response: We have included the following conflict of interest on Page 19, Line 360: “Conflict of interest: NDG is a paid consultant of Tempus Labs for infectious disease genomics..”

25. Kindly list all Multimedia Appendices before the References section. For instance, your supplemental Table 2 will be labeled in the body of the manuscript as follows:

- Multimedia Appendix 1: Genomic lineage

Response: We have labeled all multimedia appendices before the References section.

26. Create a section “Abbreviations” after your references to list and expand all abbreviations in the text.

Response: We have created an “Abbreviations” page after our references to list and expand all abbreviations in the text, page 26:

“BMI: body mass index

CAD: coronary artery disease

CKD: chronic kidney disease

COPD: chronic obstructive pulmonary disease

COVID-19: coronavirus disease of 2019

IRB: Institutional Review Board

L: Liters

LTC: long term care

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

O2: oxygen

OR: odds ratio

OSA: obstructive sleep apnea

VA: Veterans Administration

VACHS: Veterans Administration Connecticut”

### Minor Comments

27. You may want to include just the corresponding author on the manuscript and add all other authors in the metadata section of the online manuscript management system.

Response: Because we had enough space on the manuscript title page and for stylistic reasons, we have chosen to include all authors on the title page.

28. Kindly format your tables following the journal guidelines [19].

Response: We have formatted the tables according to guidelines.

29. Kindly number your tables in the body of the text in order of appearance (Table 1, 2, 3, etc).

Response: We have renumbered all the tables in order of appearance in the manuscript.

30. You need to report any *P* values based on the guidelines (eg, *P*=.05 or *P*<.001).

Response: We have reported all calculated *P* values in our manuscript according to the journal’s guidelines.

31. Review all your figures and their captions to ensure they are in line with the guidelines [20]. Apart from being uploaded as multimedia appendices, all figures must appear in the body of the text where they are first mentioned. The caption of each figure must appear at the bottom of the figure.

Response: We have moved all tables and figures up to where they should be in the text and added captions below each figure.

32. In your Discussion section, it will be appropriate to organize the “Comparison With Prior Studies” into subtitles as follows:

- 1) Predictors of hospitalization
- 2) Predictors of peak disease severity
- 3) Predictors of mortality
- 4) Genomic sequencing

Response: We thank the reviewer for this comment. We considered this but found that dividing the first part of the discussion into these four subheadings would result in small subsections. We instead took the reviewer’s prior suggestion of dividing the discussion into three subsections: Principal Findings, Comparison With Prior Studies, and Limitations. Our Discussion section has been strengthened by this.

33. I suggest starting your conclusion with a statement on the study objectives followed by a summary of findings, then lessons learned from your findings, and finally suggested direction of future research.

Response: We thank the reviewer for the suggestion and have reframed the first paragraph of our introduction to fit with the reviewer’s suggestions, pages 15 and 16, lines 288-300: “Our study found that in a cohort of veterans with average age of 63 years and a high comorbidity burden, age significantly associated with risk of hospitalization, peak disease severity, and mortality. O2 requirement upon admission correlated with peak disease severity and mortality, while dementia was an additional factor associated with higher mortality. The CDC provides a list of chronic medical conditions (May 2021) that predispose individuals to severe illness from SARS-CoV-2 infection [21], but >75% of United States adults fall under a high-risk category [22]. Veterans are a unique cohort because of advanced age on average [23], and more comorbidities. Understanding clinical factors that impact outcomes in veterans will help healthcare providers risk-stratify patients with similar demographic profiles, and future research should explore the impact of new treatments and vaccination on outcomes. The predominance of B lineage D614G in our study specimens provided valuable insight into the pace of epidemiological trend

and evolution of the virus early in the COVID-19 era through the New England region.”

34. You need to delete your “Supplemental Table 2. Lineages of genomes” from the manuscript and upload it as a Multimedia Appendix in the online manuscript submission system. All multimedia appendices must be referenced in the body of your paper. Kindly have a look at other papers published in JMIRx Med.

Response: We have changed this to “Multimedia Appendix 1,” as previously mentioned in point 25.

35. Kindly make Acknowledgments, Funding, and Conflicts of Interest subsections.

Response: We have made each of these sections as subsections, along with “Author Contributions.”

36. Your references need to be formatted following the journal guidelines. Set your reference manager to the American Medical Association (AMA) citation style and make sure to include a PubMed ID at the end of each reference. You can search the PubMed IDs of articles at <https://pubmed.ncbi.nlm.nih.gov/>. It is also possible to copy your citation directly from the PubMed site provided it has been set to the AMA style (see references to this report for examples).

For articles without PMIDs, kindly include a DOI and ensure you verify your DOIs using <https://www.doi.org/> to make sure they work.

Response: We have edited our references to include PMIDs whenever available and formatted them according to journal guidelines.

37. For referenced websites, ensure to make as much effort as possible to get and reference the PDF version of the article (ie, in the absence of a PMID and DOI).

Response: We have made every effort to reference PDF versions of articles whenever possible.

## Reviewer AV [24]

### General Comments

The authors presented a study about the clinical and genomic characterization of COVID-19 from a veteran group. I have some questions for the authors.

1. Line 85: Authors wrote, “we recorded hospitalization status, mortality, and oxygen (O<sub>2</sub>)-requirement within 24 hours of admission.” Here, can authors clarify if they recorded each single patient’s clinical information within 24 hours of admission or they collected them from chart review? In addition, for O<sub>2</sub>, the 2 should be subscript.

Response: We thank the reviewer for helping us clarify this. We did gather this information from manual chart review and have updated our methods to read, page 8, lines 160 and 161: “Our categorical outcomes, also derived from manual chart review, were hospitalization status, mortality, and oxygen (O<sub>2</sub>)-requirement within 24 hours of admission from manual chart review.”

We have also changed O<sub>2</sub> throughout the manuscript to have a subscript.

2. Lines 105 and 106: The disease name should be capitalized.

Response: We thank the reviewer for this comment; however, disease names are not typically capitalized unless they are an abbreviation.

3. Line 113: Authors did not provide a transition between the univariate regression and multivariate regression. Univariate analysis was simply mentioned in the first sentence without any explanation or discussion. Authors should indicate the reason why they conducted multivariate analysis (eg, univariate was not specific enough). Additionally, in general, the factors should have the first letter capitalized, for example, Age, non-White race.

Response: We thank the reviewer for this comment. As in our response to reviewer W, we have edited our description and clarified our univariate and multivariate analyses, pages 8 and 9, lines 168-172: “We used STATA v16 (College Station, TX) for logistic regressions to predict our hospitalization and mortality, and ordinal logistic regression to predict peak disease severity. We first conducted a univariate analysis, then used significant variables from the univariate analysis ( $P < 0.05$ ) to use in a multivariate model for each of our outcomes to assess the impact of several variables at once, which has been frequently used in COVID-19 literature.”

We have ensured that White and non-White are capitalized where present. Age is usually not capitalized.

4. Line 129: Authors wrote, “our study found that in an older cohort of veterans.” Here, older cohort could cause some confusion to some readers. When one reads the paper a few years later, he or she probably cannot understand what the older cohort is related to. Authors can add a time frame to it.

Response: This is a thoughtful comment, and we thank the reviewer for these comments and have added age to help support it, page 15, lines 288-290: “Our study found that in a cohort of veterans with an average age of 63 years and a high comorbidity burden, age significantly associated with risk of hospitalization, peak disease severity, and mortality.”

5. Line 131: Similar to point 4, authors should add the Centers for Disease Control and Prevention (CDC) report date.

Response: We have included a date, page 15, lines 291-293: “The CDC provides a list of chronic medical conditions (May 2021) that predispose individuals to severe illness from SARS-CoV-2 infection”

6. Line 133: Authors wrote, “veterans are a unique cohort because of advanced age on average, and more comorbidities. Understanding clinical factors that impact outcomes in veterans will help clinicians risk-stratify patients with similar demographic profiles.” Many veterans could be young in some Veterans Affairs (VA) medical centers. It may be right to general veteran populations, but authors need to cite references to support this claim.

Response: We thank the reviewer for this comment, and we agree that we need to cite a reference for this claim. We have

included the following reference, page 16, line 294: Profile of Veterans: 2017. In: National Center for Veterans Analysis and Statistics UDoVA, ed. <https://tinyurl.com/2p82akdb>

7. Line 137: Authors wrote, “in our study, age was a significant predictor for all of our outcomes and was a confounder for other variables.” Most scientific papers are written from the third point of view. Therefore, it is not common to state the study outcomes as “our outcome.” Authors should use a better phrase, such as in line 151: “This may explain the outcomes in our study.”

Response: We agree with the reviewer and have rephrased this sentence to be, page 16, lines 304 and 305: “In our study, age was a significant predictor for all of the studied outcomes and was a confounder for other variables.”

8. Line 138: Authors wrote, “interestingly, LTC status predicted all three of our outcomes on univariate analysis, but not on multivariate analyses. Earlier in the COVID-19 pandemic, residents of nursing homes had higher rates of infection as well as severe illness and mortality [25].” There is no transition between these two sentences. The first few sentences in the paragraph discussed age as a predictor. However, the sentence “earlier in the COVID-19 pandemic...” did not show an immediate connection with the age issue. Maybe the authors would like to express that nursing homes have older patients. If this is the case, the authors need to provide some connection or background information here.

Response: We do agree that we were trying to say nursing homes may have older patients. We have connected the two ideas, page 16, lines 304-307: “In our study, age was a significant predictor for all of the studied outcomes and was a confounder for other variables. Accordingly, LTC status predicted all three of our outcomes on univariate analysis, but not on multivariate analyses, possibly because LTC units tend to have older residents.”

9. Line 140: Authors wrote that “our study shows that among veterans in LTC facility, disease outcomes were not impacted by their residence status.” Here, authors should provide some discussion or reasons for their findings.

Response: We thank the reviewer for pointing this out. We intended to carry on the previous thought that after adjusting for age, residents of a long-term care (LTC) facility did not have worse outcomes. We have reworded this sentence, page 16, lines 308 and 309: “Our study shows disease outcomes were not impacted by their residence status, after adjusting for age.”

10. Line 148: Authors wrote, “our study supports data from previous reports that non-White patients are at increased risk of hospitalization but have similar peak severity and mortality outcomes [26-29].” Are these non-White patients in the United States or in other countries? This could change the dynamic and purpose of citing the reference. Please clarify.

Response: These studies are from the United States, and we have clarified this point on page 17, lines 315-317: “Our study supports data from previous reports that non-White patients in the United States are at increased risk of hospitalization but have similar peak severity and mortality outcomes.”

11. Line 156: Authors concluded that, for patients with dementia, they could have a high risk of death because of biological factors. Another possibility is the lack of self-report ability in patients with dementia. As a result, they probably do not understand their body’s changes, which could delay the needed care.

Response: We thank the reviewer for this comment and have added in this explanation, page 17, lines 318-321: “This may be explained by a host of biological factors but also may be a result of inability to self-report symptoms. This finding emphasizes the importance of extra care and monitoring required when approaching a patient with dementia.”

12. For the Discussion section, authors may add subtitles to different issues they would like to discuss. The current writing may be a little bit confusing to some readers.

Response: We thank the reviewer for this comment and have added subsections entitled, “Principal Findings,” “Comparison With Previous Studies,” and “Limitations” to our Discussion section.

13. In the Discussion, the authors mentioned multivariate analysis of many potential risk factors as their strength. It is true that the multivariate model is a powerful tool, but it is not necessarily fit for the COVID-19 situation very well. Authors need to cite references about other cases of using the multivariate model for COVID-19 outcome analysis.

Response: We thank the reviewer for this comment and have added several references to other studies using multivariate models after the following sentence in the methods, pages 8 and 9, lines 169-172: “We first conducted a univariate analysis, then used significant variables from the univariate analysis ( $P < 0.05$ ) to use in a multivariate model for each of our outcomes to assess the impact of several variables at once, which has been frequently used in COVID-19 literature.”

Mason KE, Maudsley G, McHale P, Pennington A, Day J, Barr B. Age-Adjusted Associations Between Comorbidity and Outcomes of COVID-19: A Review of the Evidence From the Early Stages of the Pandemic. *Front Public Health*. 2021;9:584182. PMID: 34422736. doi: 10.3389/fpubh.2021.584182.

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Merzon E, Green I, Shpigelman M, Vinker S, Raz I, Golan-Cohen A, et al. Haemoglobin A1c is a predictor of COVID-19 severity in patients with diabetes. *Diabetes Metab Res Rev*. 2021;37(5):e3398.

Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054-1062.

14. Figures and supplemental tables: Authors should include more details in the titles. Simply writing “genomes” or “hospitalization” in the title is not standard in scientific papers.

Response: We have renamed the titles to be “Hospitalization by patient demographics and comorbidities (%)” and “Mortality by patient demographics and comorbidities (%)”.

15. Figure 1: Authors should provide a better maximum likelihood tree. The current figure has many branches stacked to each other, barely providing any helpful information to readers.

Response: We thank the reviewer for this comment, and we are showing only the branches in which we have a sequence. From this figure, we are hoping to show the diversity of lineages, with the main branch points labeled. For more in-depth information on the exact lineages that our study included, we have provided the frequencies in list format in Multimedia Appendix 1.

## Round 2 Review

### Reviewer W

#### General Comments

The authors of the paper titled “COVID-19 Outcomes and Genomic Characterization of SARS-CoV-2 Isolated From Veterans in New England States: A Retrospective Analysis” have addressed all concerns raised close to full satisfaction. The paper is in much better shape now; however, there still are a few concerns worth noting. Kindly refer to the minor comments.

#### Specific Comments

##### Minor Comments

1. Under “Study Design,” the second and third sentences should be moved to the “Study Setting” and the last sentence moved to “Ethical Considerations.” The justification for the study design initially recommended was to cite any studies on the topic that have used similar methods (if possible).

Response: We have made these changes. We have also cited another study that used similar methods in the veteran population to justify the methodology.

2. Tables 1 and 2 still need to be formatted according to the guidelines.

Response: Tables have been placed where they are referenced in the text and the format is according to instructions. Font size has been changed to normal size, and tables have been reformatted to fit the window in portrait orientation. Soft line breaks have been removed in favor of separate table rows.

3. I still see the captions of figures appearing above the figures, contrary to the guidelines.

Response: We have checked our submitted figures again and did not find captions in the latest submission. All figures are uploaded as supplementary files and follow the journal guidelines. We have removed the older figure files to remove any confusion. The correct files are the supplementary figure files submitted as revised figures on September 14, 2021.

4. Kindly maintain the heading “Multimedia Appendix: Lineages of genomes” in the manuscript but remove the table and upload it in the online manuscript management system.

Response We have removed said table from the manuscript, and it is available as a multimedia appendix in the online manuscript management system. The heading has been maintained in the manuscript as the reviewer suggested.

5. Ensure that all reported percentages in your manuscript are accompanied with the absolute values on which they were calculated, for instance, 25% (5/20) or (25%, 5/20).

Response: Thank you. We have double-checked and added the absolute values where they were missing.

### Reviewer AV

The authors presented an updated manuscript after taking the reviewers’ suggestions. I have a few minor comments.

1. Authors added reference [30] but did not indicate or cite it in the paper. I guess it should be listed here: “which has been frequently used in COVID-19 literature [9,31-33].”

Response: We thank the reviewer for catching this. We have added the citation now.

2. Authors wrote, “this study included all veterans who tested positive for COVID-19 from April 8, 2020, to September 16, 2020 at one of the six New England VA hospitals.” Previously authors wrote, “Connecticut had been entrusted with testing for SARS-CoV-2 for all six VA healthcare centers.” Does this mean the patients enrolled in this study are from one of six VA hospitals, or they are from all six hospitals?

Response: The study included veterans at all six New England VA hospitals. We have clarified this now by changing the word *one* to *any* in the subheading “Participants (Sample Size and Inclusion Criteria).”

3. Authors wrote, “the CDC provides a list of chronic medical conditions (May 2021) that predispose individuals to severe illness from SARS-CoV-2 infection [21], but >75% of United States adults fall under a high-risk category [22].” In general, if the word “but” is in the sentence, readers will pay attention to the words following “but,” which means the first part may not be important or critical. Authors can kindly use another connection word.

Response: We have modified this to the following, to help explain better: “The CDC provides a list of chronic medical conditions (May 2021) that predispose individuals to severe illness from SARS-CoV-2 infection [21]. Based on this list, >75% of United States adults fall under a high-risk category [22], therefore making it important to have select populations evaluated for uniquely applicable risk factors.”

4. In the Abstract, the authors wrote “Multiple SARS-CoV-2 lineages were distributed in patients in New England early in the COVID-19 era, mostly related to viruses from New York with D614G mutation.” Can the authors kindly clarify if it is New York State or New York City?

Response: We have clarified this by adding the word state.

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## Abbreviations

- AMA:** American Medical Association
- CDC:** Centers for Disease Control and Prevention
- LTC:** long-term care
- ROC:** receiver operating characteristic
- VA:** Veterans Affairs
- WGS:** whole genome sequencing

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Original Paper

# Comparison Between Male and Female Survivors of Sexual Abuse and Assault in Relation to Age at Admission to Therapy, Age of Onset, and Age at Last Sexual Assault: Retrospective Observational Study

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## Abstract

**Background:** Sexual abuse and sexual assault are complex phenomena that involve many factors (or correlates) and have many health and financial implications for individuals, families, and society. Every correlate needs to be studied in detail, individually and in relation to other correlates. Only with a thorough understanding of these correlates can more efficient and targeted prevention and intervention programs be designed.

**Objective:** The purpose of this study was to examine the differences between male and female survivors of sexual abuse and sexual assault regarding the correlates of the survivors' age of onset of assault, age at the last assault, and age at which they entered therapy.

**Methods:** Therapists at eight sexual assault centers in the province of Alberta, Canada, completed a questionnaire on each of their clients over a period of 7 years. A total of 3302 participants, of whom 2901 (87.86%) were female and 401 (12.1%) were male survivors of sexual abuse and assault, were included in this study. Mostly descriptive analyses were carried out on the 4 variables of concern in this study.

**Results:** Regarding the number of survivors who sought therapy, female survivors outnumbered male survivors by a ratio of 7:1, with different ratios for different age groups. As children age, their risk of being sexually assaulted for the first time decreases. Male children are more likely to be sexually abused at a younger age, whereas female children are more vulnerable to being assaulted at all ages, particularly in adolescence. The mean age of onset of sexual abuse was found to be 6.71 (SD 2.86) years, and the odds of experiencing the first sexual assault during childhood, as opposed to adolescence, were 4:1 for females and 9:1 for males. Male survivors were two times more likely than female survivors to experience their first sexual assault in childhood. The vast majority of survivors sought help many years after being sexually assaulted, and male survivors waited an average of 3 years longer from the last sexual assault before seeking therapy.

**Conclusions:** The majority of survivors of sexual abuse and sexual assault live with the consequences for many years before they seek help, and a large proportion of male survivors are not likely to seek help.

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## KEYWORDS

sexual abuse; sexual assault; age of onset; sex; gender; age; therapy; abuse; assault; mental health; victim; childhood; children; gender disparity; violence

## Introduction

Although numerous studies have been conducted on various correlates of child sexual abuse (CSA) and sexual assault, not every correlate receives equal attention. A quick survey of the literature shows that prevalence and incidence studies [1-3] and the psychological effects of sexual abuse and assault [4-8] receive the most considerable attention. The sex and age of survivors [9-11] receive more attention than the age of the survivors when the first act of sexual abuse or assault occurred (age of onset) and when the last act of sexual abuse or assault was experienced. Although the ages of survivors at first and last sexual abuse or assault are sometimes mentioned, they have not been the focus of studies [12-14].

A 2014 report by the World Health Organization on violence prevention noted that the lifetime prevalence rate of CSA is 18% for girls and 7.6% for boys, with Africa having the highest rates of 33% for girls and 14% for boys [15]. The US Department of Health and Human Services' reports of 1999, 2005, and 2017 indicated, based on substantiated investigations, that 11.3%, 9.3%, and 8.6% of children were sexually abused, respectively, and the 1999 data showed that females were 4 times more likely to be sexually abused than males [16-18]. The comprehensive Canada-wide statistics on Canadian incidence of child maltreatment reported that 8.4% of all cases substantiated by the Department of Child Welfare involved sexual abuse of children in 1998 [19]; this percentage was 3% in 2003 [20] and 2008 [21]. The Australian Commonwealth Department of Family and Community Services report of 2017 indicated, based on substantiated investigations, that 9% of children were sexually abused and that girls were more likely to be sexually abused than boys (11% vs 7%, respectively) [22]. In 2002, the World Health Organization noted in its report, based on several studies, that when a broader definition of CSA was used, the prevalence jumped to 19% for males and 45% for females [23].

Indeed, the literature contains numerous prevalence studies that vary widely and lack consistency. The variety of definitions of CSA, cultural factors, legal regulations, and methods used to collect data are the major contributors to this lack of consistency. Rates based on CSA cases reported by survivors, especially those reporting retrospectively, tend to be much higher than those of cases that are reported to authorities. Studies based on self-report questionnaires might be biased toward overestimation, while studies using interviews might be biased toward underestimation of the prevalence [2,24]. Hence, rates based on official reports of CSA are lower than rates based on self-reports by youth and adults because only a small proportion of CSA cases are reported to authorities [25-27] and because

only those whose allegations were substantiated after disclosing to the authorities were included in the official report data. For example, estimates of CSA based on a review of 217 studies conducted between 1998 and 2008 found rates based on self-reports to be approximately 30 times higher than rates based on official reports (law enforcement and child protection) (12.7% vs 0.4%, respectively) [28]. A survey of 122 adult survivors of sexual abuse found that only 32% reported the abuse when they were children, whereas 68% reported the abuse after adulthood [29]. Another study concluded that 30% of male and 16% of female survivors had never reported their abuse [30]. A review of several disclosure studies found that approximately 30% to 80% of survivors do not report their experiences of sexual abuse until adulthood [31]. Based on these studies and many others, it seems that there is a ratio of approximately 3 to 1 in favor of those who do not report sexual abuse. Even when children are in the care of the state, many do not report sexual abuse, as was observed by the Mullighan Commission of Inquiry on Children in State Care in Australia [32].

It may seem that estimates based on self-reports are more accurate and, therefore, a realistic reflection of the prevalence of child sexual abuse. However, when relying on self-reports, the probability of false positive and false negative reports increases, thereby undermining the accuracy of the results [33,34]. However, the risk of false negative reports is judged to be small enough not to undermine prevalence rates based on self-reports and therefore to present minimal risk to the accuracy of the results [34,35]. False positive reports are rare [34,36], and the fact that many survivors of CSA do not disclose their abuse to anyone is likely to render any false positive results negligible. In fact, estimates based on self-reports may be somewhat conservative. Based on these studies, the use of survivors' retrospective reports of sexual abuse in this study is appropriate and justified.

Regardless of the definition of CSA, cultural factors, legal regulations, or the method used to estimate prevalence and incident rates, it seems that the majority of studies found girls to be at least twice as likely to be sexually abused as boys, that girls are more likely to seek help than boys, and that the risk of being sexually abused increases with age into late adolescence. Furthermore, although girls are at 2 to 3 times greater risk of being sexually abused than boys, this ratio does not seem to change during adolescence [3,10,24,28,36].

A few studies have not supported the finding that the rates of CSA among girls are higher than among boys. For example, one study using South African students found that the prevalence of CSA for boys, at 60%, was approximately 7% higher than for girls, at 53.2% [37]. Another study using Portuguese parents

found the prevalence of CSA for boys and girls to be approximately the same, at 2.7% [38]. The difference between boys and girls in reporting may be due to the reluctance of males to disclose experiences of CSA. This reluctance is reflected by the length of time male survivors take to reveal CSA. Males may take as long as 10 years to disclose, whereas females take much shorter periods [39]. Adolescents experience a higher number of sexually abusive incidents than children [9], and at least 10% of girls experience forced intercourse before the age of 18 [3]. Based on 9 studies conducted between 1993 and 1999, the 2002 report by the World Health Organization on violence and death revealed that forced sexual intercourse before the age of 18 years was experienced by 7% to 47.6% of girls and 0.2% to 31.9% by boys [23].

Children may experience CSA when they are as young as a few months old, and the abuse may last well into their adulthood. A study found that the average age of onset of CSA was approximately 5 (SD 3.7) years and that it lasted for an average duration of approximately 7.3 (SD 4.9) years [12]. Another study found that in a sample of 246 individuals, sexual abuse generally started at the age of 6.3 (SD 3.5) years and lasted for 8.1 (SD 7.3) years [40].

In summary, it is reasonable to conclude the following: sexual abuse and sexual assault continue to be a problem worldwide; on average, approximately 10% of children experience sexual abuse; on average, female survivors outnumber male survivors by approximately 4 to 1; on average, sexual assault on children may start around the age of 2 and last for as long as 15 years; on average, the number of sexually abused children based on self-reports is much higher than the number based on official reports by at least 3 to 1; the risk of being sexually assaulted may stay the same or increase with age into late adolescence; and female survivors are more likely to seek help and to do so sooner than male survivors.

Therefore, it is important to consider the sex of survivors in relation to the age at which they seek therapy and the ages when the first and the last act of sexual assault occurred. Clearly, these four variables are related. How soon after the first act of sexual assault does a male or a female survivor seek therapy? Because sexually assaultive behaviors can last many years, is it also essential to consider how soon after the last act of sexual assault a male or a female survivor seeks therapy. How long do they live with their experience of sexual abuse or assault before they seek help? Moreover, studying the relationships among these correlates provides for the determination of vulnerability and risk. For example, which male or female age group is most vulnerable to sexual abuse or sexual assault? Furthermore, it is crucial to appreciate that data based on self-reports, unless strictly controlled, do not reflect the present. More often, people seek therapy for sexual abuse or assault that occurred many years earlier, so these self-report data provide a window to what was happening in the past. A better understanding of the correlates of sexual abuse and sexual assault and their relationships as they existed would allow for the construction of a better and more accurate picture of the past and its impact on resources in the present. A more precise description would help us anticipate the current and future needs and design better and more effective prevention and intervention programs.

Aside from national studies conducted by governmental social service and child protection agencies, almost all previous studies used small community-based samples. To date, no study has considered the relationships between the age of survivors at the time of seeking therapy, at the time of the first sexual assault, and at the time of the last sexual assault before entering treatment, using a large sample of male and female survivors. This is the first of several studies that will examine several correlates of sexual abuse and sexual assault.

This study focuses on data based on a large sample of children and adults who sought therapy for their sexual abuse or assault; these include many variables, such as the sex of the survivors, their age at the time of admission to therapy, their age at the time of the first sexual assault, and their age at the time of the last sexual assault. This study examines the differences between male and female survivors of sexual abuse and sexual assault regarding these correlates. The more general term of sexual assault is defined as any physical contact between adults (aged 18 years and older) that was traumatic and sexual in nature (kissing; fondling; oral sex; and digital, vaginal, and anal penetration) where consent was not given. When the sexual assault is committed against a minor, it is termed sexual abuse. Sexual abuse is defined as any physical contact with a minor (child under 18 years of age) that was traumatic and sexual in nature (kissing; fondling; oral sex; and digital, vaginal, and anal penetration) and was perpetrated by a blood relative, caregiver, person in a position of responsibility or control, friend, acquaintance, or date. The term *sexual assault* is inclusive of sexual abuse. Depending on the age of the survivors, an act of sexual assault may be termed as an act of sexual abuse. The term *sexual assault* is used throughout the text to refer to the act of sexual assault against anyone of any age, with the understanding that such an act is defined as sexual abuse when it is perpetrated against a person under the age of 18 years.

Although the data set is dated, there is much to be learned by examining and reporting the patterns of the relationships between these correlates. First, this examination can provide a snapshot of the prevailing patterns of relationships between these correlates before and during the period of data collection. Second, it can provide a basis for comparisons with more recent data and help establish a meaningful trend. Third, it can emphasize the importance of studying these relationships so that we may be better able to design targeted and more efficient prevention and intervention programs. Fourth, it can be used to argue for continuous funding using empirically informed prevention and intervention proposals.

## Methods

### Procedure

Eight sexual assault centers in the province of Alberta, Canada, participated in collecting the data between 1994 and 2003. These centers serve small, large, rural, and urban areas with populations of between 14,000 and 900,000 people. All centers reported data on a total of 5314 people, of whom 4317 were sexually abused or assaulted and sought therapy for the sexual abuse or assault. The archival data used in this study are based on a questionnaire, which was administered and collected under

the supervision of the author from the eight sexual assault centers. The data are based on the responses to the questionnaire provided by the survivors of sexual abuse and sexual assault who sought help from these centers.

Therapists who collected the data were instructed to complete the questionnaire as soon as the information was available and only after clients were comfortable, were informed of the purpose of the data collection, and had signed the informed consent form. Therapists were also instructed to ensure that their clients understood that intervention was not contingent or related to the data collection and that clients could refuse to be included in the survey and could withdraw their consent at any time.

Often, clients who approached these sexual assault centers for help were in crisis and needed immediate assistance. In consideration of this fact, it was decided not to ask those clients to complete the questionnaire. Clients were informed of the questionnaire only when the therapists thought it was appropriate, within the first 3 to 6 sessions, and the clients' consent was sought. A copy of the questionnaire was completed by the clients' therapist based on the clients' responses, although in some cases, and when appropriate, the client completed the questionnaire.

The completed questionnaires were sent to the author on a monthly basis. The data were entered into a database over several years by several people under the supervision of the author. Except for the respective therapists of the clients, the data were collected anonymously, clients' anonymity and confidentiality were maintained at all times, and no identifying information was extracted from the clinical files and included in the questionnaire except for the information contained in the questionnaire. Clients were informed about and consented to the data collection and the potential use of this data for funding, research, and publication. All clients signed an informed consent form for treatment as well as an informed consent form for the data collection. In cases where children were involved, the guardian of the child signed the consent form.

Some clients did not agree to participate, and not every therapist, although they were encouraged, diligently completed the questionnaire for every client. Therefore, not all survivors who received therapy received the questionnaire. The number of people who completed the questionnaire relative to the number of people seen by the centers is unknown. However, there is no reason to believe that those who did not agree to participate or

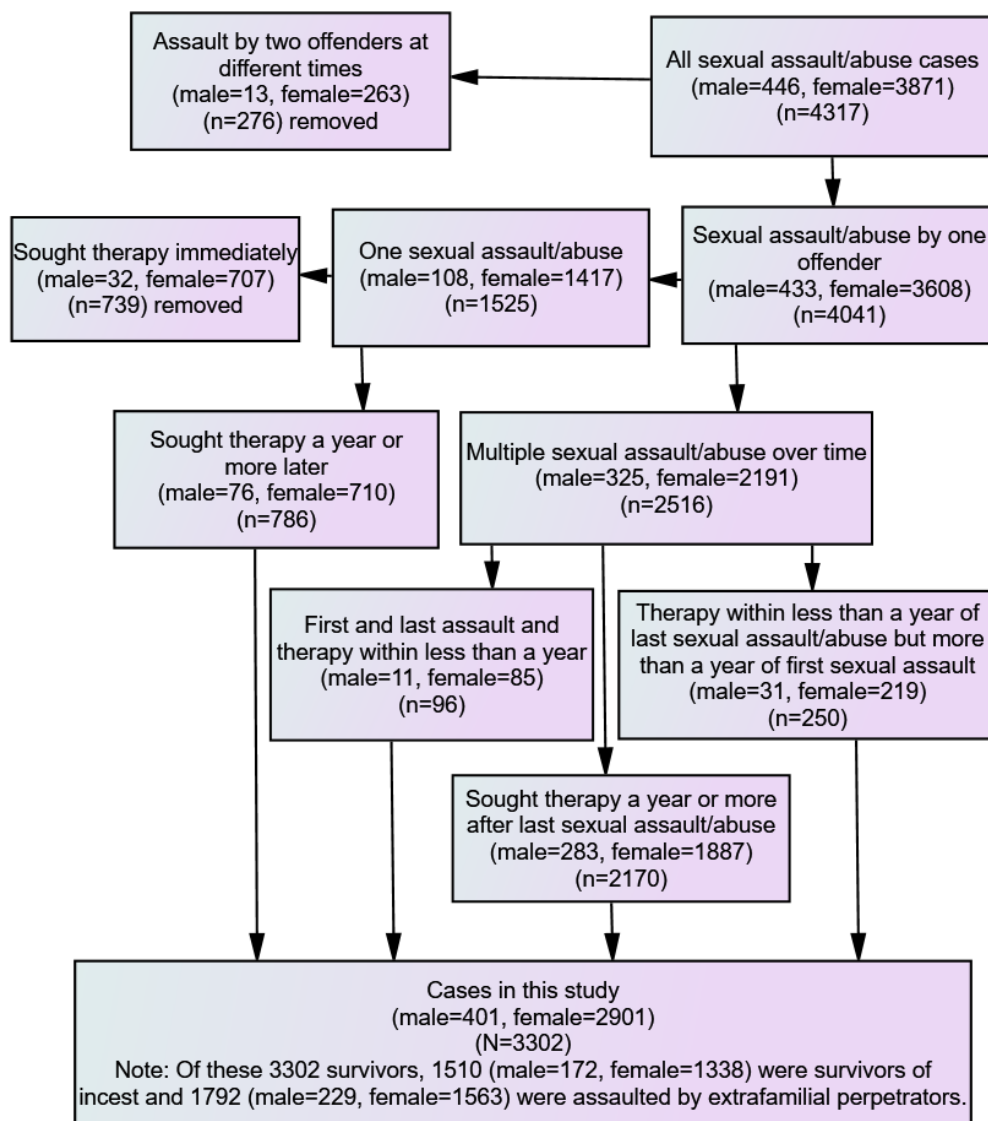
for whom data were not collected were different from those for whom data were collected. Given the size of the sample, it is reasonable to conclude that the data accurately reflect those who sought therapy at that time in those geographical areas.

## Questionnaire

The questionnaire was designed by the author and completed by the clients and their therapists who were working at these centers. The questionnaire included items that gathered information about the sex of the survivor, age at the time of admission to therapy, age at the time of the first sexual assault, age at the time of the last sexual assault, sex of the perpetrator, age of the perpetrator, survivor's relationship to the perpetrator, duration of the abuse, number of perpetrators, and type of threat used. The items in the questionnaire were developed collaboratively between the author and the therapists working at the sexual assault centers. Some questions were already part of the intake and information gathering processes at these centers.

## Participants

As shown in [Figure 1](#), a total of 4317 survivors of sexual abuse or sexual assault completed the questionnaire. Survivors who were sexually abused or assaulted by two different perpetrators at two different times ( $n=276$ ) were removed from the analysis. Survivors who were sexually assaulted once and sought therapy immediately or within days of the assault ( $n=739$ ) were also removed from the analysis. The removal of these 2 groups of survivors ( $n=1015$ ) left 3302 survivors to be the focus of this work. These survivors included those who were sexually assaulted once and sought therapy 1 year or more later ( $n=786$ ) and those who experienced multiple incidents of sexual abuse or assault over an extended period of less than 1 month to more than 15 years ( $n=2516$ ). The latter group, those with extended sexual abuse history, fell into 1 of 3 groups depending on the time they waited to seek help: those who experienced their first and last sexual assault and sought therapy within 1 year ( $n=96$ ), those who sought therapy within less than 1 year of their last sexual assault but who experienced their first sexual assault more than 1 year ago ( $n=250$ ), and those who sought therapy more than 1 year after the time of their last sexual assault ( $n=2170$ ). Furthermore, of the 3302 survivors, 1338 (40.52%) females and 172 (5.2%) males were survivors of incest, whereas 1563 (47.33%) females and 229 (6.9%) males were survivors of extrafamilial perpetrators.

**Figure 1.** The process of selection of the study participants.

## Analysis

The first part of the analysis in this study examined the sex differences of the survivors. The second part investigated the differences between males and females on the basis of the age at the time of admission to therapy, at the time of the first sexual assault, and at the time of the last sexual assault. The data were analyzed using a combination of descriptive statistics (means, standard deviations, percentages, histograms) and, where appropriate, univariate analysis using the *t* test and Cohen *d* effect size to determine any significant differences between the ages of survivors at different times. All analyses were conducted using SPSS, version 25 (IBM Corporation).

## Results

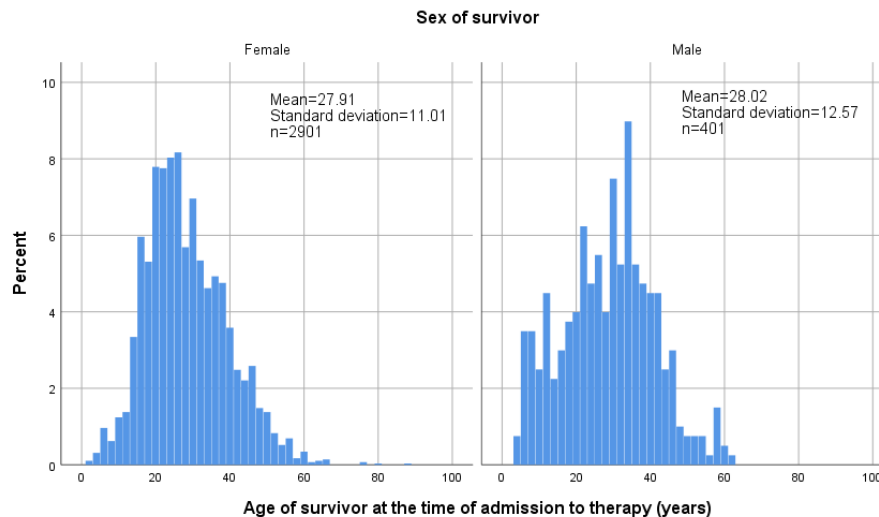
### Sex of Survivors

The population of this study was 3302 survivors of sexual abuse or assault, of whom 2901 (87.86%) were female and 401

(12.1%) were male. On average, over the 8 years of data collection, for every 7 female survivors, 1 male survivor sought therapy.

### Age of Survivors at the Time of Admission

The age of the survivors at the time of admission to therapy ranged from 2 to 88 years, with a mean age of 27.93 (SD 11.21) years. The median age at the time of admission was 26 years, and the mode was 23 years. The age of the male survivors at the time of admission to therapy ranged from 4 to 62 years, with a mean age of 28.02 (SD 12.57) years. The age of female survivors at the time of admission to therapy ranged from 2 to 88 years, with a mean age of 27.91 (SD 11.01) years. Frequency distributions of the age of male and female survivors at the time of admission to therapy are shown in [Figure 2](#).

**Figure 2.** Frequency distributions of the age of male and female sexual assault survivors at the time of admission to therapy.

To investigate these frequency distributions, the data were separated into several age groups for male and female survivors: young children (1-6 years old), children (7-12 years old), adolescents (13-17 years old), young adults (18-29 years old), and adults (30 years old and over), as shown in [Table 1](#). Young male children accounted for 4.2% of all male clients (17/401), while young female children accounted for 1.37% of all female clients (40/2901). Male children aged 7-12 years accounted for 10.5% of all male clients (42/401), whereas female children of this age accounted for 3.24% of all female clients (94/2901). Male adolescents accounted for 6.7% of all male clients (27/401), whereas female adolescents accounted for 12.20% of female clients (354/2901).

Calculations of the odds ratios (ORs) at the time of admission to therapy for male and female survivors in different age groups showed that the odds of being an older child (age 7-12 years) were approximately 5% lower for females than males, OR 0.95

(95% CI 0.5-1.9); the proportion of older children aged 7-12 years to younger children aged 1-6 years for females and males is  $(94/40) / (42/17) = 0.95$ . However, when adolescents aged 13 to 17 years were compared with children aged 1 to 12 years, the odds of being an adolescent girl were approximately 6 times greater than those of being a boy between 1 and 12 years of age (OR 5.8, 95% CI 3.5-9.5);  $(354/134) / (27/59) = 5.8 \approx 6$ .

Further examination of [Table 1](#) reveals a noticeable difference between young adult and adult male and female survivors. For the entire female sample, just under one-half (1226/2901, 42.26%) are aged between 18 and 29 years, and over one-third (1187/2901, 40.92%) are aged 30 years and older, whereas almost one-third (125/401, 31.2%) of the entire male sample were aged between 18 and 29 years and just under one-half (190/401, 47.4%) were aged 30 years and older at the time of admission to therapy.

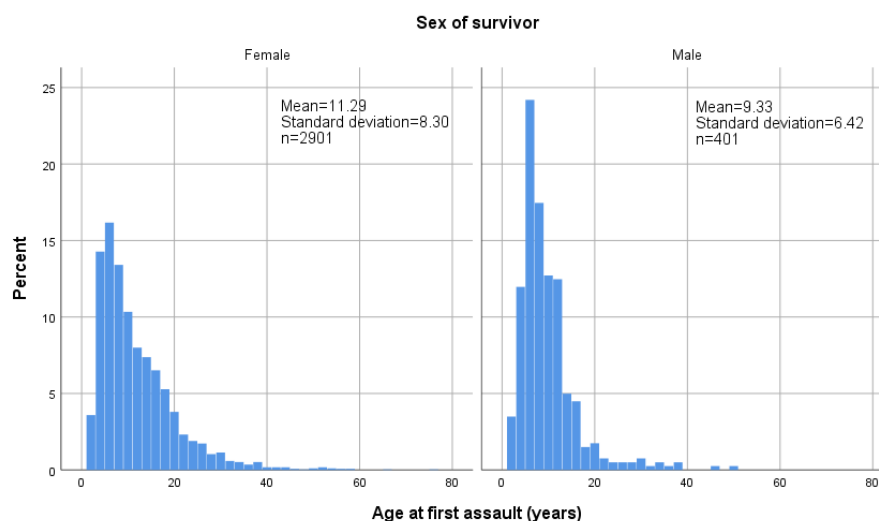
**Table 1.** Percentages of male and female sexual assault survivors by age group at the time of admission to therapy (N=3302).

Age at admission (years)	Value, n (%)	
	Male (n=401)	Female (n=2901)
1-6	17 (4.2)	40 (1.4)
7-12	42 (10.5)	94 (3.2)
13-17	27 (6.7)	354 (12.2)
18-29	125 (31.2)	1226 (42.3)
≥30	190 (47.4)	1187 (40.9)

### Age at First Assault (Age of Onset)

The age of onset at which the first sexual assault occurred was reported to be between 2-6 years by 1146 (34.71%), 7-12 years by 1092 (33.07%), 13-17 years by 525 (15.90%), 18-29 years by 418 (12.66%), and 30 years and older by 121 (3.66%) of the 3302 survivors. The ages of onset ranged from 2 to 76 years, with a mean age of 11.05 (SD 8.12) years. The mode and the

median age of onset were 5 and 10 years, respectively. The inclusion of cases in which the age of onset was after childhood inflated the mean age of onset. By restricting the age of onset to 12 years and younger, the mean age of onset was found to be 6.71 (SD 2.86) years. Frequency distributions of the ages of male and female survivors at the time of the first sexual assault are shown in [Figure 3](#).

**Figure 3.** Frequency distributions of the age of male and female sexual assault survivors at the time of the first sexual assault.

The age of onset was separated into several age groups for male and female survivors, as shown in Table 2. Among the 401 male survivors, 82.3% (n=330) reported that they had experienced their first sexually abusive act between the ages of 2 and 12 years (n=159, 39.7%, for 1-6 years and n=171, 42.6% for 7-12 years), whereas 1908 of the 2901 female survivors (65.77%) reported that they had experienced their first sexually abusive act between the ages of 2 and 12 years (n=987, 34.02%, for 1-6 years and n=921, 31.75%, for 7-12 years). During adolescence, between the ages of 13 and 17 years, 9.7% (39/401) of male survivors and 16.75% (486/2901) of female survivors reported being sexually assaulted for the first time. Of the entire sample, 8.0% (32/401) of male survivors and 17.48% (507/2901) of female survivors reported experiencing their first sexual assault after the age of 17 years. The odds of a female survivor

experiencing her first sexual assault during childhood as opposed to adolescence were approximately 4 to 1 ( $1901 \div 486 = 3.91$ ), and the odds for a male experiencing his first sexual assault during childhood as opposed to adolescence were approximately 9 to 1 ( $330 \div 39 = 8.46$ ). That is, for every female survivor in the sample who was first assaulted in adolescence, there were 4 female survivors who were first assaulted in childhood, and for every male survivor who was first assaulted in adolescence, there were 9 male survivors who were first assaulted in childhood. Taking the ratio of these two ratios showed that the odds that males would experience their first sexual assault in childhood were about twice those for females. Male survivors were 2 times more likely than female survivors to experience their first sexual assault in childhood.

**Table 2.** Percentages of male and female survivors by age of onset (N=3302).

Age at first assault (years)	Value, n (%)	
	Male (n=401)	Female (n=2901)
1-6	159 (39.7)	987 (34.0)
7-12	171 (42.6)	921 (31.7)
13-17	39 (9.7)	486 (16.8)
18-29	23 (5.7)	395 (13.6)
≥30	9 (2.2)	112 (3.9)

### Age at First Assault in Relation to Age at Admission to Therapy

The age groups at the time of admission to therapy and the age groups at the time of the first sexual assault for male and female survivors were cross-tabulated, as shown in Table 3. The diagonal of this table represents the number of survivors who sought therapy (and therefore likely came to the attention of the system) during the same period when the first sexually assaultive act occurred. Examination of Table 3 shows that 36.7% of

female adolescents (130/354) versus 19% of male adolescents (5/27) at the time of admission were first assaulted between the ages of 13 and 17 years. The remaining 63.3% of female (224/354) and 81% of male (22/27) adolescents at the time of admission to therapy reported being first assaulted between the ages of 2 and 12 years. For the 30 years and older age group, 90.56% of women (1075/1187) and 95.3% of men (181/190) were seeking therapy for sexual assaults that first occurred between the ages of 2 and 29 years.



**Table 3.** Age at admission to therapy by age at first sexual assault for male and female survivors of sexual assault (N=3302).

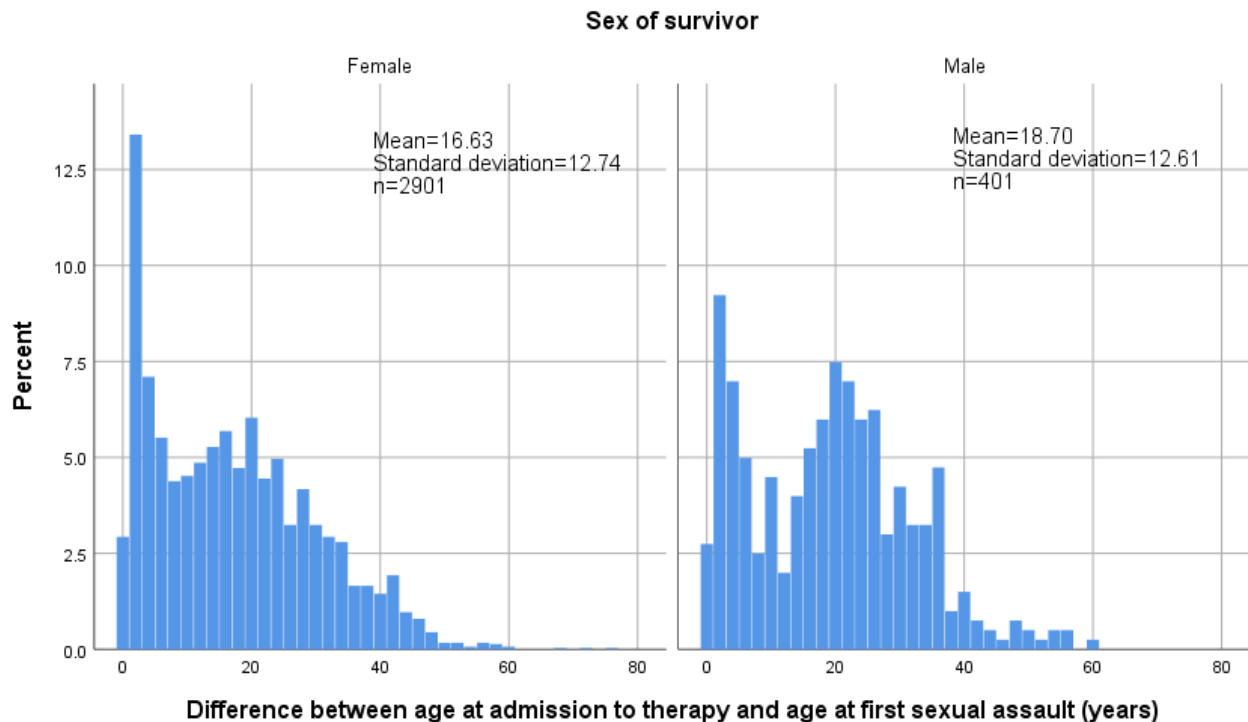
Age at admission to therapy	Age at first sexual assault (years)											
	Child (1-6)		Child (7-12)		Adolescent (13-17)		Young adult (18-29)		Adult (≥30)		Total	
	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male
<b>1-6 years</b>												
Count, n	40	17	0	0	0	0	0	0	0	0	40	17
Within age at admission group (%)	100	0	0	0	0	0	0	0	0	0	100	100
Within age groups at first assault (%)	4.05	10.69	0	0	0	0	0	0	0	0	1.38	4.24
Proportion of total (%)	1.38	4.24	0	0	0	0	0	0	0	0	1.38	4.24
<b>7-12 years</b>												
Count, n	41	25	53	17	0	0	0	0	0	0	94	42
Within age at admission group (%)	43.62	59.52	56.38	40.48	0.0	0.0	0.0	0.0	0.0	0.0	100	100
Within age groups at first assault (%)	4.15	15.72	5.75	9.94	0.0	0.0	0.0	0.0	0.0	0.0	3.24	10.47
Proportion of total (%)	1.41	6.23	1.83	4.24	0.0	0.0	0.0	0.0	0.0	0.0	3.24	10.47
<b>13-17 years</b>												
Count, n	78	11	146	11	130	5	0	0	0	0	354	27
Within age at admission group (%)	22.03	40.74	41.24	40.74	36.72	18.52	0	0	0	0	100	100
Within age groups at first assault (%)	7.90	6.92	15.85	6.43	26.75	12.82	0	0	0	0	12.20	6.73
Proportion of total (%)	2.69	2.74	5.03	2.74	4.48	1.25	0	0	0	0	12.20	6.73
<b>18-29 years</b>												
Count, n	367	53	361	49	235	14	263	9	0	0	1226	125
Within age admission group (%)	29.93	42.40	29.45	39.20	19.17	11.20	21.45	7.20	0	0	100	100
Within age groups at first assault (%)	37.18	33.33	39.20	28.65	48.35	35.90	66.58	39.13	0	0	42.26	31.17
Proportion of total (%)	12.65	13.22	12.44	12.22	8.10	3.49	9.07	2.24	0	0	42.26	31.17
<b>≥30 years</b>												
Count, n	461	53	361	94	121	20	132	14	112	9	1187	190
Within age admission group (%)	38.84	27.89	30.41	49.47	10.19	10.53	11.12	7.37	9.44	4.74	100	100
Within age groups at first assault (%)	46.71	33.33	39.20	54.97	24.90	51.28	33.42	60.87	100	100	40.92	47.38
Proportion of total (%)	15.89	13.22	12.44	23.44	4.17	4.99	4.55	3.49	3.86	2.24	40.92	47.38
<b>Total</b>												
Count, n	987	159	921	171	486	39	395	23	112	9	2901	401
Within age admission group (%)	34.02	39.65	31.75	42.64	16.75	9.73	13.62	5.74	3.86	2.24	100	100
Within age groups at first assault (%)	100	100	100	100	100	100	100	100	100	100	100	100
Proportion of total (%)	34.02	39.65	31.75	42.64	16.75	9.73	13.62	5.74	3.86	2.24	100	100

Another approach to analyzing the data was to examine histograms of the difference between the age at admission and the age of the first assault and plots of the difference between the age at admission and the age of the first assault against the age at admission for male and female survivors. The frequency distributions of the difference between the age at admission and

the age at first sexual assault for males and females are shown in [Figure 4](#). It appears that only 8.5% (34/401) of male survivors sought therapy within the first 2 years of the first sexual assault, and 19.0% (76/401) within 5 years. The majority (325/401, 81.0%) waited for up to 60 years before they sought help, with

35.2% (141/401) waiting for 16 to 26 years before they sought help.

**Figure 4.** Frequency distribution of the difference between age at the time of admission and age at the time of first sexual assault for male and female survivors of sexual assault.



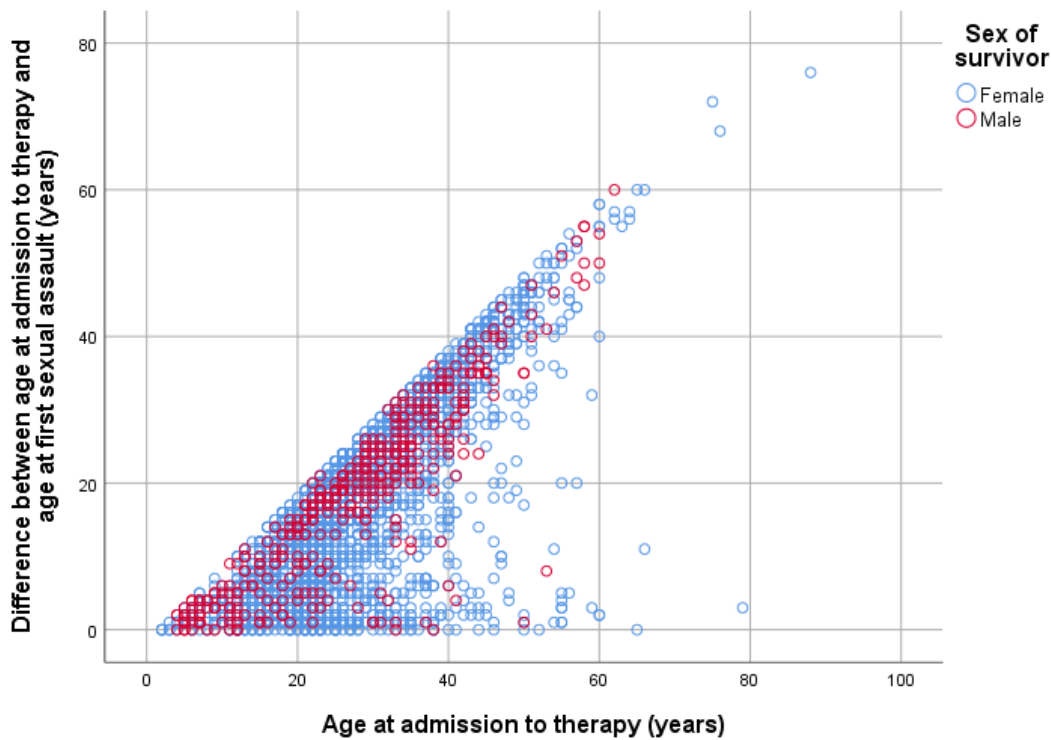
On the other hand, as shown in Figure 3, for females, approximately 15.83% (331/2901) of female survivors sought help within the first two years after the first sexual assault and about 32.52% (680/2901) within 5 years. The majority (1411/2901, 67.48%) waited for up to 76 years before they sought help, with 38.31% (801/2901) waiting for 16 to 26 years before they sought help. Clearly, more males waited a longer time than females to seek help after they were first sexually assaulted. The mean time difference between the time of admission to therapy and the time of the first sexual assault was 18.70 (SD 12.61) years for males and 16.63 (SD 12.74) years for females. The difference between these two means is statistically significant ( $t_{3300}=3.06$ ,  $P=.002$ , two-tailed), and the effect size (Cohen  $d=0.16$ , 99% CI 0.03-0.30) suggests a small but real nontrivial effect.

Scatterplots of the difference between the age at admission to therapy and the age at first sexual assault against the age at admission to therapy and the age at first sexual assault for male and female survivors are shown in Figures 5 and 6, respectively. The horizontal line at zero in Figure 5 represents the zero difference, which shows the male and female survivors across all ages who sought therapy soon after their first sexual assault. Moving up along the vertical axis, the difference between the age at which therapy was sought and the age at which the first act of sexual assault occurred increases, which is reflective of those who sought therapy after some time had passed since they experienced the first act of sexual assault. Figure 5 shows very

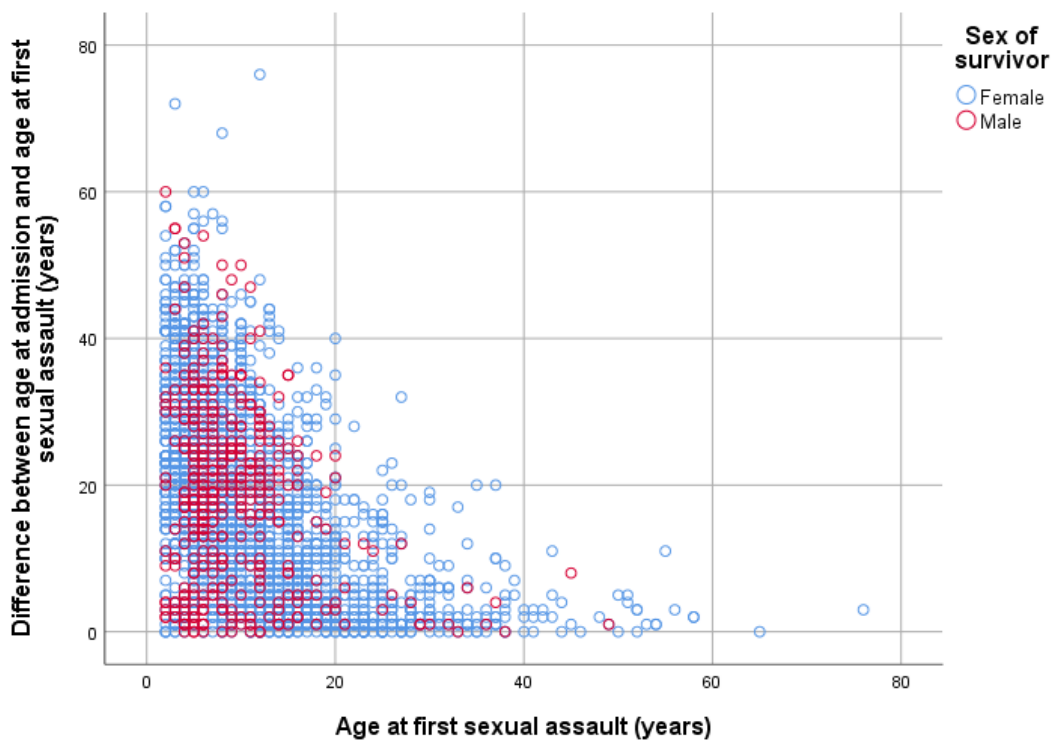
similar patterns for males and females, a positive linear relationship between the age at which therapy was sought and the number of years that had passed since experiencing the first act of sexual assault (Pearson  $r=0.75$ ,  $P<.001$ ), and that the majority of victims waited a long time after they were first sexually assaulted to seek therapy, with 36.9% (148/401) of males and 47.98% (1392/2901) of females waiting for up to 15 years to seek therapy. This leaves a majority of 63.1% of males and 52.02% of females who waited for over 15 years before seeking help.

The horizontal line at zero in Figure 6 represents the zero difference, which shows the male and female survivors who sought help soon after their first sexual assault. Moving up along the vertical axis, the difference between the age at which therapy was sought and the age at which the first act of sexual assault occurred increases, which is reflective of those who sought therapy after some time had passed since they experienced the first act of sexual assault. Figure 6 shows very similar patterns for males and females: a large proportion of survivors who were first sexually assaulted during the first 20 years of life waited a long time before seeking therapy; the older the survivors at the time of the first sexual assault, the more likely they were to seek therapy sooner than later; large proportions of males and females who were first sexually assaulted before the age of 20 years waited for more than 15 years before seeking therapy; and females who were first sexually assaulted after the age of 20 years were far more likely to seek therapy within 10 years of the assault.

**Figure 5.** Scatterplot of the difference between the age at admission and the age at first sexual assault against the age at admission for males and female survivors of sexual assault.



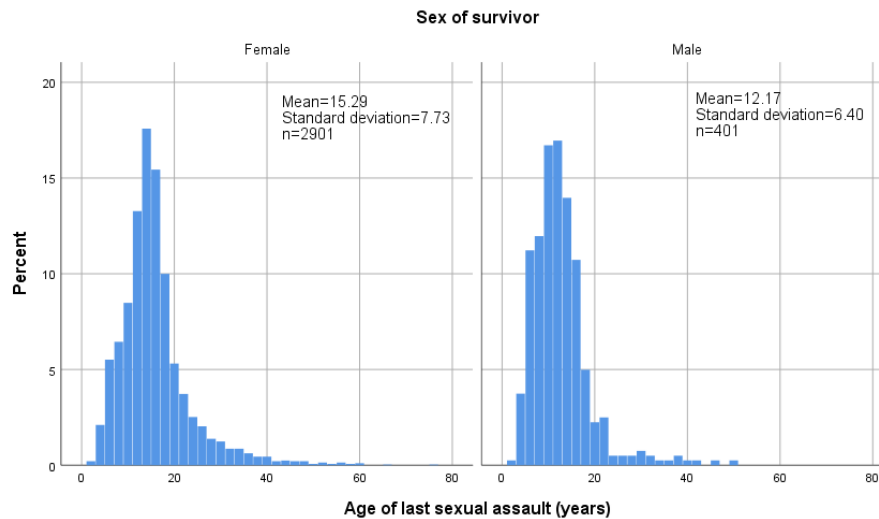
**Figure 6.** Scatterplot of the difference between the age at admission and the age at first sexual assault against the age at first sexual assault for male and female survivors of sexual assault.



**Age at Last Assault**

The age at which the 3302 survivors experienced their last sexual assault before seeking therapy was reported to be between 2 and 6 years by 288 (8.72%), 7 and 12 years by 1001 (30.31%), 13 and 17 years by 1235 (37.40%), 18 and 29 years by 606

(18.35%), and 30 years and older by 172 (5.21%). The ages at the last sexual assault ranged from 2 to 76 years, with a mean age of 14.91 (SD 7.65) years. The mode and the median age of the last sexual assault were 13 and 14 years, respectively. Frequency distributions of the age of male and female survivors at the time of the last sexual assault are shown in [Figure 7](#).

**Figure 7.** Frequency distributions of the age of male and female survivors of sexual assault at the time of last sexual assault.

The sample was separated into five groups based on the age of last sexual assault for male and female survivors, as shown in Table 4. Overall, 60.8% of all males (244/401) and 36.02% of all females (1045/2901) reported that their last sexual assault occurred between the ages of 2 and 12 years. Another 28.2% of all male survivors (113/401) and 38.68% (1122/2901) of all female survivors reported that their last sexual assault occurred between the ages of 13 and 17 years. Those who reported that their last sexual assault occurred after the age of 18 years comprised 11.0% of all male survivors (44/401) and 23.58%

(684/2901) of all female survivors. Males reporting their last sexual assault to have occurred between the ages of 2 and 12 years outnumbered females by approximately 2 to 1. In contrast, females reporting that their last sexual assault to have occurred after the age of 18 years outnumbered males by approximately 2 to 1. The 13 to 17 years at last sexual assault age group was the transitional group, wherein the proportion of females reporting sexual assaults started to increase relative to that of males.

**Table 4.** The number of male and female sexual assault survivors by age group at the time of the last sexual assault (N=3302).

Age at last sexual assault (years)	Value, n (%)	
	Male (n=401)	Female (n=2901)
1-6	61 (15.2)	227 (7.8)
7-12	183 (45.6)	818 (28.2)
13-17	113 (28.2)	1122 (38.7)
18-29	32 (8.0)	524 (18.1)
≥30	12 (3.0)	160 (5.5)

Table 5 shows the cross-tabulation of the age groups at the time of admission to therapy with the age groups at the time of last sexual assault for male and female survivors. The diagonal of this table represents the number of survivors who sought therapy (and therefore likely came to the attention of the system) during the same period when the last sexually abusive act occurred. Examination of Table 5 shows that for survivors between the ages of 7 and 12 years at the time of admission to therapy, three times as many girls (69/94, 73%) were seeking help for assaults that last occurred during the same period than for assaults that last occurred between the ages of 2 and 6 years (25/94, 27%). For boys aged 7 to 12 years at the time of therapy, 2.5 times as many (30/42, 71%) were seeking help for assaults that last occurred during the same period than for assaults that last occurred between the ages of 2 and 6 years (12/42, 29%). For

adolescents between the ages of 13 and 17 years at the time of therapy, 63.6% (225/354) of girls versus 30% (8/27) of boys were actually last assaulted during the same period. The remaining 36.4% (129/354) of girls and 70% (19/27) of boys reported their last assault to have occurred between the ages of 2 and 12 years. For young adults between the ages of 18 and 29 years at the time of therapy, 30.34% (372/1226) of women and 12.8% (16/125) of men were last assaulted during the same period. The remaining 69.66% (854/1226) of women and 87.2% (109/125) of men reported that they were last assaulted between the ages of 2 and 17 years. For those aged 30 years and older, 86.52% (1027/1187) of women and 93.7% (178/190) of men were seeking therapy for sexual abuse or assault that last occurred between the ages of 2 and 29 years.

**Table 5.** Age at admission to therapy by age at last sexual assault for male and female sexual assault survivors.

Age at admission	Age at last sexual assault (years)											
	1-6		7-12		13-17		18-29		≥30 years		Total	
	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male
<b>1-6 years</b>												
Count, n	40	17	0	0	0	0	0	0	0	0	40	17
Within age at admission group (%)	100	100	0	0	0	0	0	0	0	0	100	100
Within recent assault groups (%)	17.62	27.87	0	0	0	0	0	0	0	0	1.38	4.24
Proportion of total (%)	1.38	4.24	0	0	0	0	0	0	0	0	1.38	4.24
<b>7-12 years</b>												
Count, n	25	12	69	30	0	0	0	0	0	0	94	42
Within age at admission group (%)	26.60	28.57	73.40	71.43	0	0	0	0	0	0	100	100
Within recent assault groups (%)	11.01	19.67	8.44	16.39	0	0	0	0	0	0	3.24	10.47
Proportion of total (%)	0.86	2.99	2.38	7.48	0	0	0	0	0	0	3.24	10.47
<b>13-17 years</b>												
Count, n	20	6	109	13	225	8	0	0	0	0	354	27
Within age at admission group (%)	5.65	22.22	30.79	48.15	63.56	29.63	0	0	0	0	100	100
Within recent assault groups (%)	8.81	9.84	13.33	7.10	20.05	7.08	0	0	0	0	12.20	6.73
Proportion of total (%)	0.69	1.50	3.76	3.24	7.76	2.00	0	0	0	0	12.20	6.73
<b>18-29 years</b>												
Count, n	67	14	348	64	439	31	372	16	0	0	1226	125
Within age at admission group (%)	5.46	11.2	28.38	51.2	35.81	24.8	30.34	12.80	0.0	0.0	100	100
Within recent assault groups (%)	29.52	22.95	42.54	34.97	39.13	27.43	64.81	50.00	0.0	0.0	42.26	31.17
Proportion of total (%)	2.31	3.49	12.00	15.96	15.13	7.73	12.82	3.99	0.0	0.0	42.26	31.17
<b>≥30 years</b>												
Count, n	75	12	292	76	458	74	202	16	160	12	1187	190
Within age at admission group (%)	6.32	6.32	24.60	40	38.58	38.95	17.02	8.42	13.48	6.32	100	100
Within recent assault groups (%)	33.04	19.67	35.70	41.53	40.82	65.49	35.19	50.00	100	100	40.92	47.38
Proportion of total (%)	2.59	2.99	10.07	18.95	15.79	18.45	6.96	3.99	5.52	2.99	40.92	47.38
<b>Total</b>												
Count, n	227	61	818	183	1122	113	574	32	160	12	2901	401
Within age at admission group (%)	7.82	15.21	28.18	45.64	38.68	28.18	19.79	7.98	5.52	2.99	100	100
Within recent assault groups (%)	100	100	100	100	100	100	100	100	100	100	100	100
Proportion of total (%)	7.82	15.21	28.18	45.64	38.68	28.18	19.79	7.98	5.52	2.99	100	100

Histograms of the difference between the age at admission to therapy and the age at which the last sexual assault occurred for male and female survivors are shown in [Figure 8](#). For male survivors, approximately 10.5% (42/401) sought therapy within 1 year of their last sexual assault, and approximately 20.2% (81/401) sought help within 3 years of the last assault. The majority (79.8%) waited up to 53 years before they sought help, with 44.9% (180/401) waiting for 10 to 28 years before they sought help.

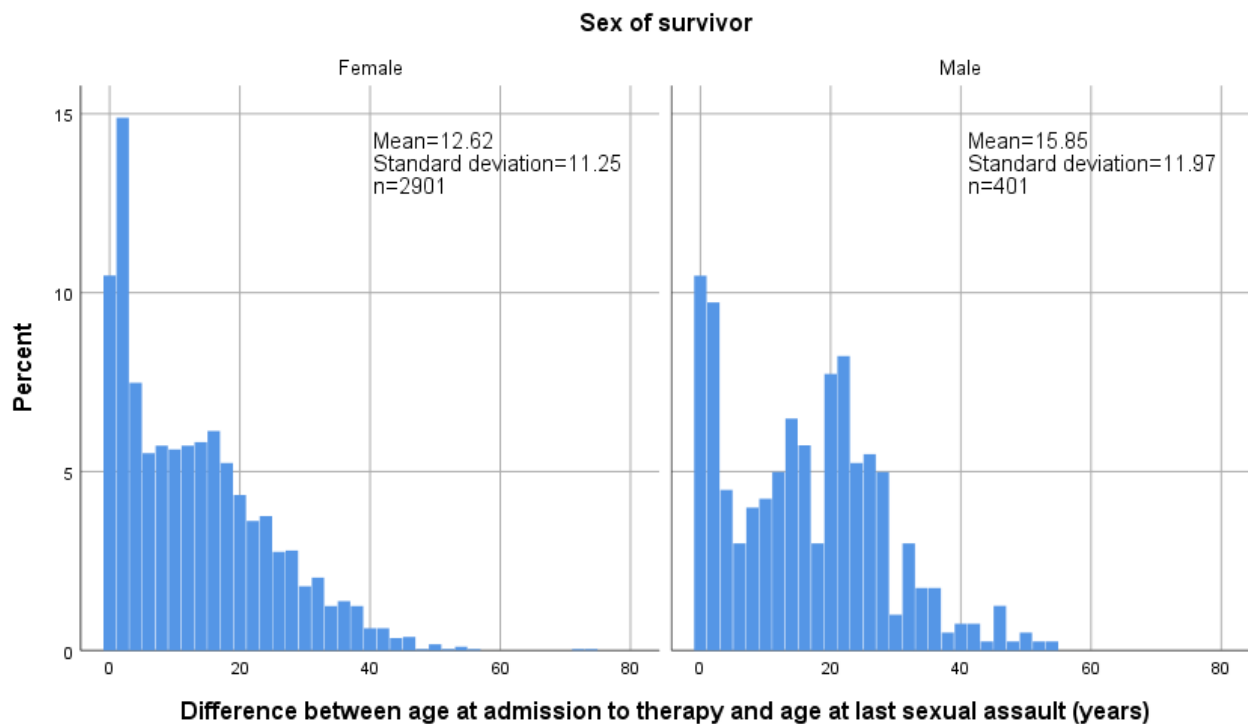
On the other hand, 10.48% of female survivors (304/2901) sought help within 1 year of their last sexual assault, and 25.37% (736/2901) sought help within 3 years of the last sexual assault.

The majority (74.63%) of females waited up to 73 years after their last sexual assault to seek therapy, with 40.19% (1291/2901) waiting for approximately 10 to 28 years before they sought help. Also, 44.50% of females waited between 6 and 18 years from the last sexual assault to seek therapy. The proportion of females who waited for a longer period than 18 years from the last assault decreased gradually as the waiting period increased.

The average time difference between the age at the time of admission to therapy and the age at the time of the last sexual assault was 15.85 (SD 11.97) years for males and 12.62 (SD 11.25) years for females. The difference between these two

means was statistically significant ( $t_{3300}=5.34$ ,  $P<.001$ , 2-tailed), with an effect size (Cohen  $d$ ) of 0.28 (99% CI 0.14-0.42), suggesting a moderate and real nontrivial effect.

**Figure 8.** Frequency distributions of the difference between the age at the time of admission to therapy and the age at the time of the last sexual assault for males and female survivors of sexual assault.



Scatterplots of the difference between the age at admission and the age at last sexual assault against the age at admission and the age at last sexual assault for male and female survivors are shown in Figures 9 and 10, respectively. The horizontal line at zero in Figure 9 represents the zero difference, which shows the males and females who sought therapy soon after their last sexual assault. Moving up along the vertical axis, the difference between the age at which therapy was sought and the age of last assault increases, which is reflective of those who sought therapy after some time had passed since their last sexual assault was experienced. Figure 9 shows very similar patterns for males and females: a positive linear relationship existed between the age at which therapy was sought and the number of years that had passed since experiencing the last act of sexual assault ( $r=0.73$ ,  $P<.001$ ); and one group of all ages sought therapy soon or waited up to 5 years after the last sexual assault, a second group aged 13 to 40 years sought therapy after waiting for up to 25 years from the time of their last sexual assault, and a third group aged 40 years and older at the time of therapy experienced their last sexual assault between the ages of 10 and 15 years.

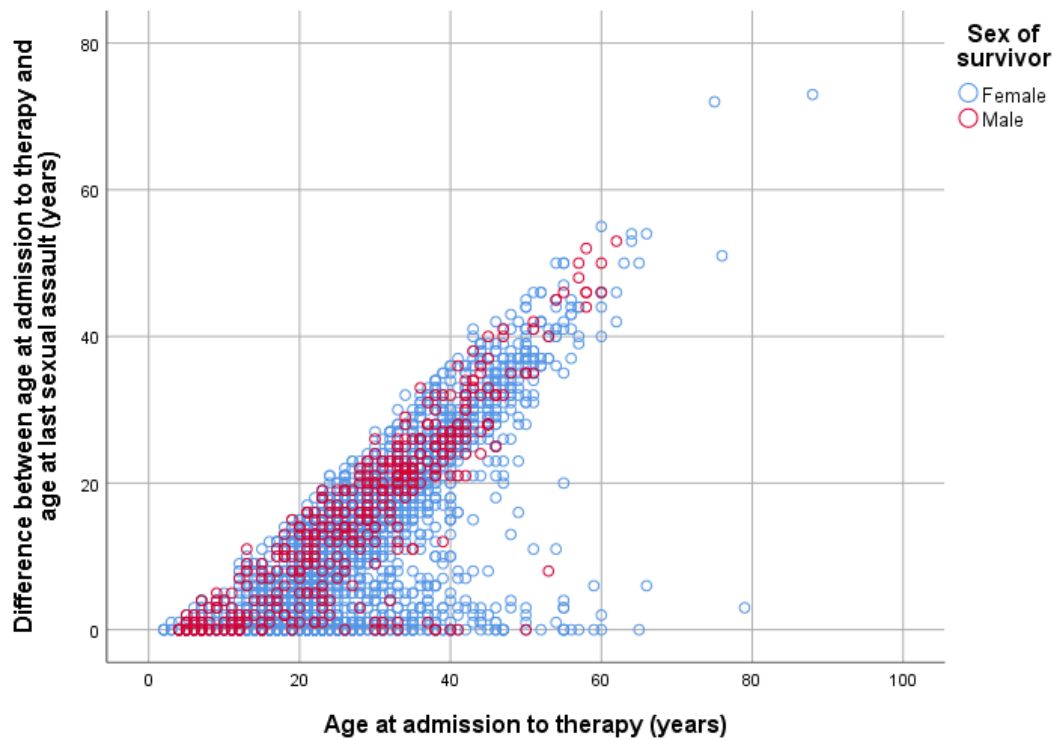
The horizontal line at zero in Figure 10 represents the zero difference, which shows the male and female survivors who sought help soon after they were last sexually assaulted. As we move up along the vertical axis, the difference between the age at which therapy was sought and the age at which the last sexual

assault occurred increases, which is reflective of those who sought therapy after some time had passed since their last act of sexual assault was experienced. Figure 10 shows that males and females follow the same pattern; that aside from the few who sought therapy soon after being sexually assaulted, the vast majority who were last assaulted between the ages of 2 and 20 years waited decades, up to 50 years, to seek therapy; that those who were last assaulted after age 20 years were more likely to seek therapy within 10 years of the assault; and that the older the person was at the time of the last sexual assault, the more likely that person was to seek therapy sooner than later.

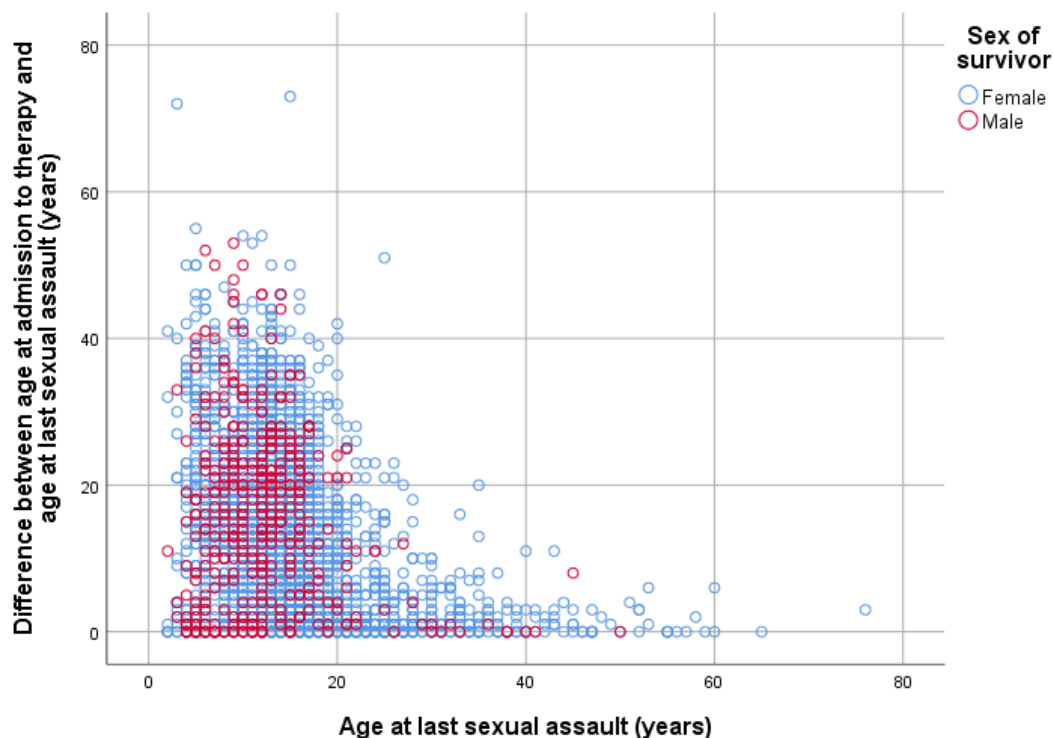
Focusing on the male survivors, Figure 10 shows that very few males sought help soon after their last sexual assault, with the vast majority of male survivors seeking help years after the last sexual assault. It appears that males who experienced their last sexual assault early in life were more likely to seek help sooner, but a large proportion of males who were last sexually assaulted at a young age waited for more than 20 years before seeking help.

Finally, it should be noted that two-thirds of the survivors in the sample were sexually abused and/or assaulted over a period of time. The mean time difference between the age at first assault and the age at last assault for males was 2.85 (SD 3.41) years, and that for females was 4.00 (SD 4.56) years.

**Figure 9.** Scatterplot of the difference between the age at admission to therapy and the age at last sexual assault against the age at admission to therapy for male and female survivors of sexual assault.



**Figure 10.** Scatterplot of the difference between the age at admission to therapy and the age at last sexual assault against the age at last sexual assault for male and female survivors of sexual assault.



## Discussion

### Principal Findings

The purpose of this study was to investigate the differences between male and female survivors of sexual abuse and sexual

assault regarding the age of onset of abuse, the age of last assault, and the age at which the survivors entered therapy. All 3302 participants sought therapy for the first time for their sexual abuse or assault by one offender, who offended against them over a period of time. Those who sought therapy immediately after one sexual assault and those who were

assaulted by two or more offenders at different times were removed from the analysis. The data were collected over a 7-year period from eight sexual assault centers in the province of Alberta, Canada. Sexual abuse was defined as a sexual act with a person under the age of 18 years, whereas sexual assault was defined as a sexual act between persons over the age of 18 years without consent.

The results show that 1 male survivor sought therapy for sexual abuse or assault for every 7 female survivors. This finding is consistent with the general perception that more female than male survivors seek help for their sexual abuse or assault. There is little doubt that females are more inclined to seek help for past and present sexual abuse or assault than males [41,42]. It should be noted that the focus of this study was on those females and males who sought help for their sexual abuse or assault; therefore, it should not be surprising if some results are inconsistent with those of several other studies. Most of those studies surveyed school, college, and university students [11,37,43]; people in the general population shortly or a long time after the discovery of sexual abuse [9,10,29,38,41]; or law enforcement and child services reports of sexual abuse or assault [16-21,25-28]. As such, the sample of this study is restricted to those who sought help, and therefore it cannot be generalized to the population of survivors of sexual abuse and assault. Therefore, the ratio of 7:1 is reflective of those female and male survivors who sought help and not those who reported incidents of sexual abuse and assault.

This large 7:1 ratio in favor of female survivors suggests that there are many male survivors of sexual abuse who are not seeking help. Even if conservative estimates are used, in which the risk of being sexually abused is the same for males and females, or females are at twice the risk of being sexually abused as males [10], the resulting large number of male survivors who are not seeking help and/or are not coming to the attention of the legal and support systems is alarming. It is reasonable to suggest that if males are unlikely to seek help, they are unlikely to report sexual abuse or assault. Indeed, females are more apt to report sexual abuse than males. A study found that 30% of males and 16% of females had never reported their abuse [30], and another argued that males' reluctance to disclose sexual abuse might explain the difference in reporting between males and females [39]. This raises a question: are females truly more vulnerable to be sexually abused, or is the ratio of female to male survivors the result of the male survivors' reluctance to report and/or seek help for the abuse? The collective findings of this study based on the different age groups who sought therapy suggest that both males and females are equally vulnerable to being sexually abused and that males are more vulnerable to being abused at younger ages, whereas females are vulnerable at all ages. Generally, these results are consistent with previous findings [3,23,24,36].

At approximately 28 years of age, the average age of male and female survivors at the time of admission to therapy does not differ. However, although there is a slight difference in the odds (5%) between male and female survivors aged 2 to 12 years at the time of therapy, when adolescents aged 13-17 years were compared with children aged 7-12 years at the time of entry to therapy, the odds of being an adolescent girl were 6 times greater

than those of being a boy between 2 and 12 years of age. These results should not be surprising, as children are likely to be brought to therapy by their caregivers, who are unlikely to treat young male and female survivors differently in terms of seeking medical or psychological help. On the other hand, adolescents are likely to be more in control of disclosure and seeking therapy; therefore, adolescent boys, considering their social upbringing and the societal norms surrounding boys, are less likely to seek therapy. This resistance to therapy seems to decrease after boys leave adolescence.

The age of onset of sexual abuse was reported to be between 2 and 6 years by one-third of the sample, with another one-third reporting the age of onset to be between 7 and 12 years. For 82.3% and 65.77% of male and female survivors, respectively, who reported ages of onset between 2 and 12 years, the average age of onset was 6.71 (SD 2.86) years. These results are consistent with the finding that CSA can begin when children are as young as a few months old and can last well into adulthood, with an average age of onset of approximately 5 (SD 3.7) years [12] and with the finding that the age of onset of sexual abuse for a sample of 246 children was 6.3 (SD 3.5) years [40].

The odds of experiencing the first sexual assault during childhood, as opposed to adolescence, are approximately 4 to 1 for females and 9 to 1 for males, and the odds that males will experience their first sexual assault in childhood are approximately twice those of females. Thus, male survivors are 2 times more likely than female survivors to experience their first sexual assault in childhood. These results are based on the reports made by those who sought therapy and are difficult to compare with the results of other studies in which investigations and disclosures are the basis of the results, such as the findings that substantiated cases of CSA consisted of 69% girls and 31% boys in 1998 [19] and 63% girls and 27% boys in 2003 [36]; the report that females show twice the risk of sexual abuse of males as children and during adolescence [10]; the finding that the CSA female to male ratio was about 2.5 [24]; and the conclusion that females have a 2 to 3 times greater risk of experiencing CSA than males and that 10% of females will experience forced intercourse before the age of 18 years [3].

At the time of admission to therapy, 66% of female and 82% of male adolescents reported being first assaulted between the ages of 2 and 12 years. Only 9% of male and 16% of female survivors sought therapy within the first 2 years of their first sexual assault; meanwhile, 19% of males and 33% of females sought help within 5 years, and 81% of males and 67% of females waited for up to 60 and 76 years, respectively, before they sought help, with 35% of males and 38% of females waiting for 16 to 26 years before they sought help. These results show that the majority of survivors waited for a long time before seeking help and that more males than females waited for longer periods to seek help after they were first sexually assaulted.

On average, the difference between the males' waiting time of 18.70 (SD 12.61) years from the time of the first assault to the time of seeking help and females' waiting time of 16.63 (12.74) years is statistically significant, with a small but real nontrivial effect size.



Positive linear relationships for male and female survivors were found between the age at which therapy was sought and the number of years that passed since the first act of sexual assault was experienced. The older the survivors were at the time of the first sexual assault, the more likely they were to seek therapy sooner. A large proportion of males and females who were first sexually assaulted before the age of 20 years waited for more than 15 years before seeking therapy, and women who were first sexually assaulted after the age of 20 years were far more likely to seek therapy within 10 years of the assault.

The conclusion that adolescents, compared to children, are more likely to have been abused at least 10 times (adolescents, 40%, vs children, 26%) [11] is understandably not supported. In this study, the focus was on those who had experienced sexual abuse involving physical contact, whereas in that study, sexual abuse was experienced at the verbal level [11]. It makes sense that adolescents may experience more verbal sexual abuse than children and, of course, that those who experience such abuse will rarely come to the attention of the system or seek help. On the other hand, when sexual abuse is defined in terms of physical contacts, the results of this study show the same trends as those reported in a study that found children were more likely to be abused than adolescents by a ratio of as much as 9 to 2 [9]. Another disturbing observation that may be made from these results is that far fewer children come to the attention of the system and seek help when they really need it. The vast majority of survivors wait until much later or until they are in their adult years to seek help for past abuse or assault, perhaps when they realize that their past experience is impacting their current life. These results are consistent with the finding that 30% to 80% of survivors do not report until adulthood [31]; the conclusion that 68% reported CSA after adulthood [29]; and the results that males may take up to 10 years to disclose CSA, compared with shorter periods for females [39].

Among the survivors, 1 in 10 males and 1 in 4 females reported their last sexual assault to have occurred after the age of 18 years. Males who were last sexually abused before the age of 12 years outnumbered females by a ratio of 2:1, and females who were last sexually assaulted after the age of 18 years outnumbered males by a ratio of 2:1. These ratios suggest that male children are more vulnerable to being sexually abused before the age of 12, and females are vulnerable to be sexually assaulted after the age of 18 years. Approximately 70% of women and 87% of men aged 18 to 29 years sought therapy for sexual assaults that occurred between the ages of 2 and 17 years. Similarly, 87% of women and 94% of men aged 30 years and older were seeking therapy for sexual assaults that last occurred between the ages of 2 and 29 years. These data suggest that, at least between 1994 and 2003, a large number of people lived in silence with their sexual abuse or assault for many years. It would be useful to know if this attitude of "living in silence" is still prevalent today, considering the amounts of exposure and education that have taken place over the past 15 years.

A statistically significant difference with a moderate real nontrivial effect size was found between male and female survivors for the average time difference between the age of the last sexual assault and the age of seeking therapy. Males waited for an average of approximately 3 years longer to seek

therapy than females. However, males and females appeared to follow a similar pattern in that the vast majority of those who were last assaulted between the ages of 2 and 20 years waited up to 50 years to seek therapy, those who were assaulted after age 20 years were more likely to seek therapy within 10 years of the assault, and the older the survivor was at the time of the last assault, the more likely they were to seek therapy sooner. As was indicated in [39], the reluctance of males to disclose experiences of CSA and sexual assault is reflected by the length of time males take to reveal such experiences. Thus, the difference between males and females in reporting may be due to males' reluctance to disclose CSA experiences.

### Limitations

There are some limitations to this study. First, the relatively small size of the male sample compared to that of the female sample poses one limitation. Second, while those who seek therapy and report sexual abuse and sexual assault may be a better and more accurate source of information about the incidence of sexual abuse and assaults, the fact that they are seeking therapy is a limitation. The results of this study are limited to males and females who sought therapy, and the results cannot be generalized to all survivors of sexual abuse. At the time of admission to therapy, proportionately, many more males than females in this sample reported being first assaulted when they were children. The presence of a large percentage of male survivors who reported being first sexually abused during childhood may be reflective of the proportion of male survivors of sexual abuse in the population or reflective of the much higher number of sexually abused male children under the age of 12 years than has been reported.

Third, the sole reliance on the survivors' memories of past sexual abuse and assault imposes another limitation. It is well established that despite their best efforts, individuals' memories are constructed and diluted. Although no details that are most susceptible to memory distortion were used, the ages at which at the first assault and last assault occurred, particularly if historical, may not be accurate.

Fourth, the events the clients described occurred between 1994 and 2003 or before 1994. The time of the collection of the data imposes another limitation. It would be of great interest to compare these results with results based on more recent data. It is to be hoped that progress has been made over the past 25 years, but the question remains: has it?

### Conclusions

Eight sexual assault centers saw a total of 4317 survivors in the province of Alberta, Canada. This study focused on a total of 3302 survivors of CSA and/or sexual assault, of whom 2901 (87.86%) were female and 401 (12.14%) were male. Overall, for every male survivor, 7 female survivors sought therapy for their sexual abuse or assault.

At the time of admission to therapy, the proportions of male survivors aged 2 to 6 and 7 to 12 years (4.2% and 10.5%, respectively) were 3 times greater than the same proportions of female survivors (1.38% and 3.24%, respectively). This pattern was reversed for those aged 13 to 17 years and 18 to 29 years, in which the proportions of male survivors (6.7% and 31.2%,

respectively) were one-half to two-thirds those of female survivors (12.20% and 42.26%, respectively). For survivors over 30 years of age, the proportion of males was 47.4%, and the proportion of females was 40.92%.

It appears that a minority of children are seeking help within a short period of being assaulted. Of those male and female survivors between 18 and 29 years of age at admission, 42.40% and 29.93% were first assaulted between the ages of 2 to 6 years, 39.20% and 29.45% were first assaulted between the ages of 7 and 12 years, and 11.20% and 19.17% were first assaulted between the ages of 13 and 17 years. This means that almost 80% of females and 93% of males aged 18 to 29 years sought therapy for sexual abuse and sexual assault that was first experienced when they were children between the ages of 2 and 12 years. It is clear that most adults seek therapy for sexual abuse or assault that occurred many years earlier during childhood.

At the time of the first sexual assault, 39.7% of male and 34.02% of female survivors were between 2 and 6 years old, 42.6% of male and 31.75% of female survivors were between 7 and 12 years old, 9.7% of male and 16.75% of female survivors were between 13 and 17 years old, and 8.0% of male and 17.48% of female survivors were over 18 years old. It seems that as children age, the risk of being assaulted for the first time decreases. That is, males and females are most vulnerable to experiencing their first sexual assault when they are children.

The presence of a large percentage of male survivors who reported being first abused as children is likely not to be reflective of the proportion of male survivors of sexual abuse in the population but rather to be reflective of those who seek therapy for sexual abuse.

Based on reports of the last sexual assault, 15.2% of males and 7.82% of females reported being sexually abused between the ages of 2 and 6 years. Boys between the ages of 7 and 12 years are at the highest risk of sexual abuse, at 45.6% (vs females, at 28.20%), whereas girls between the ages of 13 and 17 years are at the highest risk of sexual abuse at 38.68% (vs boys at 28.2%). Female adolescents as a group are more vulnerable to being sexually assaulted than their male counterparts and any other age group. Females continue to be assaulted more frequently in adulthood than males. Approximately 89% of the male survivors experienced their first sexual abuse before the age of 18 years and 11% experienced it after the age of 18 years, whereas 75% of females experienced their sexual abuse before the age of 18 years and 25% experienced it after the age of 18 years.

Prevention and intervention programs must be made available to all age groups. Intervention programs should start in preschool and continue to grade 12 on a regular and continuous basis, and they should be made part of sex education curricula.

## Conflicts of Interest

None declared.

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## Abbreviations

**CSA:** child sexual abuse

**OR:** odds ratio

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Original Paper

# Medical Brain Drain From Southeastern Europe: Using Digital Demography to Forecast Health Worker Emigration

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## Abstract

**Background:** This paper shows that the tools of digital demography, such as Google Trends, can be used for determining, estimating, and predicting the migration of health care workers (HWs), in this case, from Croatia and the Western Balkans (WB) to Germany and Austria.

**Objective:** This study aims to test the usefulness of Google Trends indexes to forecast HW migration from Croatia and the WB to Germany and Austria. The paper analyzes recent trends in HW mobility in Europe and focuses specifically on mobility patterns among medical doctors and nurses using digital demography. Without increased emigration in the last 10 years, Croatia and the WB would have 50% more HWs today, and this staff is now crucial in the fight against a pandemic. Furthermore, the COVID-19 pandemic contributed to the increase in emigration.

**Methods:** A particular problem in analyzing the emigration of HCWs from Croatia and the WB is that there is no system for monitoring this process. Official data is up to 3 years late and exists only for persons deregistered from the state system. Furthermore, during the pandemic, the “normal” ways of data collection are simply too slow. The primary methodological concept of our approach is to monitor the digital trace of language searches with the Google Trends analytical tool. To standardize the data, we requested the data from January 2010 to December 2020 and divided the keyword frequency for each migration-related query. We compared this search frequency index with official statistics to prove the significance of the results and correlations, and test the model’s predictive potential.

**Results:** All tested migration-related search queries, which indicate HCWs’ emigration planning, showed a positive linear association between Google index and data from official statistics (Organisation for Economic Co-operation and Development: Serbia  $R^2=0.3381$ , Bosnia and Herzegovina [B&H]  $R^2=0.2722$ , Croatia  $R^2=0.4515$ ). Migration-related search activities such as “job application + nurses” from Croatia correlate strongly with official German data for emigrated HWs from Croatia, Serbia, and B&H. Decreases in Google searches were correlated with the decrease in the emigration of HWs. Thus, this method allows reliable forecasts for the future.

**Conclusions:** This paper highlights that the World Health Organization’s list of countries with HWs shortages should be updated to include Croatia and the countries from the WB. The issue of the European Union drawing HWs from the EU periphery (Croatia) and nearby countries (B&H, Serbia) clearly shows a clash between the EU freedom of movement and the right to health care and

a need to ensure a health care workforce in all European regions. Understanding why HWs emigrate from Croatia and the WB, and the consequences of this process are crucial to enabling state agencies and governments to develop optimal intervention strategies to retain medical staff. The benefit of this method is reliable estimates that can enable a better response to a possible shortage of HWs and protect the functioning of the health system. The freedom of movement of workers in the EU must be supplemented with a common pension and health care system in the EU.

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## KEYWORDS

digital demography; Google Trends; the emigration of doctors and nurses; medical brain drain; Croatia; demography; brain drain; emigration; doctors; nurses; Western Balkans; health care workers; health professionals; health systems; jobs; Germany; personnel; migration; workforce; medical professionals

## Introduction

### Background

The health care system across Europe faces demographic ageing of both staff and users, increasing the demand for health needs and care. On the one hand, the demand and, on the other hand, the supply and low wages of medical labor are shaping the current situation in the European Union. One-third of the EU 27 members are affected by the shortage of nurses, and one-half of the EU 28 countries report shortages of medical doctors [1]. The COVID-19 emergency has again confirmed that all EU countries have weaknesses in their health system, and one of them is the inadequate supply of health workers [2]. Developed EU countries are tackling the shortage by immigrating health workers, mainly from Croatia and the Western Balkans (WB). At the same time, in the countries from which health workers emigrate, negative consequences are felt, which is even more pronounced during the pandemic. In addition, the pandemic will likely increase global competition for doctors [3] and nurses.

European Observatory books on health workers' mobility [4] showed in 2015 that there are gaps in understanding the magnitude of health professional mobility, particularly concerning EU enlargement. "There is also no overview of the motivators that drive the mobile European health workforce...or any systematic mapping of the impacts of health professional mobility." In addition, it is emphasized that knowledge on country responses to health professional mobility in the European Union is limited [4]. Despite this, there were no significant developments [2]. The World Health Organization (WHO) report [5] about countries with critical health workforce shortages does not even state that these issues are also relevant in European countries and that the list should be updated to include the countries Bosnia and Herzegovina (B&H), Serbia, and Croatia.

### A New Approach in the Field of Health Care Worker Migration

A particular problem in the analysis of the emigration of health care workers (HWs) from Croatia and the WB is that there is no system for monitoring this process. Official data is up to 3 years late and exists only for persons who have deregistered or, in the case of non-EU countries, requested a work visa as a medical professional. However, measuring HW mobility is a challenge for most countries, and therefore, new policy

instruments and coordination at the EU level and new methods of monitoring trends in the movement of medical staff should be introduced. This study shows that the analytical tool Google Trends (GT) can give useful complement data to the knowledge of demography, especially in the field of HW migration in the European Union.

After briefly showing the results of relevant studies in the next section, we will focus on the emigration of health care professionals from Croatia and the WB to Germany and Austria, and the results we gained with the approach of digital demography. We used Croatia, Serbia, and B&H as a case study because this region is, according to the United Nations (UN), demographically one of the most affected regions due to depopulation in the world [6] and a region with a critical shortage of medical staff. In addition, there are no studies of this type (digital demography) in Croatia and the broader region of Southeast Europe. The primary hypothesis of this paper is that the analytical tool GT is a valuable source of data for determining, estimating, and predicting migrations of HCWs.

### Emigration of Health Workers From Croatia and the Western Balkans to Germany and Austria

#### *Methodological Confusion in Data Collection About the Migration of Health Workers*

Literature on the emigration of health workers from the countries of the WB and Croatia is scarce. Particularly useful contributions specific to the WB are the works of Mara [2,7], while the works on a broader topic come from the authors Adovor et al [8], Britnell [9], and The European Observatory on Health Systems and Policies [10]. Zeisler et al [11] presented an engaging innovative methodological approach to data collection (albeit with classical methods). However, none of the papers managed to resolve the methodological confusion in data collection about the migration of health workers or estimate the exact number of emigrated nurses and doctors from Croatia and the WB. In all three analyzed countries (B&H, Serbia, and Croatia), no single authority documents health professional mobility. Therefore, this required a more comprehensive search for documentation in international sources. Official data from Eurostat, UN, Organisation for Economic Co-operation and Development (OECD), Bundesamt für Migration und Flüchtlinge, and DESTATIS were used to estimate the number of medical staff from B&H, Serbia, and Croatia who emigrated to EU countries, while digital demography was used to model future trends.

A fundamental limitation in the preparation of the paper is the shortage of official data from domestic institutions on the number of emigrated health workers. A particular problem in demographic research in Southeast Europe is the methodological inconsistency and questionability of official data at several levels (unpublished study by Jurić). Another problem is the impossibility of comparing data identically for Croatia, B&H, and Serbia due to the lack of the same methodology in collecting data. Croatian doctors and nurses as citizens of the European Union can freely migrate and work in Germany and Austria, but doctors and nurses from Serbia or B&H need visas.

### **Emigration From Croatia, Serbia, and B&H Since 2013**

Since it became a member of the European Union in 2013, an average of 50,000 people emigrate from Croatia every year, most often to Germany (85% of all emigrants) [12]. In the first half of 2019, Croatia, along with Bulgaria, had the highest percentage of emigration of all EU members [13].

Data for B&H shows that from 2014 to 2018, a net reduction in the workforce, primarily due to emigration, was 113,000 workers, or 10% of the total workforce (unpublished study by Jurić). According to Eurostat data [14] in the period 2014-2019, the number of citizens from B&H who were granted the first permit by any reason in the European Union was 226,519. The structure by country shows that most people from B&H are emigrating to Germany (35.68%), Slovenia (18.40%), Croatia

(18.13%), and Austria (10.00%). The structure of issued permits shows that, since 2016, the dominant reason for emigration is to work in another country (58.26% in 2019) (unpublished study by Jurić).

According to OECD, in the period 2014-2019, the population of Serbia decreased by 187,688. Like in B&H, most permits are issued to citizens in the category 25-45 (unpublished study by Jurić). Of this number, 60.09% emigrated to Germany, 14.16% to Austria, and 4.94% to Slovenia [15]. Eurostat data for the period 2014-2019 showed that the European Union issued 248,759 first permits for any reason for Serbian citizens [16], which is 3.59% of the total population of Serbia. Of this number, 100,315 or 40.3% were issued for work purposes (unpublished study by Jurić).

### **Nurses From Croatia and the Western Balkans in Germany**

According to the German Federal Employment Service, in 2019, over 65,000 citizens of Croatia and the WB work in Germany's health and care sector. According to estimates [17], Germany imports more than 10,000 caregivers and nurses from Croatia and the WB every year, mainly from B&H and Serbia but also from Macedonia, Kosovo, etc [18]. In 2017, of the 4600 foreign-trained nurses who moved to Germany, close to 32% originated from WB countries [2] (Table 1).

**Table 1.** Number of nurses from Croatia and the Western Balkans in Germany in 2018 and 2019 (n=57,288 from the Western Balkans and n=7500 from Croatia).<sup>a</sup>

Year	B&H <sup>b</sup> , n	Serbia, n	Kosovo, n	Albania, n	North Macedonia, n	Montenegro, n
2018	19,631	13,598	7204	5206	4094	993
2019	21,789	15,216	8050	6642	4487	1104

<sup>a</sup>Source: Own elaboration from Statistik der Bundesagentur für Arbeit [19].

<sup>b</sup>B&H: Bosnia and Herzegovina.

Abeitsagentur does not give data for Croatia, but OECD shows that in the period from 2011 to 2019, 1283 nurses emigrated from Croatia to Germany, while the Croatian chamber shows 7500. When we put these data of 65,288 emigrated HWs from this region in context, we can see that this is a higher number than the total number of nurses in Croatia and B&H together. Without such intense emigration in the last 10 years, the regions of Croatia and the WB would have 50% more HCWs today. It is necessary to emphasize that this staff is crucial in the fight against a pandemic.

Concerning the trained staff, the numbers become even more alarming. In Croatia, for example, in the last 5 years, an average of 5100 nurses have completed their education annually, while in all medical faculties in Croatia in the past 5 years, an average of 700 doctors have graduated annually [20]. At the same time, about 140 doctors annually leave the country [21]. Currently, Croatia is among the three EU countries from which most doctors and nurses emigrate [22].

According to official data, every fourth nurse has emigrated from Croatia to Germany in the last 10 years [23]. According to the HSSMS syndicate [24], Croatia had a shortage of 12,000

nurses even before this epidemic, and according to official statistics, 3180 nurses and technicians went abroad directly from the system from 2013 to 2018 alone, most often to Germany. In the period from 2009 to 2013, 4279 nurses emigrated [25]. The stated data refer only to medical personnel employed in the Croatian health care system, while the number of those who left immediately after finishing school is unknown. So, in the past 10 years alone, 7500 to 8000 nurses have left the health care system in Croatia, making one in four nurses from the system numbering 28,000 [21].

### **Emigration of Doctors**

According to the Digital Atlas of Croatian Medicine [26], more than 1000 specialist doctors emigrated from Croatia. Another 940 were looking for a letter of resignation. By 2025, the Croatian health care system will have lost another 2700 doctors due to retirement or emigration, according to the estimates by the Croatian Medical Chamber [27]. When considering that in Croatia in 2020 there were 14,094 doctors, these numbers only become alarming in context.

The average age of emigrated doctors from Croatia is 36 years, and the average age of all doctors in the Croatian system is close

to 50 years [26]. When considered with how many doctors have emigrated or are preparing for this act in 2020 and 2021 (14%) and the fact that in the next 5 years 2255 doctors will retire (which is 15% of the total number of employees in health care today), it can be concluded that Croatia will lose more than one-third of all doctors in 5 years. Primary health care is the most endangered in terms of staff, and there is already a shortage of 204 family doctors, 75 pediatricians, and 103 gynecologists [23]. There are 2142 family doctors in Croatia, but a third of them are older than 60 years. In Croatian resources, however, no trained staff can replace them [28].

The additional problem is that, due to the decreasing number of children in the family, the circle of care for older adults is decreasing. It will be increasingly difficult for future older people to find someone to provide them with immediate care [29] especially because the average pensioner in Croatia and countries of the WB cannot pay for the various types of services he may need from his current income. All this will lead to the growth of expectations from state care institutions.

In Serbia and B&H, the loss of doctors almost doubled between 2010 and 2017, reaching 14% (B&H total doctors abroad: 1688) and 8% (Serbia total doctors abroad: 3339), respectively, in 2017 [2].

OECD shows that the WB countries have the lowest density of health professionals relative to their populations, while at the same time the number of health graduates in per-capita terms is one of the lowest in Europe [30]. Therefore, a further intensification of outward mobility for this category of workers might be devastating for the region [2]. In addition, the WHO Global Code of Practice on the International Recruitment of Health Personnel [31] deems that the recruitment from health systems affected by shortages of health professionals should be avoided. Despite these warnings and although these trends are against the proclaimed values of the European Union and cohesion policy itself, no concrete measures have been taken at the EU level. Therefore, this paper again points to these issues and, regarding the WHO report [5] about countries with critical health workforce shortages, highlights that these issues are also relevant in European countries. The appeal of the paper is that the list should be updated to include the countries B&H, Serbia, and Croatia.

## The Shortage of Health Care Workers in Germany and Austria

### Germany

According to projections, the potential labor force in Germany will decrease by 16.2 million workers between 2012 and 2050 for purely demographic reasons [19]. The German generations with the highest birth rates will have left working life around 2035. According to model calculations, the net migration with countries of the European Union will soon drop significantly from the current number to slightly below 300,000 [19]. For the next 36 years, an average of between 276,000 and 491,000 people would have to immigrate from third countries every year to Germany for the labor force potential to remain constant [32]. It seems to be that Croatia and the WB are particularly targeted

here. For this reason, in 2020, Germany lifted restrictions on work for people from the WB [33,34].

According to a 2015 study by Bertelsmann Stiftung, in the year 2021, Germany must introduce around 100,000 employees in the field of medical care alone, while it was estimated that as many as 200,000 caregivers would be missing by the year 2021 [32]. In the EU health sector, an increase of 1.8 million jobs is expected by 2025 (an increase of 8.1% compared to the current situation). In the same period, 50% of health professionals in the European Union are expected to retire or leave the health sector, creating 11.6 million jobs, which is more than in any other sector [19]. Between 2000 and 2017, employment in the health sector in the European Union has been rising by 42%, compared with a 15% rise in overall employment [30]. On average, the health sector absorbs about 10% of the workforce in the European Union [30].

As previously shown, Germany and Austria today are undoubtedly addressing their HCW shortages by importing HWs from Croatia and the WB, and this trend became even more noticeable during the COVID-19 pandemic (see Results section).

According to the latest data from the German Employment Service, it is evident that every German federal state has a deficit in occupations in the field of care for older adults. In contrast, when it comes to the need for nurses, there is only one province that does not show a deficit [35]. Germany also shows a substantial need in the older adult care sector. It is estimated that in Germany between 300,000 and 600,000 migrant workers are employed in the care of older adults [18]. These are most often women from Eastern European countries and the WB who are mainly mediated to Germany through private agencies. This form of employment is mostly illegal and is becoming more common in Germany and Austria [36]. Faire Mobilität estimates that between 150,000 and 200,000 illegal workers work in the home care sector in Germany alone [37]. As German society grows older and faster, the number of registered job advertisements in geriatric care has increased 2.5 times in the last 10 years [35].

When it comes to doctors, the German official data show that the immigration of foreign doctors (in the amount of 31,000 doctors per year) has successfully filled the gap until 2013 [38]. The COVID-19 pandemic has made the shortage of doctors evident again in Germany. According to Deutsches Ärzteblatt, there are numerous cases that German doctors had to continue working even when in contact with people positive for SARS-CoV-2 due to shortage of staff [39]. The mismatch between supply and demand will continue to increase during the 2021s, while doctors from the so-called German baby boom generation are retiring, which means a 20% loss of all doctors in Germany. Namely, in 2019, 54.1% of all German doctors were older than 65 years [39].

German official policy makes no secret that the import of HCWs is a matter of primary national importance. Thus, at the end of 2019, a state agency was opened in Saarbrücken to assist in transferring carers and doctors [40]. This state agency intends to speed up immigration procedures with the German authorities for HWs recruited by private employment companies, hospitals,



and nursing homes from abroad [40]. The goal is for foreign nurses to immigrate to Germany within 3 months of applying for a visa, a process that lasted up to 2 years until 2019.

### **Austria**

In the case of Austria, the inflow of foreign-trained doctors has compensated for 60% of outward mobility, but in the case of nurses, the inflow is outpacing the outflow [7]. However, although in 2010 the number of medical graduates was more than two times higher than in the EU 28 at 22 per 100,000 inhabitants, over the past decade, this ratio has shrunk substantially by one-third to just 14 medical graduates per 100,000 inhabitants—close to the EU 28 average [2]. The number of graduate nurses per capita is below the EU 28 average and has remained unchanged from 2010 to 2017. Consequently, Austria relies much more on nurses originating from other countries, who accounted for a share of 18% as of 2019, than on medical doctors, with a share at 6% as of 2018 [2]. Shortly, the demand for health professionals in Austria is expected to surge rapidly. Close to 30% of doctors in Austria are 55 years and older. According to the European Centre for the Development of Vocational Training, there were more than 13,600 job vacancies for health professionals in Austria at the end of 2019 [2].

Regarding the mentioned WHO report, the paper emphasized that the concept of sustainability of health care systems in the European Union is unsustainable if high-income countries do not train and retain sufficient health workers to meet the need.

### **Brain Drain and the Push-and-pull Factors of Health Worker Mobility in the European Union**

#### ***Wage Differential as a Push Factor for East-West Migration***

The free movement of workers within the European Union has had an important impact on mobility patterns, especially health workers [41]. The phenomenon is complex, and its drivers are related to economic and institutional factors [8] as well as sociopolitical factors [42].

Expectations about employment opportunities are recognized as important pull factors for the mobility of HCWs. Higher levels of earnings in this sector in a potential host country and relatively high wage differentials between sending and host countries positively impact attracting health professionals in the potential host countries [2]. In 2018, average monthly wages per employee in health work activities in Croatia and the WB were 2 to 3 times lower than in the EU 28 countries [30]. OECD shows that health professionals' wage differential is a pull factor for east-west migration for this category of workers [30]. The wage differential in the health sector between the EU–Central and Eastern European (CEE) countries and Germany and Austria is substantial and, as such, is an important pull factor of mobility for health professionals from the EU-CEE, Western Balkan countries, and Croatia. Similar patterns and wage gaps apply to nurses [2]. Wage differentials in the health sector across the European countries certainly make some countries more successful at attracting health professionals than other countries that are failing to retain them [2]. Consequently, this group of countries face considerable challenges to provide health

assistance to their own rapidly ageing populations, especially in the context of the COVID-19 crisis.

### ***Motives of HW Emigration From Croatia***

As a reason for their dissatisfaction and motives for emigration from Croatia, nurses express difficult working conditions due to the insufficient number of employees and nonemployment of new nurses [43], inability to advance in the profession according to education and work experience, many unpaid overtime hours, fatigue, and exhaustion [44]. Besides, the perception of corruption in the country, the feeling of legal inequality, and the general negative social atmosphere that prevailed after the exodus of emigration since 2013 also play an essential role in this process [42].

Another issue that needs to be discussed in this section is how the pandemic reflected dissatisfaction with the working conditions of medical staff. The risk of anxiety and other negative mental health reactions among the workforce was described in a viewpoint by Shanafelt et al [45]. The toll of the crisis has been heavy on HCWs [46]. During COVID-19, a higher occurrence was found for all measured negative personal symptoms and negative professional symptoms [47]. The founded association between COVID-19 and mental health was generally the strongest for nurses, age groups 30-49 years, and residential care centers [47]. Prolonged stress at work can lead to burnout syndrome. It is associated with different consequences such as psychosomatic problems, lower employee performance, and more substantial depression and drug consumption. Teachers, police officers, nurses, and doctors have a prevalence in the population between 35% and 40% [48].

Although there are still no studies on this issue in Croatia and the WB, there are numerous testimonies of nurses and doctors in the Croatian media about dissatisfaction with working conditions during the pandemic, manifested in several strikes during the pandemic [49]. According to testimonies, this crisis also contributed to the search for better working conditions through emigration.

### ***Consequences of the Pandemic on the Brain Drain From the EU Periphery***

Humphries et al [3] illustrated how the pandemic intensified and reinforced, rather than radically altered, the dynamics of doctor emigration in the case of Ireland. According to the authors, the pandemic will likely increase global competition for doctors. The sending countries are at risk of losing out in the game of international health worker recruitment. Hospital doctors must access good working conditions, training, and career progression in the national health systems. Otherwise, the emigration of HWs could threaten the national health system's capacity to respond to future waves of the pandemic.

The European Committee of the Regions warns that the phenomenon of brain drain poses a risk to the long-term sustainability of the European project if social and economic imbalances between sending and receiving regions remain unaddressed. "It is crucial to achieving a balance between two essential principles of the European Union: free movement of labor and economic and social convergence between regions. Citizens and workers must be able to move freely within the

EU, but only because they want to and not because they are pushed from their regions by poverty and scarce economic opportunities” [50].

### ***Doctors in Germany From Croatia, Serbia, and B&H***

The number of foreign-trained doctors working in OECD countries increased by 50% between 2006 and 2016 (to reach nearly 500,000 in 2016), while the number of foreign-trained nurses increased by 20% over the 5 years from 2011 to 2016

(to reach nearly 550,000) [30] (see [Table 2](#) for Croatia, Serbia, and B&H).

In some countries of the European Union, the percentage of foreign-trained doctors has reached 30% and, in some specializations, has risen to 40%. According to Knez et al [22], both economic and noneconomic factors influence nurses' and doctors' choices to emigrate. Benefits of emigration for Croatian nurses and doctors are high satisfaction with living standards, income, professional development, and better work conditions [22].

**Table 2.** Doctors in Germany from Serbia, Croatia, and B&H.<sup>a</sup>

Year	2010, n	2011, n	2012, n	2013, n	2014, n	2015, n	2016, n	2017, n	2018, n	2019, n
Overall number of doctors from B&H <sup>b</sup> in Germany	118	150	165	202	236	270	327	397	470	505
Annual inflow from B&H	N/A <sup>c</sup>	32	15	37	34	34	57	70	73	35
Overall number of doctors from Serbia in Germany	246	292	381	501	648	826	1026	1236	1364	1504
Annual inflow from Serbia	N/A	46	89	120	147	178	300	210	128	140
Overall number of doctors from Croatia in Germany	137	158	175	196	254	295	341	380	412	428
Annual inflow from Croatia	N/A	21	16	21	63	57	48	46	42	26

<sup>a</sup>Source: Own elaboration from Organisation for Economic Co-operation and Development (2021) [51].

<sup>b</sup>B&H: Bosnia and Herzegovina.

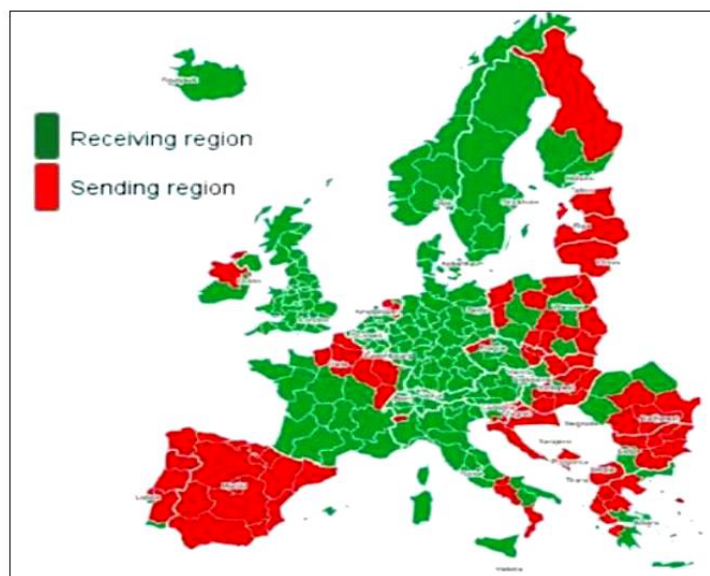
<sup>c</sup>N/A: not applicable.

### ***Who Benefits From the Freedom of Movement of Workers in the European Union?***

According to Lutz et al [52], the European Union's future labor force is likely to be smaller but better educated. Simultaneously, overall, in the European Union, the total cost of ageing (public spending on pensions, health care, long-term care, education, and unemployment benefits) is expected to increase by 1.7 percentage points to 26.7% of gross domestic product (GDP) between 2016 and 2070 [52].

The European Committee of the Regions report shows that intra-EU mobility concerns only a small percentage of Europeans. In 2017, out of a total population of about 511 million citizens, there were almost 17 million EU 28 movers (ie, about 3%) [53]. The ESPON project shows that the sending regions have an average GDP per capita that is 64% of the EU 28 average, while receiving regions have an average GDP per capita of 108% of the EU 28 average. Further, it is indicated that emigration flows follow east-west, south-north, and rural-urban patterns, and that peripheral region are mostly sending regions [54] (see [Figure 1](#)).

**Figure 1.** Intra-European Union mobility: receiving and sending countries, nomenclature of territorial units for statistics classification NUTS-2, 2017.



Freedom of movement of workers in the European Union has doubled since the beginning of the century and is largely beneficial from east to west. Alcidi and Gros [55] examined the factors driving growth in intra-EU labor mobility and showed that just under 4% of EU citizens of working age (20-64 years) now reside in a member state that is not that of their citizenship, ranging from 1.0% of German nationals living and working abroad to 14% of Croatian and 20% of Romanian nationals [55]. Although this mobility is beneficial for receiving states and contributes to a well-functioning monetary union, it can negatively affect the sending countries, resulting in a brain drain and an erosion of public finances [55,56].

## Methods

### Google Trends as a Source of Data for Predicting the Migration of Health Care Workers

Digital footprint monitoring is the primary source of innovation in the context of digital demography [57,58]. Namely, as more and more people are leaving their digital traces on the web, the use of these data for different types of research is becoming more common. In recent years, significant efforts have been made to devise new methods that, in addition to the existing ones, can provide some answers to open questions in the field of demography and public health [57,58].

According to Jurić [59] and Choi and Varian [60], GT data have been used in various types of research: US unemployment, flu outbreak, predicting consumer behavior, predicting inflation rates, predicting the housing market, predicting stock market changes, modeling tourism demand, etc. All the research results showed that the use of GT analytical tools could reveal valuable insights about intentions [61]. Analysis of data obtained through the Google Search engine is therefore gaining in importance in many social sciences [62], and this paper will show that this approach can be beneficial in forecasting the migration of health workers.

The need for such nonstandard approaches to modeling emigration assessments of medical staff is necessary on the one

hand due to delays in official data and on the other because there is substantial uncertainty regarding the sustainability of the medical system in connection with the current COVID-19 pandemic. Traditional data sources, based either on surveys or registers, generally fail to provide statistical information on migration flows quickly and do not facilitate correct anticipation of these flows in the short term [63].

Google is the first source of information for most users planning to relocate [64]. Several studies have used immense data sources to analyze migration-related phenomena directly. The first successful analysis of this type of data was in 2009, and the first study in the field of migration examined, during the 2015 migration crisis, searches for particular terms in Arabic in Turkey and Germany according to selected terms such as “Greece” or “Germany” [65]. A study by the Pew Research Center showed that digital prints left by internet searches could provide insight into the movement of migrants. Namely, during their travels in 2015 and 2016, many migrants used smartphones that provided access to information, maps, and travel tips via social media. It was then unequivocally proven that these indicators could be used to predict migration (unpublished study by Jurić). In addition, Böhme et al [66] used a combination of economic and migration-related keywords to predict the levels of migration between groups of countries, with a rather good predictive power.

Compared to approaches using social networks [57,58], the advantage of GT is that limitations related to penetration rates, variable-level social network use, and fake accounts are not prevalent [64]. The main advantage of this approach is the timely detection and identification of external migration, which is an essential analytical indicator for public health, from the labor market to preserving the health system. With this approach, insights into migration trends are obtained a year earlier than official data, which can be used to model projections and predict different trends.

Every year, the global spread of the internet and digital technologies radically transforms the way people communicate

with each other, and with the advent of COVID-19, that process has been further accelerated. The COVID-19 outbreak and lockdown accelerated the adoption of digital solutions at an unprecedented pace, creating unforeseen opportunities for scaling up alternative approaches to social science [67]. As a result of the fourth digital revolution and the pandemic, individuals have begun to leave an increasing number of traces online [62]. According to Internet World Stats [68], when it comes to the use of internet services, Croatia, Serbia, and B&H are in the group younger than 50 years, generally comparable to the EU average.

As the internet penetration rate accelerates and increases substantially compared to the creation of credible registration systems for monitoring migration and changes in public health [69], developing tools that retrieve alternative new sources of information is likely to become an accepted additional approach to monitoring demographic trends of all kinds [62]. Although the pandemic accelerated the uptake of digital solutions in data collection techniques [70], the research on the use of substantial data sources (big data) in the field of migration in Southeastern Europe, except our forthcoming study (unpublished study by Jurić), does not exist.

Understanding why health care personnel emigrate from Croatia and the WB, and the consequences of this process are crucial to enabling state agencies and governments to develop optimal intervention strategies to retain this staff and protect the functioning of the health system [71]. For this purpose, we created a method that can be useful for monitoring this process and further predictions of the general interest in emigration.

### Methodological Concept

Internet data (ie, digital traces) could become transformative for demography, especially in migration studies (unpublished study by Jurić). The main advantages of this approach are that those data are easily collected and generated in real time, they are incredibly robust, and they provide a profound insight into the opinions of individuals [72]. This data can be used to gather insights into what was going on in the user's mind through a noninvasive manner [73]. Moreover, digital traces provide documentation of both movement and activities, which can help researchers bypass possible sources of error in survey data, such as inability to recall and bias. Finally, digital traces can provide access to groups that are difficult to reach or are generally underrepresented by traditional research techniques [74].

The European Commission examined the feasibility of using big data to study demographic issues [57] and concluded

similarly to the UN that big data sources do not replace traditional data sources but can complement them, and they can still be used to assess trends. However, these data are also characterized by several shortcomings, as well as data from traditional demographic sources, which we show in the following section.

The primary methodological concept of our approach is to monitor migration-related searches with the analytical tool GT [75]. This tool shows the popularity of a specific term and shows if a trend is rising or falling. GT does not provide information on the actual number of keyword searches. Instead, it standardizes search volume on a scale of 0 to 100 over the period being examined, with higher values indicating the time when the search volume was the greatest, allowing for verifiable metrics (unpublished study by Jurić) [62]. It should be borne in mind, however, that each of these searches was conducted for its reason and does not answer the researchers' questions, so Googling the term "Germany" is not necessarily an implication that someone wants to move to Germany but may be interested in living conditions, tourist information, or just looking for the German Bundesliga (unpublished study by Jurić) [62]. Therefore, it is essential to choose the correct terms and pay attention to the overall context by interpreting the results.

The Google Search index cannot estimate the exact number of searches, so with the help of this tool, the exact number of emigrants cannot be estimated, but the increase of the trend can be noticed precisely (unpublished study by Jurić) [62,76]. We tested the method in Croatia, B&H, and Serbia by comparing the findings obtained with GT and official statistics. The findings show that the increase in migration-related searches such as "Krankenschwester/ Krankenpfleger + Bewerbung" (Nurse, application for job Germany, Austria) is correlated with increased emigration of HCWs recorded by official statistics and that the decrease in results correlates the decrease of emigrated HWs.

To standardize the data, we requested the data for the period from January 2010 to December 2020 and then divided the keyword frequency for selected words, giving a search frequency index. This index is then compared with official statistics to prove the significance of the results (see further explanations by Wilde et al [77] and Wanner [64]).

Initially, keywords were chosen by brainstorming possible words that we believed to be predictive, specific, and common enough to forecast HCW migration. After the significance screen, we selected the following keywords and topics (Textbox 1).

**Textbox 1.** Keyword and topic selection criteria.

<p><b>General terms</b></p> <ul style="list-style-type: none"> <li>• Arbeit (work)</li> <li>• Job in Austria, Germany</li> <li>• Gehalt (salary)</li> <li>• Lohn (salary)</li> <li>• Job in Germany, Austria</li> <li>• License</li> </ul> <p><b>Job</b></p> <ul style="list-style-type: none"> <li>• Arbeit + Krankenschwester (work + nurse)</li> <li>• Arbeit + Arzt (work + doctor)</li> <li>• Posao + medicinska sestra + Austrija + Njemačka (work + nurse + Austria + Germany)</li> <li>• Posao + doktor + Austrija + Njemačka (work + doctor + Austria + Germany)</li> </ul> <p><b>Application for job</b></p> <ul style="list-style-type: none"> <li>• Krankenschwester/Krankenpfleger + Bewerbung (nurse, application for job Germany, Austria)</li> <li>• Arzt + Bewerbung (doctor + application for job Germany + application for job Austria)</li> </ul>
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**Limitations of the Methodological Concept**

Like all others of this type, this study has significant limitations that we want to highlight. Although previous research in this area has shown the feasibility of using digital data for demography, at the same time, we highlight the problems associated with assessments and conclusions (unpublished study by Jurić) [57,62,74,78]. Namely, it is unquestionable that there are still significant open methodological issues with the questionable integrity of the data obtained using the sources of large data sets (unpublished study by Jurić) [62,74].

- The Google Search index cannot estimate the exact number of searches, so with the help of this tool, the exact number of emigrated HCWs cannot be estimated, but the increase of the trend can be noticed precisely, which can serve as an indicator.
- Although the data obtained with GT are robust data with large samples, which provide information qualitatively different from what can be obtained from the official statistics report, Eurostat, OECD, and other official databases, they are not representative of the observed population. It is also a problem that GT does not provide data on which the population was sampled or how it was structured [62].
- A particular problem exists in the researchers' education, who must be skilled in computational methods, be transparent about their methods to ensure repeatability, and be accustomed to the interdisciplinary environment.
- The last item is both a limitation and an advantage of this approach. Namely, in a traditional research process, a researcher with a predefined theoretical framework and

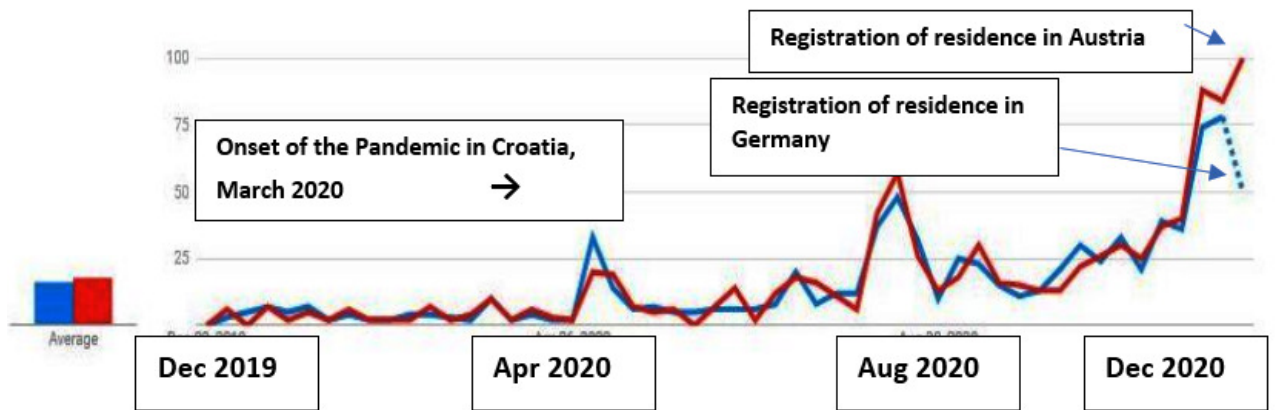
questions collects data from a survey using a carefully crafted set of definitions for each item in the survey. With digital data, the reverse process of operationalizing the research concept occurs. The researcher first observes all the activities and then puts them in a theoretical framework [73].

Unquestionably, this model has unresolved issues related to the reproducibility of the findings and the validity of the measurements, which arise from the characteristics of the GT system used. Although these open-ended issues pose serious challenges for making precise estimates, statistics offer various tools available to deal with imperfect data (unpublished study by Jurić) [62].

**Results****Use of the Google Trends Analytical Tool to Forecasting the Migration of Health Workers****Croatia**

Searching for job applications in Croatia during 2020 (German: "Bewerbung + Krankenschwester") was more common than the search for the equivalent in Croatian (Croatian: "zamolba za posao + medicinska sestra"). It is also evident that this is an upward trend. This is a strong indication that Croatian citizens continue planning to emigrate to Austria and Germany (unpublished study by Jurić). A further indication is a search for terms related to residence registration in Austria and Germany in combination with the entry "PCR [polymerase chain reaction] test" (Figure 2).

**Figure 2.** Search queries in German from Croatia "Registration of residence in Germany + PCR" or "Registration of residence in Austria + PCR Test" (searching for a term in Croatian and German from Croatia; 2019-2020). PCR: polymerase chain reaction.



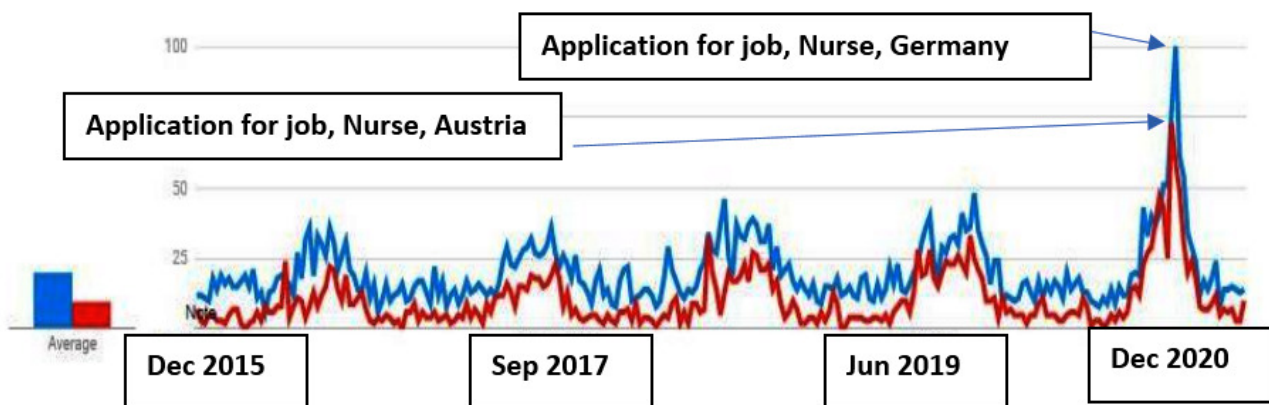
Search queries regarding an application for a job as a nurse in Germany and Austria increased during the 2020 pandemic.

Search queries in German from Croatia "Krankenschwester/Krankenpfleger + Bewerbung Deutschland" and "Austria" (nurse + application for job Germany + application for job Austria) increased particularly during the

2020 pandemic (Figure 3). This could be correlated with the difficult working conditions of HCWs in Croatian hospitals during the pandemic [26] but also with the mentioned increased recruitment of HWs from Germany.

The same phenomenon is also observed in the case of the emigration of doctors (Figure 4).

**Figure 3.** Search queries in German from Croatia "Krankenschwester/Krankenpfleger + Bewerbung Deutschland" and "Austria" (nurse + application for job Germany + application for job Austria; 2015-2020).



**Figure 4.** Search queries in German from Croatia "Arzt + Bewerbung, Deutschland" and "Arzt + Bewerbung + Austria" (doctor + application for job Germany + application for job Austria; 2015-2020).



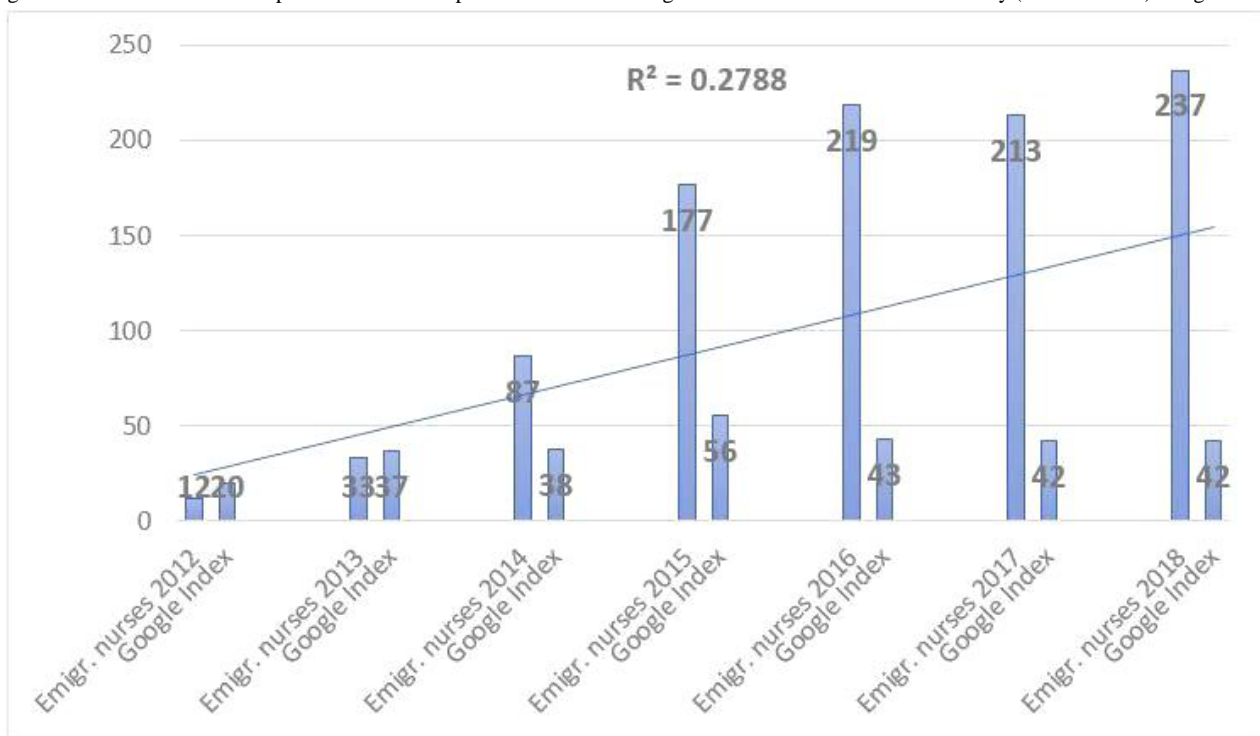
In further proceedings to standardize the data, we requested the data from January 2010 to December 2020 and divided the keyword frequency for each word and compared this search

index with official statistics to prove the significance of results [79].

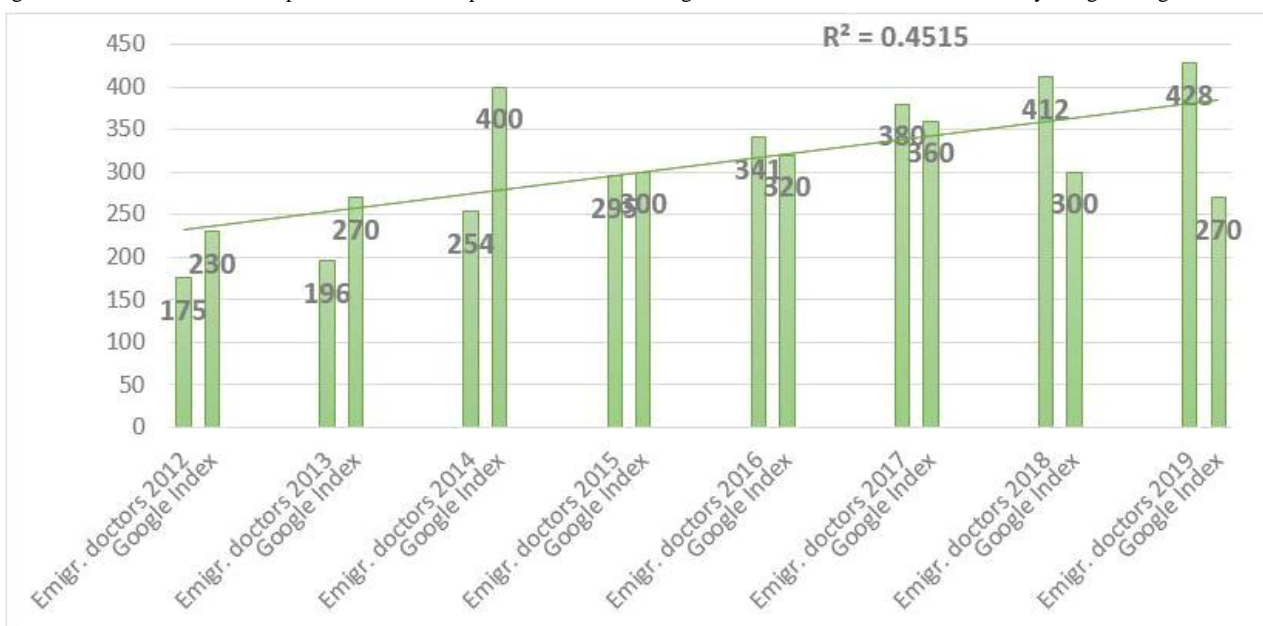
Figure 5 shows that the increase in Google Search for the query “posao u Njemačkoj + medicinska sestra” (work in Germany + nurses) correlates with the increase of emigrated nurses to Germany. In the following, we show that the verification can also be performed in the opposite way (ie, from Croatia in German), which again gives reliable estimates.

Figure 6 shows that, in the case of emigration of doctors, the increase in the Google Search query “Arbeit in Deutschland + Arzt” (work in Germany + doctor) was correlated with the increase of emigrated doctors to Germany.

**Figure 5.** Correlation between Google Search index for query "posao u Njemačkoj + medicinska sestra" (work in Germany + nurses) in Croatian and the Organisation for Economic Co-operation and Development statistics for emigrated nurses from Croatia to Germany (annual inflow). Emigr: emigrate.



**Figure 6.** Correlation between Google Search index for query "Arbeit in Deutschland + Arzt" (work in Germany + doctor) in German in Croatia and the Organisation for Economic Co-operation and Development statistics for emigrated doctors from Croatia to Germany. Emigr: emigrate.

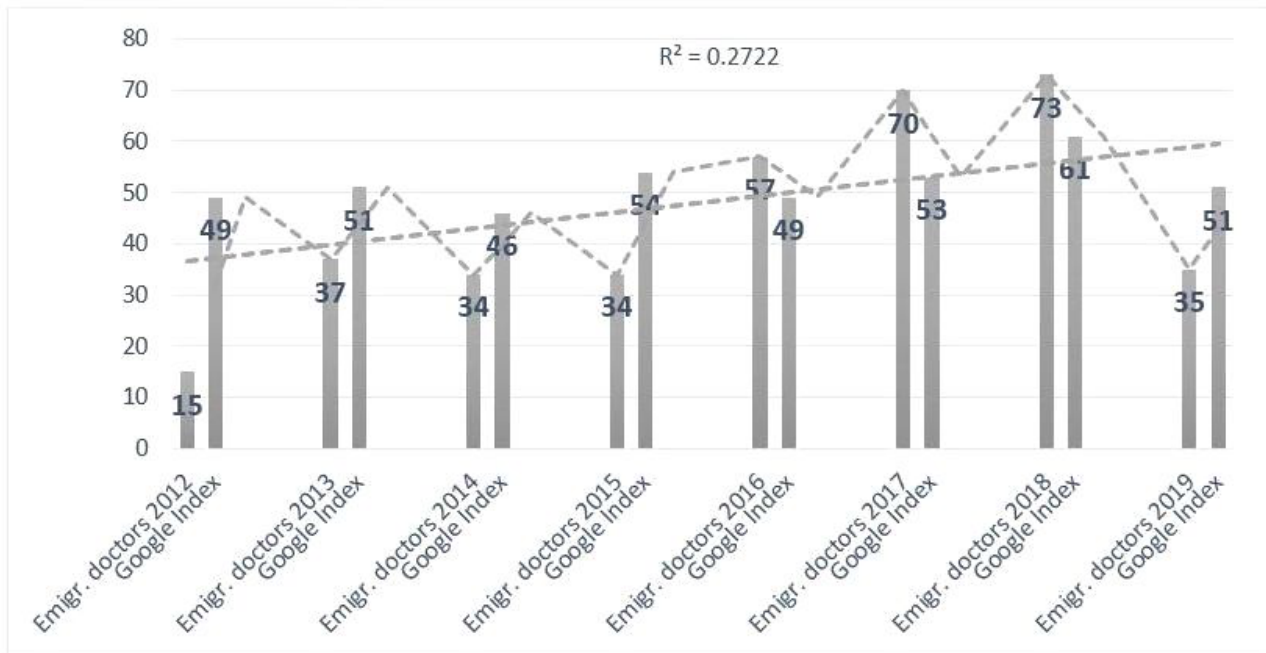


### B&H and Serbia

In the case of B&H, we calculated the annual inflow of B&H doctors to Germany and compared these data with the GT index (Figure 7). As in the case of Croatia, there was a positive correlation.

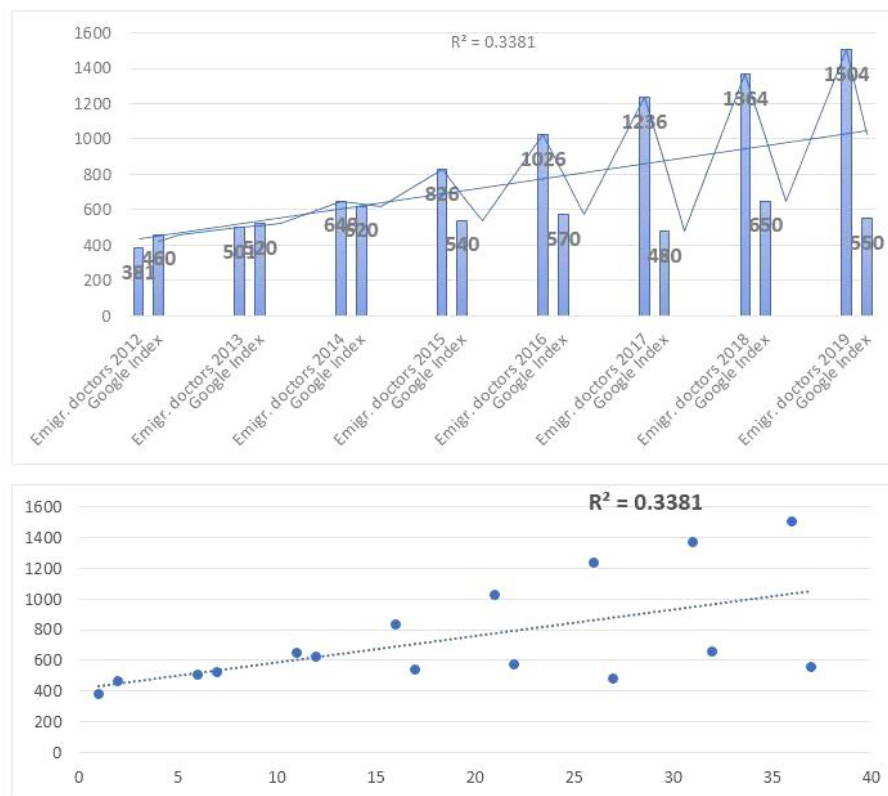
In addition, in the case of Serbia (Figure 8), the increase in Google Search for the query “posao u Nemačkoj + Doktor” (work in Germany + doctor) correlated with the increase of emigrated doctors to Germany. There is a positive linear association between the Google index and data from official statistics (OECD).

**Figure 7.** Correlation between Google Search index for query "Arbeit in Deutschland + Arzt" (work in Germany + doctor) in Bosnia and Herzegovina (B&H) and the Organisation for Economic Co-operation and Development statistics for emigrated doctors from B&H to Germany (annual inflow). Emgir: emigrate.





**Figure 8.** Correlation between Google Search index for query "Arbeit in Deutschland + Arzt" (work in Germany + doctor) in Serbia and the Organisation for Economic Co-operation and Development statistics for emigrated doctors from Serbia to Germany. Emigr: emigrate.



## Discussion

From 2010 to 2020, 65,288 HWs emigrated from Croatia and the WB. Without such intense emigration in the last 10 years, Croatia and the WB would have 50% more HWCs today. It is necessary to emphasize that this staff is crucial in the fight against a pandemic.

During the pandemic, the “normal” ways of data collection are simply too slow (particularly when EU countries are fast tracking health workers into the European Union). The methods presented here show a way of generating timely insights into intent to migrate among health workers. All tested migration-related search queries that show an indication about HCWs’ emigration planning showed a positive linear association between Google index and data from official statistics (OECD: Serbia  $R^2=0.3381$ , B&H  $R^2=0.2722$ , Croatia  $R^2=0.4515$ ). The increase in Google Search is correlated with the increase in the number of emigrated HWs from Croatia, Serbia, and B&H. The decrease in Google Search is correlated with the decrease in the emigration of HWs.

This method contributes in a way that proves the feasibility of predicting further migrations from Croatia, Serbia, and B&H in this specific case of HCWs to Germany and Austria, which allows reliable forecasts for the future. This procedure also presents a new methodological approach to how data obtained through GT can be standardized for comparison with official databases.

The insights are particularly relevant for national and EU policy makers, and can help design appropriate strategies to retain

HCWs. The method can enable state agencies and the government to prepare and better respond to the shortage of HWs in the future and protect the functioning of the health system. Regarding the WHO report about countries with critical health workforce shortages, this paper highlights that these issues are also relevant in European countries and that the list should be updated to include the countries B&H, Serbia, and Croatia. In addition, it is emphasized that the concept of health care system sustainability in the European Union is unsustainable if high-income countries do not train and retain sufficient health workers to meet the need.

Although this mobility is beneficial for receiving states and contributes to a well-functioning monetary union, it negatively affects the sending countries, resulting in a brain drain and an erosion of public finances [55]. The issue of the European Union drawing HWs from the EU periphery (Croatia) and nearby countries (B&H, Serbia) clearly shows a clash between the EU free movement and the right to health care and a need to ensure a health workforce in all European regions (as per the WHO global code and the UN Sustainable Development Goals).

This method could be useful for policy makers but only if they respond and react to the data. An important question for policy makers is how they can retain health workers during a pandemic. Increased salaries and improved working conditions is certainly a good way. What precisely could the European Union do to address this problem? One approach would be to strengthen fiscal transfers to the member states and countries of the European periphery that are most affected by the harmful effects of freedom of movement [56]. However, fiscal transfers can never fully compensate for the loss of population. For example,

financial compensation cannot fully compensate the departure of a nurse who left a Croatian hospital and now works in Germany until a Croatian hospital finds a replacement. Otherwise, the specific hospital will still lack a nurse, which is reflected in Croatia's general quality of health care. That is why we proposed a compensation solution so that Germany funds centers of excellence for the education of nurses in Croatia and the WB, if they remain to work in their homeland for 5 years after completing their education. In this context, it welcomes the appeal of the WHO that calls on high-income countries to strive for self-sufficiency through educating, retaining, and sustaining enough doctors and nurses to staff their health care systems [22].

In a situation where there is only freedom of movement of workers but not a common pension and health care system in the European Union, or a guaranteed minimum wage, nothing significant will change at the EU level. This means that the EU framework remains a structure in which the wealthy members will continue to become richer and the poor members increasingly poorer, which also applies to the whole European periphery. Moreover, with the onset of the pandemic, the situation worsened.

Without systemic regulation of this issue at the EU level, such trends of the emigration of HWs will threaten the national health system's capacity to respond to the needs of an ageing population and possible new waves of the pandemic.

## Conflicts of Interest

None declared.

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## Abbreviations

**B&H:** Bosnia and Herzegovina  
**CEE:** Central and Eastern European  
**GDP:** gross domestic product  
**GT:** Google Trends  
**HW:** health care worker  
**OECD:** Organisation for Economic Co-operation and Development  
**PCR:** polymerase chain reaction  
**UN:** United Nations  
**WB:** Western Balkans  
**WHO:** World Health Organization

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Original Paper

# Information Technology Ambidexterity, Digital Dynamic Capability, and Knowledge Processes as Enablers of Patient Agility: Empirical Study

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## Abstract

**Background:** There is a limited understanding of information technology's (IT) role as an enabler of patient agility and the department's ability to respond to patients' needs and wishes adequately.

**Objective:** This study aims to contribute to the insights of the validity of the hypothesized relationship among IT resources, practices and capabilities, and hospital departments' knowledge processes, and the department's ability to adequately sense and respond to patient needs and wishes (ie, patient agility).

**Methods:** This study conveniently sampled data from 107 clinical hospital departments in the Netherlands and used structural equation modeling for model assessment.

**Results:** IT ambidexterity positively enhanced the development of a digital dynamic capability ( $\beta=.69$ ;  $t_{4999}=13.43$ ;  $P<.001$ ). Likewise, IT ambidexterity also positively impacted the hospital department's knowledge processes ( $\beta=.32$ ;  $t_{4999}=2.85$ ;  $P=.005$ ). Both digital dynamic capability ( $\beta=.36$ ;  $t_{4999}=3.95$ ;  $P<.001$ ) and knowledge processes positively influenced patient agility ( $\beta=.33$ ;  $t_{4999}=3.23$ ;  $P=.001$ ).

**Conclusions:** IT ambidexterity promotes taking advantage of IT resources and experiments to reshape patient services and enhance patient agility.

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**KEYWORDS**

IT ambidexterity; dynamic capabilities; digital dynamic capability; knowledge processes; patient agility; hospitals; information sciences; information technology; digital health; health care; digital transformation; research models

## Introduction

### Background

In the age of digital transformation, modern hospitals need to simplify their current care delivery processes and sustainable business models to contain the rising health care costs and address the needs of the more engaged and informed patient. At the same time, hospitals need to adequately address the confluence of dynamic and unpredictable market forces in which they operate, optimally deploy, and enable their information technology (IT) assets; resources; and organizational, IT, and knowledge capabilities and focus on the state-of-the-art patient service delivery [1-6]. Physicians and other health care providers can use innovative IT solutions and the available exponential volumes of patient-generated data—including the patient's medical history in a single, easy-to-find location—to enhance the quality of care delivery [7-9]. As a result, hospitals today need to deal with a myriad of substantial organizational, political, and technological challenges over the coming years, also in the process of fully leveraging digital technologies [10,11]. Emerging technologies like big data analytics, the Internet of Things, distributed ledger technologies, social media, artificial intelligence (AI), and cloud-based solutions are, in essence, more than promising. These innovative technologies can truly disrupt the quality of processes and services, the effectiveness of medical outcomes, and the productivity of employees, and ultimately change lives [12-16]. Hospitals can now redefine their role in the hospital ecosystem so that the patient service quality and value might ultimately translate into substantial societal benefits [17].

Despite a wealth of attention for IT adoption and IT-enabled transformation in health care research [6,18-25], there is still a limited understanding of the role of IT as a crucial enabler of organizational sensing and responding capabilities to address the needs, wishes, and requirement of patients adequately [26-29]. Moreover, the extant scholarship has contended that IT could also hamper the process of gaining organizational benefits [30-33]. Understanding the facets that drive IT investment benefits is valuable in clinical settings [34]. As can be gleaned from this, substantial gaps remain in the extant literature. This paper, therefore, responds to two crucial limitations in the extant research. First, this paper tries to unfold how hospital departments can develop the ability to simultaneously pursue *exploration* and *exploitation* in their management of IT practices (ie, IT ambidexterity [35,36]) by practitioners often referred to as bimodal IT (eg, [37,38]) to drive a hospital departments' digital dynamic capability. This technical-oriented dynamic capability, in essence, represents the degree to which qualities and competencies are developed to manage innovative digital technologies for new, exceptional, and effective patient service development [39]. As such, this capability requires substantial undertakings toward embracing new digital technologies [39,40]. Second, this study tries to unfold the complementary effect of IT ambidexterity and digital

dynamic capability on hospital departments' knowledge processes and their ability to adequately sense and respond to patient needs and wishes (ie, patient agility). Health care processes require close collaboration between different clinical departments and disciplines, and IT is crucial in facilitating effective knowledge processes between key stakeholders (eg, physicians, nurses, and health information management professionals) [8,41-43]. Hence, IT-driven knowledge processes can enhance patient treatment processes and patient agility.

Gaining these insights is essential, as hospitals are actively exploring their digital options and innovations, and transforming their clinical processes and interactions with patients using digital technologies [43,44]. For instance, clinicians who use digital innovations in their clinical practice (eg, mobile handheld devices and apps) can increase error prevention and improve patient-centered care [45-48]. In addition, digital options and innovations provide ways for clinicians to be more agile in their work, improve clinical communication, remotely monitor patients, and improve clinical decision support [49-52], and hence improve the patient treatment process and quality of medical services [51,53]. Moreover, recent scholarship advocates the deployment of knowledge assets, processes, and digital-driven sense and responding capabilities as a way of achieving higher quality and patient-centered care and financial performance benefits in hospitals [46,54,55]. Moreover, Fadlalla and Wickramasinghe [56] argue that patient-centered (care that is respectful of and responsive to individual patient preferences, needs, and values) sensing, responding, and digital capabilities are crucial in facilitating high-quality care.

These insights are also important for hospitals in the Netherlands, as Dutch hospitals are bound to care production agreements (ie, so-called turnover ceilings) between hospitals and health insurers. The Dutch Healthcare Authority, an autonomous administrative authority falling under the Dutch Ministry of Health, Welfare, and Sport, oversees that these agreements focus more on patient quality and value creation than production. Therefore, more contract negotiations will be driven by focusing on the quality of care and patient value, achieving patient agility seems a valuable endeavor. Thus, this research tries to extend existing work on IT-enabled transformation in health care and does so by sufficiently capturing clinicians' attitudes toward IT ambidexterity, digital dynamic capability, knowledge processes, and patient agility of their hospital departments. In doing so, we adopt a practitioner-based approach [57,58].

Throughout this study, the dynamic capabilities framework is embraced [40,59,60]. As such, this study distinguishes between IT resources, a lower-order technical dynamic capability, and higher-order dynamic capabilities (ie, knowledge processes and patient agility) [40,61-63].

To summarize, the study's main research questions are:

- How does IT ambidexterity lead to perceived patient agility of the hospital department?
- What is the role of digital dynamic capability and knowledge processes in the process of converting the contributions of IT ambidexterity on the department's perceived patient agility enhancements?

This study's IT business value approach aligns with the industries' focus on operational and clinical excellence, patient-centered value, and a streamlined patient journey [64,65].

Hence, this paper proceeds as follows. First, it reviews the theoretical development by highlighting key literature on IT resources and ambidexterity, the dynamic capabilities view (DCV), and organizational agility. Second, section 3 highlights the study's research model and associated hypotheses. Third, section 4 details the methods used in this study, after which section 5 outlines key results. Finally, this study discusses the outcomes, including theoretical and practical contributions, and ends with concluding remarks.

## Theoretical Background

### *IT Resources and IT Ambidexterity*

Organizations need to pursue and make trade-offs in practice between two seemingly opposing paths (ie, the ability to adapt existing IT resources to the current business environment and demands, and their focus on developing IT resources that contribute to long-term organizational benefits) [36,66]. The balance between these two objectives is referred to, in the literature, as ambidexterity [67-70]. Organizations' simultaneous engagement of *exploration* and *exploitation* will likely provide them with superior business benefits [67-70]. IT exploration concerns the organization's efforts to pursue new knowledge and IT resources [35,66], for instance, thinking about acquiring new IT resources (eg, potential IT applications and critical IT skills) and an organization's ability to experiment with new IT management practices. On the other hand, IT exploitation is typically conceptualized as a construct that captures the degree to which organizations take advantage of existing IT resources and assets (eg, the reuse of existing IT applications and services for new patient services and the reuse of existing IT skills) [71,72].

### *Digital Dynamic Capability*

Digital dynamic capabilities can be considered the "organization's skill, talent, and expertise to manage digital technologies for new product development" [39]. Hence, it can be conceived as an organization's ability to master digital technologies, drive digital transformations, and develop new innovative patient-centered services and products. Our study embraces a hierarchical capability view [35,40,59,60]. Thus, the digital dynamic capability is conceptualized as a lower-order technical dynamic capability that organizations could embed and leverage in the process of developing higher-order dynamic organizational capabilities such as innovation ambidexterity, absorptive capacity, and organizational adaptiveness [40,61,62]. This current conceptualization is also in line with the previous scholarship. However, the digital dynamic capability is tough to mimic and establish within organizations as it requires specific, idiosyncratic, and heterogeneous competencies to

develop [73,74]. As such, this capability requires substantial undertakings toward embracing new digital technologies [39,40].

### *Dynamic Capabilities and Knowledge Processes*

As its definition and conceptualizations suggest, digital dynamic capability builds upon a rich foundation of the DCV [74-78]. The DCV is a foundational strategic framework within the management and information system (IS) field [79,80], and is built from a multiplicity of theoretical roots [81]. The DCV claims that under conditions of high economic turbulence, traditional resource-based capabilities do not provide organizations with a competitive edge [82-84]. Instead, within this framework, organizations seek a balance between strategies to remain stable in the process of delivering current business services distinctively and mobile so that they can anticipate and effectively address market disruptions and business changes [84].

These dynamic capabilities have been defined and conceptualized as sets of measurable and identifiable routines that have been widely validated through empirical studies [78,85,86]. In general, these capabilities can be conceived as the organizations' routines to integrate, build, reconfigure, gain, and release internal competences and resources to address changing market and business ecosystem demands [74,76]. In short, these capabilities can represent an organization's ability *to act* under changing circumstances [59,87], a first *derivative* of traditional resource-based capabilities: the ability to contribute to maintaining a competitive edge continuously.

Although the knowledge-based view of organizations strongly builds upon the organizational learning theories and literature [88,89], recent studies converged both strategic management streams toward the core idea of knowledge-related dynamic capabilities. Knowledge processes represent the crucial operations for the input of knowledge assets [90]. They focus on generating, analyzing, and distributing customer information for strategy formulation and implementation [55,91,92]. In addition, hospital knowledge processes are important for patient care, as acquiring new medical knowledge and insights can substantially impact patients' treatment [41]. Knowledge processes foster clinicians and medical staff to exchange and share medical and patient knowledge, and as such, these processes can be regarded as an effective way to integrate medical knowledge, enhance knowledge flow, and cultivate the use of evidence-based care that will likely have a positive impact on the quality of care [93,94]. As conceived in this study, knowledge processes are conceptualized as a dynamic capability [95,96].

### *The Concept of Organizational and Patient Agility*

The DCV argues that organizations can respond to changing conditions while simultaneously and proactively enacting influence in the environment. Organizational agility has been considered a critical capability for sustained organizational success under the DCV [84]. This particular capability has been defined and conceptualized in many ways and through various theoretical lenses in the IS literature [26,97,98]. For instance, Park et al [99] ground their conceptualization and operationalization in the information-processing theory [100]



and argue that information processing capabilities strengthen the organization's sense-response processes to adapt to changing environmental conditions. Lu and Ramamurthy [101] embrace a complementarity perspective and perceive agility as the organization's ability to seize market opportunities and operationally adjustment capacity. Chakravarty et al [26] adopt a contingency factors perspective and operationalize the multidimensional concept of agility through the organization's ability to anticipate and proactively respond to market dynamics (ie, entrepreneurial agility and the organization's ability to react to events without needing substantial strategic changes, that is, adaptive agility). A multidimensional view is also adopted by Lee et al [35], who likewise perceive organizational agility as a higher-order multidimensional dynamic capability that allows organizations to effectively and efficiently sense and respond to environmental conditions. Roberts and Grover [102] synthesized that, although there seems to be ambiguity in definitions as reflected by the concepts' operationalized capabilities, a set of high-level characteristics can be devised from the extant literature. Hence, to a certain degree, all studies show two high-level organizational routines: deliberately *sensing* and *responding* to business events in the process of capturing business and market opportunities. These two organizational

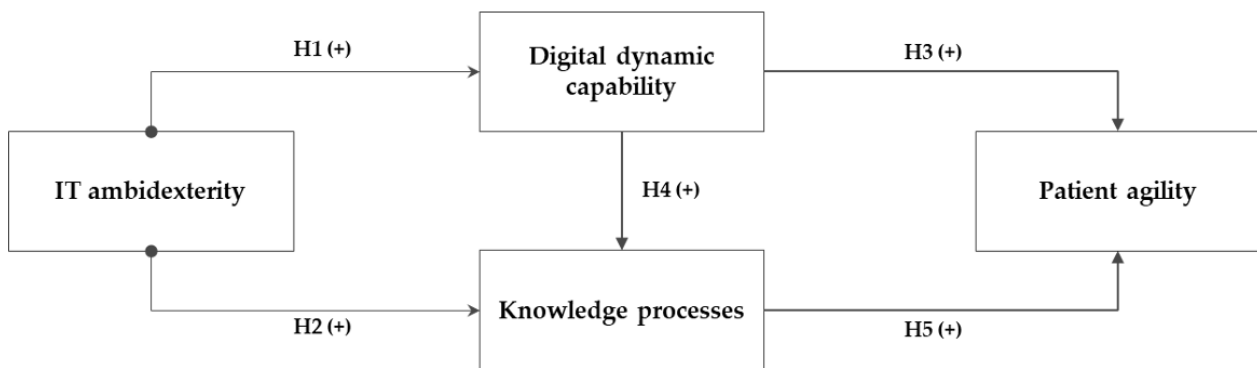
capabilities are crucial for organizations' success [31]. Hence, our paper perceives patient agility as a higher-order manifested type of dynamic capability that allows hospital departments to adequately *sense* and *respond* to patient needs, demands, and opportunities within a turbulent and fast-paced hospital ecosystem context [43,84,102,103].

By addressing these crucial questions, this paper contributes to the medical informatics and IS literature by unfolding the mechanisms through which the dual capacity of IT exploration and IT exploitation simultaneously drives patient agility in hospital departments.

### Research Model and Hypotheses

IT ambidexterity as a core organizational IT resource is expected to enhance hospital departments' level of patient sensing and responding capability (both conceptualized as higher-order dynamic capability) through digital dynamic capability (as a lower-order technical dynamic capability) and knowledge processes. Figure 1 demonstrates the research model and the associated hypotheses that will be clarified further in the paper. For the sake of simplicity, the figure does not demonstrate included control variables.

**Figure 1.** Research model. H: hypothesis; IT: information technology.



IT can be a transformative force in hospitals and contribute to enhanced patient services, efficiency and effectiveness gains, and clinical care [10,104]. However, IT implementations in hospitals are often exposed to cultural, organizational, and social challenges and inertia forces [10,104,105]. Therefore, an ambidextrous IT implementation strategy should be embraced, whereby short-term contributions (exploitation of current IT resources) and continuous progress of the IT resource portfolio (exploratory mode) drive IT-driven business transformation simultaneously [106]. When both short-term goals and ambitions are synchronized with the longer-term objectives, hospital departments are better equipped to develop digital capabilities and knowledge options, and to frame the hospital's business strategy and clinical practice [39,98,107].

IT exploration can be considered an enabler of digital dynamic capability. This mode promotes the use of and experimentation with new IT resources (eg, new IT platform implementation, decision support functionality, big data and clinical analytics, and social media) as a basis to reshape existing patient services. On the other hand, IT exploitation focuses on using, enhancing, and repackaging existing IT resources (eg, reuse or redesigning

current electronic medical record for new patient service development and ensuring hospitalwide accessibility to clinical patient data and information). Therefore, digital dynamic capability relates well to the dual capacity to aim for two disparate modes of operandi in managing the department's skills, qualities, and competencies to manage digital technologies and developments—like mobile, social media, big data analytics, robotic process automation, AI, cloud computing, and Internet of Things—for new patient service delivery. However, in practice, many organizations struggle to reach IT ambidexterity results because of resource constraints and conflicting ambitions and motives [108]. As the individual qualities of IT ambidexterity may, to some extent, strengthen hospital departments' digital options, they will likely not enhance the hospital department's digital dynamic capabilities in isolation [98]. The simultaneous engagement of IT exploration and IT exploitation will enhance the qualities and competencies to manage innovative digital technologies for new patient service development, as they depend primarily on the organization's investment decision to deploy simultaneous short-term improvement activities and long-term innovations [109].

Thus, IT resources play a substantial role in acquiring, processing, organizing, and distributing knowledge, and providing digital processes and knowledge options as enablers of agility [35,98,110]. This study argues that departments that can simultaneously exploit and explore their current IT resources portfolio will be better equipped to integrate existing and leverage new patient information sources, ensuring hospitalwide accessibility to clinical data and driving effective knowledge processes [111,112]. By leveraging the two modes of IT management practices, hospital departments can effectively integrate and analyze patient knowledge, use it for interdepartmental meetings, and identify new health service development needs.

In line with this reasoning, this study defines the following hypotheses:

- Hypothesis 1: The greater the hospital department's IT ambidexterity, the higher the degree of its digital dynamic capability will be.
- Hypothesis 2: The greater the hospital department's IT ambidexterity, the more effective its knowledge processes will be.

Digital dynamic capability is a crucial dynamic capability necessary to innovate and enhance business operations [39,61,113,114]. Various prior studies investigated the benefits that result from developing a digital dynamic capability. Wang et al [115] argue that digital dynamic capability allows leveraging IT and knowledge resources to deliver innovative services that customers value and that contribute to organizational benefits. Coombs and Bierly [116] empirically showed that a sophisticated digital dynamic capability enables competitive advantages. Thus, the extant literature shows that digital dynamic capability drives organizations to learn from experience in turbulent economic and competitive environments actively. Hence, in such an environment, it is essential to search continuously, identify, and absorb new knowledge and technological innovation such that they can be used to respond to changing customer behavior, demands, and wishes timely, adequately, and innovatively [28,113]. These claims are likewise consistent with results from Westerman et al [117], Khin and Ho [39], and Ritter and Pedersen [118], who showed that digital dynamic capability is crucial to deploy new innovative business models, enhance customer experiences, and improve business agility. Organizations can succeed in their digital options, products, and services by actively managing the opportunities provided by innovative technologies and responding to digital transformation [39].

A technological-driven capability is crucial for hospital departments that want to strive for patient agility in clinical practice because the process of achieving new digital patient service solutions is exceedingly dependent on its ability to manage digital technologies [39]. It requires proactively responding to digital transformation, mastering the state-of-the-art digital technologies, and deliberately developing innovative patient services using digital technology. Such a capability goes well beyond the notion of IT capabilities (ie, aggregation of IT resources and IT competencies in the vast majority of empirical studies) [119-121]. The development of

a digital dynamic capability is tough to mimic and establish within hospital departments, as it requires specific, idiosyncratic, and heterogeneous competencies to develop [73,74].

The digital dynamic capability allows hospital departments, for example, to absorb and process sensitive patient information better, support clinicians in their decision-making processes, exchange clinical data, and facilitate patient health data accessibility [43,122]. As such, developing this capability makes the department more receptive to new patient data and information. The accumulation and storing of knowledge necessary to develop these new technologies also improve a firm's ability to engage in transformation processes through its evaluation, use, and implementation. Finally, as a firm engages more in developing and mastering new technologies, they become more efficient in deploying the existing knowledge and, thus, generate more exploitative activities [123].

Hence, hospitals that actively invest and develop such a capability are likely to anticipate their patients' needs (of which they might be physically and mentally unaware) and respond fast to changes in the patient's health service needs using digital innovations and assessments of clinical outcomes [39,102,103]. Therefore, such a strategically significant capability is crucial for the departments' focus on quality, efficiency, essential patient information, and enhancing the patient's clinical journey. Based on the aforementioned arguments and building upon the DCV, the following two hypotheses are defined:

- Hypothesis 3: The more developed the hospital department's digital dynamic capability, the higher the hospital department's patient agility.
- Hypothesis 4: The more developed the hospital department's digital dynamic capability, the more effective the hospital department's knowledge processes will be.

Previous scholarship demonstrated that knowledge-based capabilities and agility are two crucial capabilities that mediate the impact of IT resources and capabilities on business benefits [98,124]. In the context of hospital departments, substantial investments in processing and analyzing patient data and information, and adequate interdepartmental knowledge and information flow will drive the department's ability to anticipate the patients' current and future needs [92]. In clinical practice, the diagnosis and treatment processes are composed of a multitude of interactions and coordination between care activities in different activity levels and multiple types of knowledge [53]. Moreover, departments that are more aware of their patient needs through information knowledge processes are likely to harness new patient knowledge more effectively, make better clinical practice decisions, and support the treatment process [53,92,124]. Thus, through knowledge processes, the department can develop and redesign its core processes and capabilities. Mature knowledge-based processes drive transfer of knowledge across and within the department, uniquely deploy knowledge resources, and allow hospital departments to enhance business processes and services, and better sense and seize business and patient service opportunities that ultimately can enhance business performance [55,84,87]. Recently, scholars showed that data and knowledge-driven capabilities, as intermediate constructs, contribute to hospital performance

enhancements [125,126]. Moreover, in hospital departments, patient agility as a crucial capability describes the competence of the health care providers' ability to create patient value and drive patient satisfaction in a way that uniquely uses knowledge resources and processes [46,55].

In sum, this study argues that knowledge processes are crucial in the process of reconfiguring its existing patient sensing and responding capabilities [96] and that these capabilities, to a great extent, rely on the integration of knowledge processes in the department [55,88,112]. Hence, this study defines the following:

- Hypothesis 5: The more effective the hospital department's knowledge processes, the higher the hospital department's patient agility.

## Methods

A deductive and quantitative approach was used to address the study objectives. Hence, hypothesized relationships among key constructs are analyzed by first cross-sectionally collecting field data and then analyzing the obtaining survey data.

### Data Collection Tool and Procedure

An online survey was developed to capture clinicians' attitudes toward IT ambidexterity, digital dynamic capability, knowledge processes, and patient agility of their hospital departments. Hence, we adopted a practitioner-based approach that used subjective measures because hospitals are typically more willing to provide subjective data than sensible objective performance metrics (eg, [57,58]). In practice, perceptual measures on processes and practices positively correlate with objective data [127].

This survey was pretested on multiple occasions by 5 master's students and 6 medical practitioners and scholars to improve the survey items' content and face validity. The medical practitioners all had sufficient knowledge and experience to assess the survey items effectively to provide valuable improvement suggestions. Within the survey, comprehensible construct definitions were provided, and the survey followed a logical structure. In one of the final questions, the participants were asked if they wanted to receive critical insights from the study. Various controls were also built during the data collection process so that each department completed the survey only once.

### Study Population

The target population was (clinical) department heads and managers, team leads, and physicians under the assumption that, at the hospital department level, these health care providers are actively involved in contact with patients or at least have intelligible insight into the department's patient interactions and the use of IT. Moreover, these are the foremost stakeholders who can provide insights into the unique and sometimes complicated situations where medical knowledge is exploited, enabling a unique treatment course [55]. This approach is a similar approach taken by many other key publications in the field surveying clinicians to obtain insights into how patient-based information affects the diagnosis, therapy, patient safety, and overall clinical practice and care to patients

[55,128-130]. Therefore, these providers were considered to be the most important subject in this survey. In addition, our single informant strategy is consistent with prior literature on specialized not diversified units and departments [131].

### Sampling Techniques

Data were conveniently collected between November 10, 2019, and January 5, 2020, sampled from Dutch hospitals through the 5 master's students' professional networks within Dutch hospitals. Convenient sampling is a nonprobability sampling method where the sample is taken from a group of people easy to contact or reach and fit the profile [132].

### Sample Size and Inclusion and Exclusion Criteria

The survey software registered 230 active and unique participants. However, 101 cases had to be removed because of unreliable data entries or no entries at all. Additionally, 1 respondent (administrative function) did not belong to our target population and had to be removed from the sample. In a final step, 21 additional participants had to be removed due to substantial missing values (ie, more than 15%). Therefore, this study used 107 complete survey responses for final analyses.

### Constructs and Items

The selection of constructs and measures was made following previous empirically validated work. Additionally, this study includes only measures that were suitable for departmental-level analyses. Since this research was done in a health care setting, some original items had to be slightly reworded to fit the particular context. *IT ambidexterity* is operationalized using the item-level interaction terms of IT exploration and IT exploitation [35,69]. Items were adopted from Lee et al [35]. This study used three measures from Khin and Ho [39] for *digital dynamic capability* to represent the department's capability to manage innovative digital technologies for new patient service development. *Patient knowledge processes* refer to critical activities within the department that focus on generating, analyzing, and distributing patient-related information for strategy formulation and implementation. Six items based on the work of Jayachandran et al [92] are adopted. *Patient agility* concerns the departments' ability to sense and respond to patient needs adequately and is modeled as a higher-order (second) dynamic capability comprising the first-order dimensions *patient sensing capability* and *patient responding capability* [28,31,98]. Hence, this study used 10 empirically validated measures from Roberts and Grover [28] (see [Multimedia Appendix 1](#) for a complete overview of the construct and their associated items with their respective item-to-construct loadings [ $\lambda$ ], mean values [ $\mu$ ], and the SDs). All of the aforementioned items were measured using a 7-point Likert scale.

This study controlled the outcomes for both *size*, measured as full-time employees (log-normally distributed), and *age* of the department (5-point Likert scale, 1: 0-5 years; 5: >25 years).

### Ethics Considerations

Participants were allowed to complete the survey anonymously, and we did not log anything in the survey system that could trace participants. The participants could withdraw their entries if they wanted to. In addition, reusable personal data was not

requested, and the survey did not include questions about personal or sensitive topics [132]. Furthermore, before starting the survey, the participants had to sign a consent form. This approach is in line with the General Data Protection Regulation. Finally, participants were given the option to leave their email addresses to receive a research report. These email addresses were removed from the data set after this report was sent.

## Data Analyses and Management

### Model Estimation Procedure

The research model's hypothesized relationships are tested using partial least squares (PLS) structural equation modeling (SEM). To estimate and model parameters, SmartPLS version 3.2.9. was used [133]. In essence, PLS-SEM allows assessing both the measurement model (ie, outer model) [134] and the structural model (ie, inner model) of the research model so that hypotheses can be tested [135]. The PLS algorithm establishes latent constructs from the factor scores. It, thereby, seemingly avoids factor indeterminacy [136] so that these scores then be applied in the following analyses [137]. A fundamental justification for using PLS-SEM is that its use is appropriate in exploratory contexts and for the objective of theory development [136]. In this research, the focus is on prediction as to which the PLS algorithm assesses the explained variance ( $R^2$ ) for all dependent constructs [136]. Additionally, PLS is less strict in terms of particular data distributions [134].

### Sample Justification

Another reason to justify the variance-based approach is that the current sample is relatively small [138]. However, the sample size does exceed minimum threshold values to obtain stable PLS outcomes [139]. A power analysis was done using G\*Power [140]. Hence, this study assumes the conventional 80% statistical power and a 5% probability of error as input parameters, while the maximum number of predictors in the research model is three (when including the nonhypothesized direct effect of IT ambidexterity on agility). Based on

G\*Power's output parameters, a minimum sample of 38 cases were needed to detect an  $R^2$  of at least 24%. The current sample of 107 far exceeds this minimum requirement. The estimation procedure makes use of the general recommended path weighting scheme algorithm [133].

### Nonresponse Bias

This study accounts for possible nonresponse bias by using a  $t$  test to assess whether or not there is a significant difference between the early participants ( $n=66$ ) and the late subsample ( $n=41$  participants) on the responses on the Likert scale questions. This assessment is crucial as nonresponse bias can significantly impact the study outcomes and requires careful examination [141,142]. Hence, this study included various elements, including department age, the number of patients, and all construct items in the assessment. Furthermore, no significant difference could be detected after running the analyses and assessing the Levine equality test (of variances) and the  $t$  test for equality of mean values. Hence, this confirms the absence of nonresponse bias. Finally, per suggestions of Richardson et al [143] and Podsakoff et al [144], Harman single-factor analysis was applied using exploratory factor analysis (using SPSS Statistics v24, IBM Corp) to restrain possible common method bias [143,144]. Hence, this study sample is not affected by method biases, as no single factor is attributed to the majority of the variance.

## Results

### Sample Demographics

Within the final sample of 107 participants, 36 (33.6%) work for a university medical center, 41 (38.3%) work for a specialized top clinical (training) hospital, and the final 30 (28%) work for general hospitals. Table 1 shows the demographics of the participating hospital department (see also Multimedia Appendix 2 for an overview of the survey responses per medical department).

**Table 1.** Demographics of participating hospital departments.

Element and categories	Participants, n (%)
<b>Hospital type</b>	
University medical center	36 (33.6)
Top clinical training hospital	41 (38.3)
General hospital	30 (28)
<b>Department age (years)</b>	
0-5	28 (26.2)
6-10	20 (18.7)
11-20	20 (18.7)
20-25	8 (7.5)
>25	31 (29.0)
<b>Experience at this particular department (years)</b>	
0-5	49 (45.8)
6-10	18 (16.8)
11-20	28 (26.2)
20-25	6 (5.6)
>25	6 (5.6)
<b>Amount of patients</b>	
<4000	25 (23.4)
4000-6500	21 (19.6)
6500-9000	12 (11.2)
9000-11,500	12 (11.2)
11,500-14,000	11 (10.3)
≥14,000	26 (24.3)

### Assessment of the Measurement Model

Various analyses were done to determine the reliability and validity of the study constructs. This is a crucial step before testing the study's hypotheses and evaluating the quality of the research.

In the first step, the internal consistency reliability is investigated using both the Cronbach alpha measure and the composite reliability estimation value. In a subsequent step, this study assessed the convergent validity—using the average variance extracted (AVE)—of the first-order latent constructs [133]. All the AVE values exceeded the lowest recommended mark of 0.50 [145]. Construct-to-item loadings were likewise investigated to determine the degree to which a variable contributes to explaining the variance of a particular construct while considering the other measurements. These loading also exceeded minimum thresholds. In a final step, discriminant validity was established through the assessment of three tests. First, cross-loadings were investigated [146]. Analyses show that all items load more strongly on their intended latent constructs than they correlate on other constructs (see also [Multimedia Appendix 3](#)). Second, the well-known

Fornell-Larcker criterion is used [145]. In doing so, the square root of the AVE (see the diagonal entries in italics in [Table 2](#)) is compared with cross-correlation values. With this, each square root value should be larger than the cross-correlations [135]. As can be gleaned from [Table 2](#), all Fornell-Larcker values (ie, square root of the AVE) are higher than the shared variances of the constructs with other constructs in the model. In a final step, a newly developed measure, the heterotrait-monotrait ratio of correlations (HTMT), was used [147]. In general, acceptable outcomes of this analysis are HTMT values that are below 0.85 (upper bound). Discriminant validity is established between constructs. The HTMT analyses show that all values are well below the threshold value of 0.85. [Table 2](#) summarizes the entire assessment. The higher-order (formative) construct of patient agility was assessed using variance inflation factor (VIF) values for the constructs patient sensing and patient responding capability. These VIF values were well below the conservative threshold of 3.5. Hence, no multicollinearity was present within the research model [148].

As the reliability and validity of the model are now established, the model's associated fit indices can be assessed as well as the hypothesized relationships using the structural model.

**Table 2.** Convergent and discriminant validity assessment.

Constructs	AVE <sup>a</sup>	CA <sup>b</sup>	CR <sup>c</sup>	EXPLR <sup>d</sup>	EXPLO <sup>e</sup>	DDC <sup>f</sup>	PSC <sup>g</sup>	PRC <sup>h</sup>	KP <sup>i</sup>
EXPLR	0.888	.867	0.919	0.942 <sup>j</sup>					
EXPLO	0.790	0.937	0.960	0.502	0.889				
DDC	0.783	0.862	0.916	0.584	0.631	0.885			
PSC	0.723	0.904	0.929	0.375	0.502	0.588	0.850		
PRC	0.792	0.934	0.950	0.313	0.341	0.452	0.508	0.890	
KP	0.616	0.875	0.906	0.463	0.512	0.552	0.713	0.393	0.785

<sup>a</sup>AVE: average variance extracted.

<sup>b</sup>CA: Chronbach alpha measure.

<sup>c</sup>CR: composite reliability estimation.

<sup>d</sup>EXPLR: information technology exploration.

<sup>e</sup>EXPLO: information technology exploitation.

<sup>f</sup>DDC: digital dynamic capability.

<sup>g</sup>PSC: patient sensing capability.

<sup>h</sup>PRC: patient responding capability.

<sup>i</sup>KP: patient knowledge processes.

<sup>j</sup>The square root of the AVE was compared with cross-correlation values.

### Model Fit Assessments

This study used three metrics, that is, (1) standardized root mean square residual (SRMR; note, however, that the first two metrics for model fit should be interpreted with caution as these metrics are not fully established PLS-SEM evaluation criteria), (2) Stone-Geisser test, and (3) the variance explained by the model ( $R^2$ ) to assess the model's goodness-of-fit. We tried to get insights into how well the research model fits with the data obtained with these analyses.

First, the newly developed SRMR metric was calculated. The SRMR metric calculates the difference between observed correlations and the model's implied correlations matrix [135,149]. The obtained SRMR of 0.059 is well below the conservative threshold mark of 0.08, as proposed by Hu and Bentler [149]. Second, the Stone-Geisser test ( $Q^2$ ) was calculated using the blindfolding procedure to assess the model's predictive relevance. Hence, the current model's  $Q^2$  values (for endogenous constructs) all far exceed 0, indicating the overall model's predictive relevance.

Finally,  $R^2$  values were analyzed. The structural model explained 47% of the variance for digital dynamic capability ( $R^2=0.47$ ). The explained variance for patient knowledge processes is 36% and for patient agility 51%. These  $R^2$  outcomes are considered moderate to substantial effects [150]. Based on the assessed four metrics, it can be concluded that the research model performs well compared with the base values and that sufficient model fit was obtained to test the hypotheses.

### Assessment of the Structural Model and Hypotheses Testing

Following the model fit assessments and the assessment of the measurement model, we tested the hypotheses of the study that we developed in the section Research Model and Hypotheses.

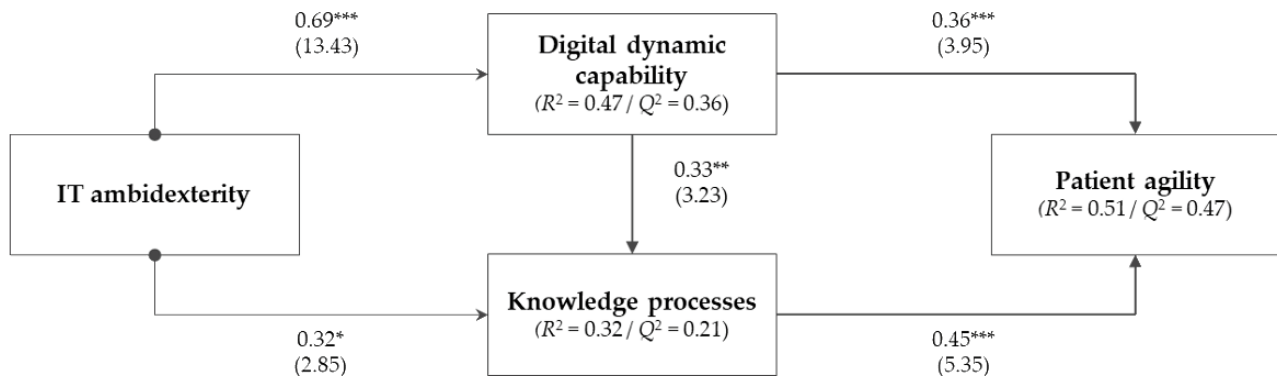
Based on the outcomes of the nonparametric bootstrap resampling procedure [135], this study found support for the first hypothesis, that is, IT ambidexterity positively impacts digital dynamic capability ( $\beta=.69$ ;  $t_{4999}=13.43$ ;  $P<.001$ ). Thus, our results showed that IT exploration and exploitation's simultaneous engagement enhances the qualities and competencies to manage innovative digital technologies for new patient service development. Likewise, this study found support for hypothesis 2 (ie, IT ambidexterity  $\rightarrow$  knowledge processes:  $\beta=.32$ ,  $t_{4999}=2.85$ ;  $P=.005$ ). Therefore, the outcomes showed that hospital departments that exploit and explore their current IT resources portfolio integrate and leverage patient information sources and drive effective knowledge processes.

Digital dynamic capability was positively associated with patient agility ( $\beta=.36$ ;  $t_{4999}=3.95$ ;  $P<.001$ ), providing support for hypothesis 3. The outcomes proved that digital dynamic capability is crucial for hospital departments that strive for patient agility in clinical practice. In addition, the structural model results support hypothesis 4 (ie, digital dynamic capability  $\rightarrow$  knowledge processes:  $\beta=.33$ ;  $t_{4999}=3.23$ ;  $P=.001$ ). Hence, hospital departments that engage in developing and mastering new technologies are more efficient in deploying the existing knowledge and, thus, generate more exploitative activities and effective knowledge processes. The results also showed that digital dynamic capability *partially* mediates the effect of IT ambidexterity on knowledge processes [135,151]. Finally, the results support hypothesis 5 (ie, knowledge processes are positively associated with patient agility:  $\beta=.45$ ;  $t_{4999}=5.35$ ;  $P<.001$ ). Therefore, these outcomes suggested that patient agility relies on the integration of knowledge processes in the department to a great extent. Furthermore, it can be concluded that also partial mediation characterizes the triangular relationship between digital dynamic capability, knowledge processes, and patient agility.

The bootstrapped PLS results showed nonsignificant effects for the included control variables: *size* ( $\beta=-.10$ ;  $t_{4999}=0.79$ ;  $P=.86$ )

and *age* ( $\beta=-.01$ ;  $t_{4999}=0.17$ ;  $P=.43$ ). Figure 2 summarizes the structural model assessment results.

**Figure 2.** Structural model results. IT: information technology.



\*  $P \leq 0.05$ , \*\*  $P \leq 0.01$ , \*\*\*  $P \leq 0.001$

## Discussion

### General Discussion

The digital transformation brings about an unprecedented challenge for modern day hospitals [152,153]. Decision makers and stakeholders across the hospital need to make sure that digital resources and technological innovations are aligned and deployed with care to enhance efficiencies, decision-making, and quality of services so that personalized and patient-centered care can be delivered [154]. Thus, it is needless to say that digital innovations can improve existing processes and medical procedures for diagnostics and patient treatment.

Using data from 107 hospital departments in the Netherlands, this study showed that the simultaneous engagement of IT exploration and IT exploitation within hospital departments (ie, IT ambidexterity) enhances the qualities and competencies to manage innovative digital technologies for new patient service development (ie, digital dynamic capability). In addition, the outcomes showcase that the greater the hospital departments' IT ambidexterity, the more effective are its knowledge processes. Furthermore, our results show that actively investing in digital dynamic capability is essential when departments want to enhance quality and patient clinical journeys. In particular, our study demonstrates that the more developed the hospital department's digital dynamic capability, the more effective will be the hospital department's knowledge processes. This outcome is important, as knowledge processes facilitate transforming clinical data into patient-related insights, thereby supporting clinicians within hospitals to make informed decisions concerning diagnosis and treatment. Our study shows that these data-driven processes allow clinicians to improve the patient treatment process and medical quality services and be more agile in their work, which is in line with the theory by Li et al [53]. Finally, our results show that digital dynamic capability is a crucial driver of patient agility, conceptualized as a dynamic capability. This capability provides the hospital department with adequate responsiveness by enabling the flexibility to sense and respond to patient demands and needs.

This study makes substantial theoretical and practical contributions, which will be discussed next.

### Implications for Theory and Practice

The process of digitizing existing patient services and developing new digital solutions remains time-consuming and challenging in many ways. In addition, from a research perspective, there is still a limited understanding of how IT resources and the digital capability-building processes can facilitate patient agility and contribute to the much needed insights on obtaining value from IT at the departmental level [35,155,156]. This study aims at addressing these particular gaps in the literature. Notably, this study designed and tested a research model, using a sample of 107 hospital departments from the Netherlands, arguing that IT ambidexterity would drive a department's patient agility by first enabling digital dynamic capability and knowledge processes. Outcomes of this study found support for these foundational claims. Furthermore, this study's structural model analyses unfolded that IT ambidexterity, which is a crucial antecedent of digital dynamic capability and knowledge processes. These crucial capabilities and processes, in turn, substantially impact the departments' ability to adequately sense and respond to patient needs and wishes (ie, patient agility).

Evidence unfolded that digital dynamic capability partially mediates the relationship between IT ambidexterity and knowledge processes. Similarly, a partial mediation characterizes the triangular relationship between digital dynamic capability, knowledge processes, and patient agility. These outcomes corroborate existing IT-enabled agility and dynamic capability studies [102,124,157,158]. The results also support the core idea that the hospital department's capacity to obtain value from its knowledge assets is a crucial success factor in achieving patient agility [110,158].

This study embraces the dynamic capabilities and knowledge-based view of IT resource deployments and advances the current insights on the resource and capability-building perspective [74,98,101,155]. It does so by unfolding the

nomological path from *resources* to the *IT-enabled value perspective* [21].

Outcomes of this study suggest that hospitals—that are committed to the process of ambidextrously managing their IT resources—are more proficient in promptly sensing and responding to patients' medical needs and demands. These theoretical contributions are valuable as these particular insights remained unclear in the extant literature, and future research can take these insights into account when investigating the IT benefits in hospitals. Likewise, unfolding the benefits of hospital departments' dual capacity to aim for two disparate things at the same time using empirical data is relevant from a practical perspective, as the business value of IT and the preceding IT investments can be justified [35,159,160]. The outcomes corroborate with the “theory of swift and even patient flow” [44] in that digital capabilities support the process of optimizing current hospital assets and help adequately respond to patient's needs by improving hospital operations (eg, better diagnoses, scheduling, and coordination of patient care). Hence, it supports the *call* for researchers to demonstrate the best ways to optimize digital health care solutions [21].

This study provides hospital department managers and decision makers with valuable practical implications. Hospital departments must direct IT investments to bring about the highest IT business value, given the many substantial challenges to ensure high quality across the patient care delivery continuum. This research shows that IT ambidextrous departments can adequately develop new innovative digital opportunities and patient services to enhance the hospital department's knowledge processes and patient agility levels. This development path is crucial for successful hospital departments that strive to enhance the patient's clinical journey and provide patients with fitting health services. However, it is important to note that IT ambidexterity can help hospital departments indirectly obtain high levels of patient agility. However, this development might be hindered if departments do not fully leverage their dual IT exploration and exploitation capacity to drive digital dynamic capability and knowledge processes and enhance patient agility.

Digital dynamic capability is crucial in the development of knowledge processes and patient agility. Hospital department managers should develop the core competencies, knowledge, and skills to process patient information better, adequately respond to digital transformation, master the state-of-the-art digital technologies, and deliberately develop innovative patient services using digital technology. Hospital department managers should also be aware of the crucial role of knowledge processes. Mature knowledge processes enhance decision-making processes and drive patient agility in hospital departments. Therefore, they should dedicate their resources to leverage these capabilities fully so that they are better equipped to search, identify, and absorb new technological innovations; integrate, process, and exchange patient information; and use them for decision-making processes, and to anticipate and respond fast to changes in the patient's health service needs. Our study results highlight the need for hospital departments to focus more on patient agility, a crucial antecedent of enhanced patient care. Hospital

department managers and decision makers should also deliberately pay attention to end user's psychological meaningfulness, stakeholder involvement, and providing adequate resourcing and infrastructures when implementing new digital technologies [33,161-163]. These aspects are crucial when implementing new digital technologies so that the hospital staff is supported and perceived value can be related to individual behavior changes and key stakeholders' needs and expectations. The outcomes are particularly relevant for practitioners now, as hospitals worldwide need to take action to transform health care delivery processes using digital technologies and increase clinical productivity during the COVID-19 crisis [164].

In summary, hospital departments should strive to be agile in the modern turbulent economic environment. This study provides crucial insights and guidance to achieve this.

### Limitations and Future Studies

Several study limitations should be mentioned. These limitations suggest future research avenues. This study used self-reported data to test the developed hypotheses as obtaining objective measures is typically a challenging endeavor. The decision to use self-reported data is still justifiable as empirical outcomes, as these data types are strongly correlated to objective measures [127,165,166]. Another concern is that data were collected using the single informant strategy. As such, method bias could still be a concern. This study did pay considerable attention to account for possible measurement errors and method bias. Future research could embrace a matched-pair design where different participants address independent (explanatory) and dependent constructs. Another opportunity for future research is triangulating the included measures with, for example, potentially available archival data from public sources. These insights, next to possibly applying the current model to other countries, could help validate the outcomes further. In addition, a more substantial sample of hospital departments will further contribute to the robustness of the results. Scholars could confirm this research's outcomes using a replication study in different (non-Western) countries. Future research could also investigate patient agility, focusing on specific departments, as this study encompasses various participating departments. Focusing on a few departments with more responses could capture a richer view of the subject matter.

Finally, this study did not include patient service performance outcomes and benefits beyond this paper's scope. Hence, it would be interesting to investigate the relationships between patient agility and the hospital department's performance outcomes, as patient agility is considered a crucial ingredient in delivering high-quality patient value and overall streamlined patient journeys. Hence, this research's outcomes inform further research about whether patient agility impacts clinical care quality and efficacy. Scholars could then investigate patient agility's contribution to increasing, for example, clinical productivity and quality enhancement during different stages of the COVID-19 pandemic [164]. Finally, future work could also involve the patient engagement and digital technology co-design perspectives [163,167,168].



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## Conflicts of Interest

None declared.

### Multimedia Appendix 1

Survey constructs and items and descriptive statistics.

[[DOCX File , 19 KB - xmed\\_v2i4e32336\\_app1.docx](#) ]

### Multimedia Appendix 2

Survey response per medical department.

[[DOCX File , 16 KB - xmed\\_v2i4e32336\\_app2.docx](#) ]

### Multimedia Appendix 3

Cross-loading analysis for the first-order factors.

[[DOCX File , 18 KB - xmed\\_v2i4e32336\\_app3.docx](#) ]

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## Abbreviations

- AI:** artificial intelligence
- AVE:** average variance extracted
- DCV:** dynamic capabilities view
- HTMT:** heterotrait-monotrait ratio of correlations
- IS:** information system
- IT:** information technology
- PLS:** partial least squares
- SEM:** structural equation modeling
- SRMR:** standardized root mean square residual
- VIF:** variance inflation factor

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Original Paper

# COVID-19 Outcomes and Genomic Characterization of SARS-CoV-2 Isolated From Veterans in New England States: Retrospective Analysis

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## Abstract

**Background:** Clinical and virologic characteristics of COVID-19 infections in veterans in New England have not been described. The average US veteran is a male older than the general US population. SARS-CoV-2 infection is known to cause poorer outcomes among men and older adults, making the veteran population an especially vulnerable group for COVID-19.

**Objective:** This study aims to evaluate clinical and virologic factors impacting COVID-19 outcomes.

**Methods:** This retrospective chart review included 476 veterans in six New England states with confirmed SARS-CoV-2 infection between April and September 2020. Whole genome sequencing was performed on SARS-CoV-2 RNA isolated from these veterans, and the correlation of genomic data to clinical outcomes was evaluated. Clinical and demographic variables were collected by manual chart review and were correlated to the end points of peak disease severity (based on oxygenation requirements), hospitalization, and mortality using multivariate regression analyses.

**Results:** Of 476 veterans, 274 had complete and accessible charts. Of the 274 veterans, 92.7% (n=254) were men and 83.2% (n=228) were White, and the mean age was 63 years. In the multivariate regression, significant predictors of hospitalization (C statistic 0.75) were age (odds ratio [OR] 1.05, 95% CI 1.03-1.08) and non-White race (OR 2.39, 95% CI 1.13-5.01). Peak severity

(C statistic 0.70) also varied by age (OR 1.07, 95% CI 1.03-1.11) and O2 requirement on admission (OR 45.7, 95% CI 18.79-111). Mortality (C statistic 0.87) was predicted by age (OR 1.06, 95% CI 1.01-1.11), dementia (OR 3.44, 95% CI 1.07-11.1), and O2 requirement on admission (OR 6.74, 95% CI 1.74-26.1). Most (291/299, 97.3%) of our samples were dominated by the spike protein D614G substitution and were from SARS-CoV-2 B.1 lineage or one of 37 different B.1 sublineages, with none representing more than 8.7% (26/299) of the cases.

**Conclusions:** In a cohort of veterans from the six New England states with a mean age of 63 years and a high comorbidity burden, age was the largest predictor of hospitalization, peak disease severity, and mortality. Non-White veterans were more likely to be hospitalized, and patients who required oxygen on admission were more likely to have severe disease and higher rates of mortality. Multiple SARS-CoV-2 lineages were distributed in patients in New England early in the COVID-19 era, mostly related to viruses from New York State with D614G mutation.

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## KEYWORDS

infectious disease; COVID-19; epidemiology; veteran; outcome; sequencing; genetics; virus; United States; impact; testing; severity; mortality; cohort

## Introduction

### Background

Disease severity and outcomes of COVID-19 caused by SARS-CoV-2 vary among individuals who become infected, with several factors that have been suggested as predictors of mortality, including Charlson comorbidity index score, age, and BMI [1-6]. Other comorbidities such as cardiovascular disease, diabetes, and dementia are prevalent in patients who are hospitalized and can predict worse outcomes and complications following infection, but the current literature shows variable impacts of comorbidities in different populations [7-15].

Virologic characteristics have been suggested to impact the severity of disease, and concern has been raised about several variants being more transmissible or more lethal [16-18]. A dynamic nomenclature system (Pangolin) was developed to classify SARS-CoV-2 and identify lineages and mutations that could impact infectivity and virulence [19]. In the early era of COVID-19, there was significant concern about the D614G variant being more infectious, and SARS-CoV-2 with this mutation had been found to cause infections in New York State [17,20]. Evaluation of prevalence of this virus in the nearby states therefore became of substantial interest. Viral epidemiology and regional evaluation of viral variants, with their clinical correlations, are important to provide a full understanding of the disease.

### Study Rationale

Given the high variability and conflicting data in predicting who will have poor outcomes, assessment of specific populations is necessary to give providers the best clinical picture on their patients. The US veteran population is predominantly male (89%) with an average age of 58 years, compared to the general US population that has a median age of 38.5 years and a gender distribution of 98.2 males to every 100 females [21,22]. Both older age and male sex have been found to be independent predictors of greater disease severity and mortality in COVID-19 infections [8,13,23-26]. Evaluation of clinical outcomes among US veterans, a population predisposed to poorer outcomes because of these demographic variables, therefore, is important. Clinical outcomes of veterans with COVID-19 in New England

and SARS-CoV-2 genomics have not been described. Outcome assessment based on unique demographic and clinical variables in people infected with novel viruses cannot be overemphasized. Given the high mutability of SARS-CoV-2, changing epidemiological trends over time, and known impact of virological factors on clinical outcomes, this study becomes even more important as it will provide an insight into this unique regional population with COVID-19 at a relevant time period in the evolution of the virus.

### Study Aims

We aimed to describe patient characteristics, comorbidities, and disease factors that impact patient outcomes and present data on the genomic composition of the SARS-CoV-2 infecting these patients.

## Methods

### Specific Objectives

This study aims to determine the clinical and virologic factors impacting outcomes in veterans with COVID-19.

### Study Design With Justification

We conducted a retrospective chart review to gather demographic and clinical variables as well as clinical outcomes. The Veterans Affairs (VA) health care system has electronic medical records that can be accessed to extract this information. We have conducted such chart reviews before to help inform management decisions based on predictors of outcomes [27].

### Study Setting

In 2020, the VA health care system in West Haven, Connecticut had been entrusted with testing for SARS-CoV-2 for all six VA health care centers in New England states (Connecticut, Massachusetts, Maine, New Hampshire, Rhode Island, Vermont). The virus, isolated from samples testing positive, was then sent for whole genome sequencing (WGS) under an agreement funded by the Centers for Disease Control and Prevention (CDC).

## Participants (Sample Size and Inclusion Criteria)

This study included all veterans who tested positive for COVID-19 from April 8, 2020, to September 16, 2020, at any of the six New England VA hospitals. Inclusion criteria included patients with accessible chart records and a diagnosis of COVID-19 based on one of three polymerase chain reaction-based tests: Xpert Xpress SARS-CoV-2 (Cepheid), Simplexa COVID-19 Direct Kit (DiaSorin), and Roche cobas 6800 system.

## Data Collection

We manually reviewed charts and recorded demographics (age, gender, race, BMI, long-term care [LTC] facility status, and state of residence when diagnosed with COVID-19). Comorbidities recorded were immunosuppression, dementia, diabetes mellitus, chronic kidney disease stage 3, chronic liver disease, coronary artery disease (CAD), heart failure, atrial fibrillation, chronic obstructive pulmonary disease, asthma, and active tobacco use. All data collection was retrospective after a diagnosis of COVID-19 had been confirmed. If chart review occurred while a veteran was hospitalized, the chart was again reviewed retrospectively after discharge from the hospital.

## Sample Collection and Handling

Handling of nasopharyngeal specimens or isolated virus was carried out by the VA Connecticut Healthcare System (VACHS) clinical laboratory as part of clinical care, following standardized Clinical Laboratory Improvement Amendments guidelines [28]. Our viral repository was populated by the positive test results of all New England veterans. The VACHS laboratory handled specimens, isolated the SARS-CoV-2 RNA, and shipped it for WGS to a non-VA laboratory. We obtained the details of the platform used to diagnose, the cycle threshold (Ct), and the date of test from the laboratory. Sequencing of viral genomes was conducted at the non-VA laboratory by our coauthors as follows.

## Genomic Sequencing and Phylogenetic Analysis

Whole virus genomes were sequenced ( $\geq 20\times$  coverage depth across  $\geq 70\%$  of the genome) using the Illumina ( $n=238$ ) and Nanopore ( $n=61$ ) platforms. WGS was conducted on SARS-CoV-2 isolates with a Ct value  $<36$  and provided near-complete or complete genome results where the Ct value was  $<30$ . Using BWA-MEM version 0.7.15 (GNU Project), we aligned reads to the Wuhan-Hu-1 reference genomes (GenBank MN908937.3). With iVar v1.2.1 (Andersen Lab), we trimmed sequencing adaptors and primer sequences, and called bases by simple majority ( $>50\%$  frequency) at each site to generate consensus genomes. An ambiguous N was used when  $<10$  reads were present at a site. We aligned consensus genomes with MAFFT (GNU Project) [29] and masked problematic sites [30]. We built a phylogenetic tree with IQTree (IQ-Tree) [31] using

an HKY substitution model and 1000 bootstraps, visualized it with Python module baltic v0.1.5 (Python Software Foundation), and assigned lineages with Pangolin [19].

## Outcome Measures

Our categorical outcomes, also derived from manual chart review, were hospitalization status, mortality, and oxygen ( $O_2$ ) requirement within 24 hours of admission from manual chart review. We divided patients based on their peak disease severity (ordinal) into five categories depending on oxygenation requirements: (1) no  $O_2$  requirement, (2) 1 to 3 liters by nasal cannula (NC), (3) 4 to 6 liters by NC, (4)  $>6$  liters  $O_2$  or noninvasive positive pressure ventilation, and (5) mechanical ventilation. Mortality was defined as death within 60 days from the date of diagnosis.

## Data Analysis

We used STATA v16 (StataCorp) for logistic regressions to predict our hospitalization and mortality, and ordinal logistic regression to predict peak disease severity. We first conducted a univariate analysis, then used significant variables from the univariate analysis ( $P<.05$ ) to use in a multivariate model for each of our outcomes to assess the impact of several variables at once, which has been frequently used in COVID-19 literature [9,10,32-34]. Assumptions for logistic regressions (binary outcome, linearity, no outliers, and multicollinearity) were tested and met, with maximum variance inflation factors of 2. Genomic characteristics were reported descriptively.

## Ethical Considerations

The VACHS Institutional Review Board approved the creation and maintenance of a data repository of all veterans in New England diagnosed with COVID-19 and a viral repository of the SARS-CoV-2 RNA received from all six New England facilities. This study was conducted in accordance with the Declaration of Helsinki, keeping all private health information secure in approved secure folders behind a VA firewall. The RECORD (Reporting of Studies Conducted Using Observational Routinely-Collected Data) statement guidelines were used to maintain transparency in the reporting of this study [35].

## Results

### Participant Characteristics

Of 476 veterans in six New England states with confirmed SARS-CoV-2 during the study period, 274 had complete and accessible charts. Of 274 veterans, 93% ( $n=254$ ) were men, 83% ( $n=228$ ) were White, the mean age was 63 (SD 17.6) years, and over one-third resided were in LTC ( $n=92$ ; Table 1). The most common comorbidities were CAD ( $n=74$ ), diabetes ( $n=68$ ), and tobacco use ( $n=62$ ).

**Table 1.** Patient characteristics (n=274).

Demographics	Participants
Age (years), mean (SD)	62.9 (17.6)
<b>Gender, n (%)</b>	
Male	254 (93)
Female	20 (7)
<b>Race, n (%)</b>	
White	228 (83)
Non-White	46 (17)
BMI >30, n (%)	110 (40)
From LTC <sup>a</sup> , n (%)	92 (34)
<b>State, n (%)</b>	
Connecticut	89 (32)
Massachusetts	150 (55)
Maine	4 (1)
New Hampshire	9 (3)
Rhode Island	20 (7)
Vermont	2 (1)
<b>Comorbidities, n (%)</b>	
Immunosuppressed	10 (4)
Dementia	42 (15)
Diabetes	68 (25)
CKD <sup>b</sup> 3	18 (7)
Chronic liver disease	32 (12)
<b>Chronic heart disease</b>	107 (39)
CAD <sup>c</sup>	74 (27)
Heart failure	29 (11)
Atrial fibrillation	40 (15)
<b>Chronic lung disease</b>	97 (35)
COPD <sup>d</sup>	44 (16)
Asthma	19 (7)
OSA <sup>e</sup>	55 (20)
Tobacco use	62 (23)

<sup>a</sup>LTC: long-term care.

<sup>b</sup>CKD: chronic kidney disease.

<sup>c</sup>CAD: coronary artery disease.

<sup>d</sup>COPD: chronic obstructive pulmonary disease.

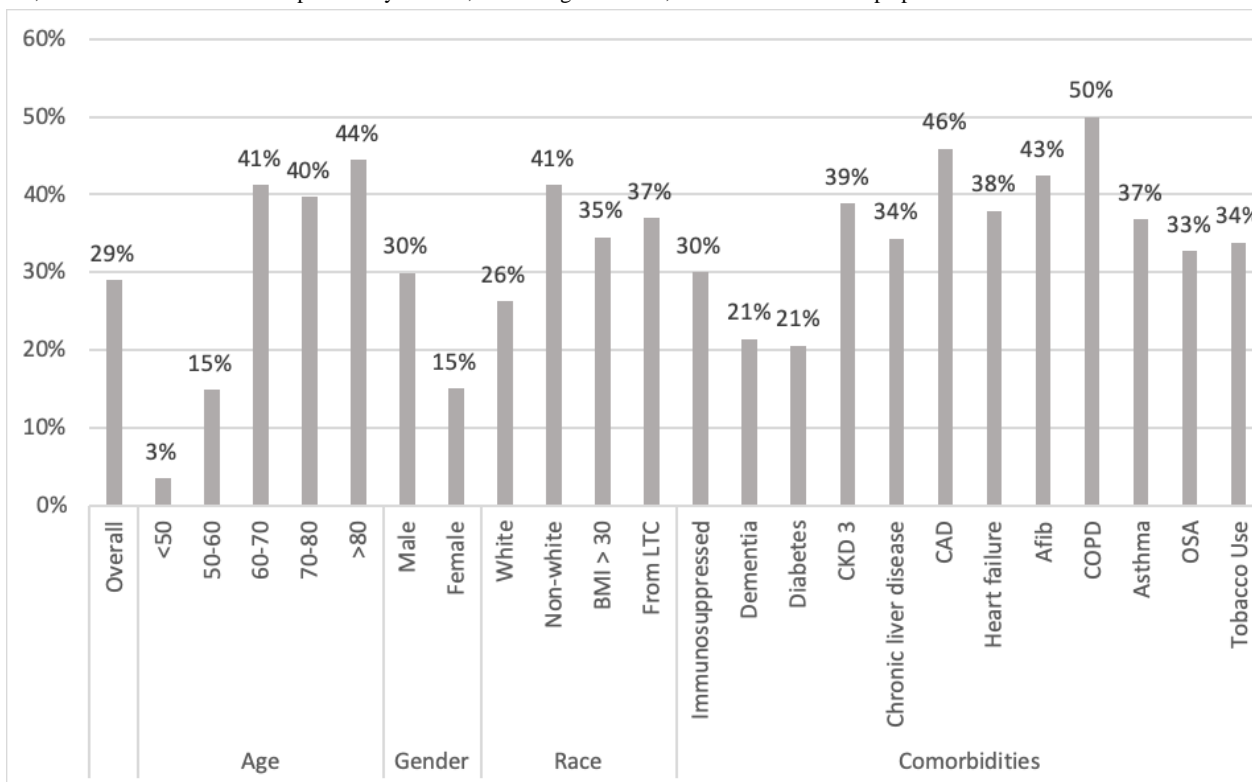
<sup>e</sup>OSA: obstructive sleep apnea.

### Rates and Predictors of Hospitalization, Peak Severity, and Mortality

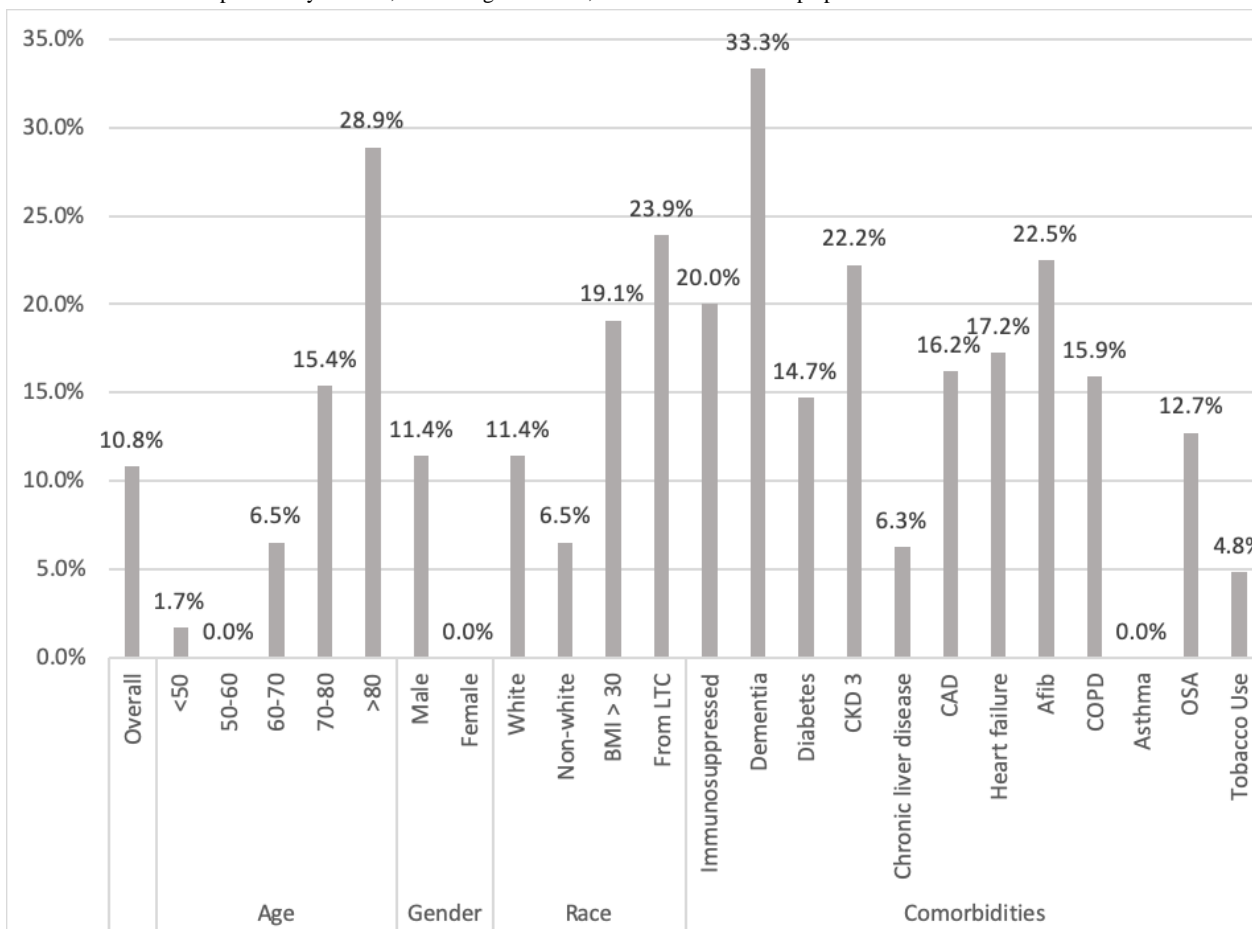
Notably, 12% (n=33) of patients required O<sub>2</sub> above their baseline home O<sub>2</sub> requirement within 24 hours of admission, and 21% (n=58) of all patients required O<sub>2</sub> support at some point during

hospitalization. In terms of peak severity, 79% (n=216) required only room air, 11% (n=30) required 1 to 3 liters O<sub>2</sub>, 4.0% (n=11) required 4 to 6 liters O<sub>2</sub>, 3.6% (n=10) required >6 liters O<sub>2</sub> or noninvasive positive-pressure ventilation, and 2.2% (n=6) were intubated. The hospitalization rate was 29% (n=79; [Figure 1](#)), and the overall mortality rate was 11% (n=30; [Figure 2](#)).

**Figure 1.** Percent of patients hospitalized based on patient demographics and comorbidities. CAD: coronary artery disease; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; LTC: long-term care; OSA: obstructive sleep apnea.



**Figure 2.** Percent of patients who died based on patient demographics and comorbidities. CAD: coronary artery disease; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; LTC: long-term care; OSA: obstructive sleep apnea.



Univariate regression analysis results are reported in [Table 2](#). In the multivariate regression ([Table 2](#)), significant predictors of hospitalization (C statistic 0.75) were age (odds ratio [OR] 1.05, 95% CI 1.03-1.08) and non-White race (OR 2.39, 95% CI 1.13-5.01; [Table 2](#)). Peak severity (C statistic 0.70) also varied by age (OR 1.07, 95% CI 1.03-1.11) and O<sub>2</sub> requirement on admission (OR 45.7, 95% CI 18.79-111). Mortality (C

statistic 0.87) was predicted by age (OR 1.06, 95% CI 1.01-1.11), dementia (OR 3.44, 95% CI 1.07-11.1), and O<sub>2</sub> requirement on admission (OR 6.74, 95% CI 1.74-26.1). In other words, for every year increase in age, the odds of hospitalization increased by 5%, peak severity increased by 7%, and mortality increased by 6%.

**Table 2.** Univariate and multivariate regression analysis of factors that predict hospitalization, peak severity, and death.

	Hospitalization		Peak severity		Death	
	Unadjusted OR <sup>a</sup> (95% CI)	<i>P</i> value	Unadjusted OR (95% CI)	<i>P</i> value	Unadjusted OR (95% CI)	<i>P</i> value
<b>Univariate regression</b>						
Age	1.06 (1.03-1.08)	<i>&lt;.001</i> <sup>b</sup>	1.06 (1.04-1.09)	<i>&lt;.001</i>	1.1 (1.06-1.14)	<i>&lt;.001</i>
Female gender	0.41 (0.12-1.45)	.17	0.42 (0.95-1.9)	.26	N/A <sup>c</sup>	N/A
Non-White race	1.97 (1.02-3.8)	.04	1.3 (0.6-2.6)	.55	0.54 (0.16-1.9)	.33
From long-term facility	1.78 (1.04-3.07)	.04	2.8 (1.5-5.1)	.001	7.9 (3.2-19.2)	<i>&lt;.001</i>
BMI <30	1.52 (0.9-2.7)	.14	1.1 (0.6-2)	.77	5.8 (2.1-15.9)	.001
Dementia	0.63 (0.29-1.4)	.25	1.6 (0.7-3.3)	.26	7.2 (3.2-16.6)	<i>&lt;.001</i>
COPD <sup>d</sup>	3.04 (1.6-5.9)	.001	1.5 (0.74-3.2)	.25	1.8 (0.7-4.5)	.22
Heart failure	1.6 (0.7-3.5)	.25	1.8 (0.8-4.0)	.18	1.9 (0.67-5.5)	.23
CAD <sup>e</sup>	2.93 (1.66-5.2)	<i>&lt;.001</i>	2.1 (1.2-3.9)	.02	2.1 (0.9-4.6)	.07
Atrial fibrillation	2.05 (1.03-4.1)	.04	3 (1.4-5.9)	.002	3.1 (1.3-7.4)	.01
Hospitalization	N/A	N/A	N/A	N/A	2.58 (1.18-5.65)	.02
O <sub>2</sub> on admission	N/A	N/A	46.2 (19.9-107.3)	<i>&lt;.001</i>	4.34 (1.77-10.6)	.001
<b>Multivariate regression</b>						
Age	1.05 (1.03-1.08)	<i>&lt;.001</i>	1.07 (1.03-1.11)	<i>&lt;.001</i>	1.06 (1.01-1.11)	.02
Non-White race	2.39 (1.13-5.01)	.02	N/A	N/A	N/A	N/A
From long-term facility	0.70 (0.36-1.38)	.31	1.18 (0.55-2.55)	.67	2.0 (0.58-6.88)	.27
BMI <30	N/A	N/A	N/A	N/A	2.95 (0.81-10.75)	.10
Dementia	N/A	N/A	N/A	N/A	3.44 (1.07-11.1)	.04
COPD	1.73 (0.84-3.35)	.14	N/A	N/A	N/A	N/A
CAD	1.44 (0.75-2.81)	.27	0.71 (0.32-1.55)	.39	0.57 (0.209-1.57)	.28
Atrial fibrillation	0.984 (0.45-2.16)	.97	1.11 (0.46-2.64)	.82	1.25 (0.42-3.69)	.69
Hospitalization	N/A	N/A	N/A	N/A	1.36 (0.40-4.65)	.63
O <sub>2</sub> on admission	N/A	N/A	45.7 (18.79-111)	<i>&lt;.001</i>	6.74 (1.74-26.1)	.006

<sup>a</sup>OR: odds ratio.

<sup>b</sup>Italics indicate that *P*<.05 (exact values reported).

<sup>c</sup>N/A: not applicable.

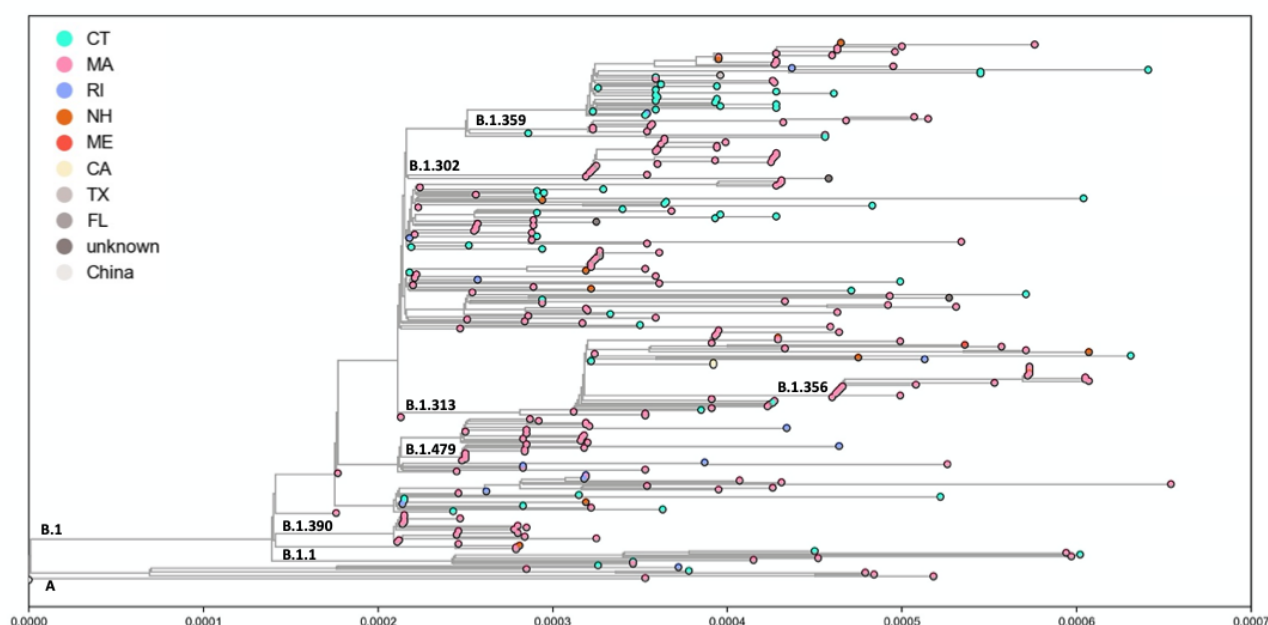
<sup>d</sup>COPD: chronic obstructive pulmonary disease.

<sup>e</sup>CAD: coronary artery disease.

## Genomic Characteristics

For the genomic characteristics, among the 476 patients, 299 patients' genomes had adequate coverage for analysis. We found the majority of our specimens (154/299, 51.5%) were from SARS-CoV-2 lineage B.1 or a sublineage of B.1 (eg, B.1.302, B.1.303, B.1.356; 137/299, 46%), all of which are defined by

D614G substitution ([Figure 3, Multimedia Appendix 1](#)). Only 2.4% (7/299) were from the lineage A that lack the D614G mutation. There were 41 different SARS-CoV-2 lineages detected in our cohort, and we did not have the power to test for clinical correlates. Our sequencing data does inform us that the outcomes presented in this VA cohort are dominated by the impacts of the B lineage D614G mutation.

**Figure 3.** Maximum likelihood tree of genomes.

## Discussion

### Principal Findings

Our study found that in a cohort of veterans with an average age of 63 years and a high comorbidity burden, age was significantly associated with risk of hospitalization, peak disease severity, and mortality.  $O_2$  requirement upon admission correlated with peak disease severity and mortality, while dementia was an additional factor associated with higher mortality. The CDC provides a list of chronic medical conditions (May 2021) that predispose individuals to severe illness from SARS-CoV-2 infection [6]. Based on this list, >75% of US adults fall under a high-risk category [36], therefore making it important to have select populations evaluated for uniquely applicable risk factors. Veterans are a unique cohort because of advanced age on average [22] and more comorbidities. Understanding clinical factors that impact outcomes in veterans will help health care providers risk-stratify patients with similar demographic profiles, and future research should explore the impact of new treatments and vaccination on outcomes. The predominance of B lineage D614G in our study specimens provided valuable insight into the pace of epidemiological trend and the evolution of the virus early in the COVID-19 era through the New England region.

### Comparison With Prior Studies

Many COVID-19 studies have found age to be a predictor of worse outcomes [3,37-40]. In our study, age was a significant predictor for all of the studied outcomes and was a confounder for other variables. Accordingly, LTC status predicted all three of our outcomes on univariate analysis but not on multivariate analyses, possibly because LTC units tend to have older residents. Earlier in the COVID-19 pandemic, residents of nursing homes had higher rates of infection and severe illness

and mortality [41]. Our study shows disease outcomes were not impacted by their residence status after adjusting for age.

Concurrent work from our group suggests that  $O_2$  requirement within 24 hours of admission predicts poor outcomes in veterans, which has helped inform the triage guidelines at our health care system. This is an important finding because other ways of determining oxygenation status can frequently change and thus become difficult for clinicians to use in practice [22].

Our study supports data from previous reports that non-White patients in the United States are at increased risk of hospitalization but have similar peak severity and mortality outcomes [42,43]. Many studies have shown that minorities often have delays in seeking care, causing higher risk of hospitalization when they do seek care [44,45]. This may explain the outcomes in our study. It is critical to continue ongoing efforts to combat medical inequities and target prevention efforts and education to communities and racial groups most affected by COVID-19.

After adjusting for age and other comorbidities, we found that patients with dementia had a higher risk of death. This is similar to other studies on patients with COVID-19 and dementia [37,46,47]. This may be explained by a host of biological factors but also may be a result of the inability to self-report symptoms. This finding emphasizes the importance of extra care and monitoring required when approaching a patient with dementia.

### Limitations

Limitations of this study include the smaller sample size. Furthermore, our study is specific to veterans, which is a largely male and older cohort, and results may not therefore be generalizable. The time period of this study was prior to established medical therapies for COVID-19, and our reported outcomes are likely worse than expected today. Strengths of

our study include its comprehensive scope, wide geographic range, manual chart review process allowing for the capturing of all comorbidities and oxygenation parameters that may not be available otherwise in a database, and multivariate analysis of many potential risk factors.

### Conclusion

Our study found that in an older cohort of veterans from the six New England states with a high comorbidity burden, age was

the single strongest predictor of hospitalization, peak severity, and mortality. Non-White veterans were more likely to be hospitalized, and patients who required oxygen on admission were more likely to have severe disease and higher rates of mortality. Furthermore, patients with dementia were more likely to die. Multiple genomic variants of SARS-CoV-2 were distributed in patients in New England early in the COVID-19 era, mostly from a B.1 sublineage with the spike D614G mutation.

### Acknowledgments

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### Authors' Contributions

The authors confirm contribution to the manuscript as follows. ML and SG participated in the conception, design, data collection, analysis and interpretation of results, and manuscript preparation. YHS and MR participated in the data collection, analysis and interpretation of results, and manuscript preparation. MP and NDG participated in the conduction, analysis and interpretation of whole genome sequencing, and manuscript preparation. DC participated in the data collection and analysis and interpretation of results. CBFV, JRF, and TRA participated in the conduction and analysis of whole genome sequencing.

### Conflicts of Interest

NDG is a paid consultant of Tempus Labs for infectious disease genomics.

Multimedia Appendix 1

Lineages of genomes.

[[DOCX File , 14 KB - xmed\\_v2i4e31503\\_app1.docx](#) ]

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## Abbreviations

**CAD:** coronary artery disease

**CDC:** Centers for Disease Control and Prevention

**Ct:** cycle threshold

**LTC:** long-term care

**NC:** nasal cannula

**OR:** odds ratio

**REPORT:** Reporting of Studies Conducted Using Observational Routinely-Collected Data

**VA:** Veterans Affairs

**VACHS:** VA Connecticut Healthcare System

**WGS:** whole genome sequencing

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Original Paper

# Influence of the COVID-19 Lockdown on the Physical and Psychosocial Well-being and Work Productivity of Remote Workers: Cross-sectional Correlational Study

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## Abstract

**Background:** Lockdowns imposed during the COVID-19 pandemic have impacted the living and working habits of millions of people, with potentially important implications for their physical, mental, and social well-being.

**Objective:** The primary objective of this study was to investigate the impact of the COVID-19 pandemic on remote workers who were not directly affected by COVID-19.

**Methods:** This was a correlational cross-sectional study (with an additional qualitative component) of 184 remote workers surveyed during the first COVID-19 lockdown in the United Kingdom. Standard measures of mental health (Kessler-6 Distress Scale), productivity (Brief Instrument to Assess Workers' Productivity During a Working Day), and physical activity (International Physical Activity Questionnaire) were used, and respondents were further surveyed on changes to their dietary, exercise, smoking, drinking, and socialization habits to produce a well-being change index.

**Results:** The results revealed associations between sedentary behavior and poorer mental health ( $\tau_b=0.14$ ) and between poorer mental health and low work productivity ( $\tau_b=-0.39$ ). However, both positive and negative lifestyle changes were reported; a self-reported increase in well-being (with respect to diet, exercise, smoking, alcohol consumption, and socialization) since the start of the pandemic was associated with both better mental health ( $\tau_b=-0.14$ ) and better work productivity ( $\tau_b=0.14$ ). Of note, among respondents without a mental health diagnosis (137/184, 74.4%), we observed rates of moderate (76/137, 55.5%) and severe (17/137, 12.4%) psychological distress, which were markedly higher than those reported in large prepandemic studies; moreover, 70.1% (129/184) of our respondents reported more sedentary behavior, 41% (69/168) increased their alcohol consumption,

and 38.6% (71/184) increased their overall food intake. However, 46% (75/163), 44.8% (39/87) and 51.8% (57/110) of respondents reported spending more time walking and engaging in more moderate and vigorous exercise, respectively. Qualitative analysis revealed many positive adaptations to lockdowns (eg, decreased commuting expenses, flexibility) but also a number of structural obstacles to remote working (eg, lack of support and high expectations from employers, childcare duties).

**Conclusions:** These findings may be of practical importance for policy makers and employers in a world in which work involves long-term remote or hybrid employment arrangements; strategies to promote more sustainable remote working are discussed.

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## KEYWORDS

COVID-19; pandemic; remote workers; mental health; health policy; employment; policymakers; wellbeing

## Introduction

### Background

The COVID-19 pandemic has had catastrophic effects on global economies, with significant reductions in commercial and business activities projected [1] as well as increasing unemployment and underemployment with associated loss of income [2,3]. In a study of Vietnamese remote workers, 61% of respondents reported losses of income as a result of the country's first national lockdown, with women more financially affected than men [4]. The COVID-19 pandemic has further forced a work strategy paradigm shift in a very short period of time, and it does not provide the flexibility that home working would offer under normal conditions [5]. In several industries, working remotely has become a prominent solution to continued employment (eg, higher education delivery; business and operational management; administrative/secretarial work) during the pandemic. With uncertainty surrounding the prolonged impacts of COVID-19, and companies accelerating their plans to shift to remote working as a new default [6,7], there is an urgent need to understand the direct and indirect impact of remote working [8]. The impact of such sudden changes to working routines needs to be addressed in an attempt to understand the broad impacts of COVID-19 on work productivity and well-being [9].

In the United Kingdom, lockdown and social distancing measures were imposed starting in March 2020 [10]. By April, almost half of UK employees were working remotely, 90% of them having transitioned to this form of working because of the lockdown [10]. However, to date, little attention has been directed toward understanding the health, well-being, and societal impacts of remote working. This has most likely reflected (1) the need to increase epidemiological understanding and direct impacts on frontline services and patients; (2) prepandemic evidence demonstrating the benefits of remote working due to its flexibility [11] and financial convenience [12]; and (3) the low risk that people working remotely will contract the infection due to reduced social contact and isolation [13]. However, the validity of prepandemic evidence is questionable in the current climate, where societal and economic issues are profoundly different. Accordingly, this paper will present insight into the effects of remote working to establish an understanding of its impacts upon physical health, psychosocial well-being, and work productivity.

Although remote (or distant) working is not a new phenomenon, before 2000, only 2.5% of UK workers (2/3 of them women) worked remotely. Historically, the logic behind flexible work arrangements has been to avoid losing valuable labor to factors such as childcare and family commitments [5,14], as well as to promote a more environmentally friendly way of working (eg, decreasing resources to commute) [15,16]. Well-being has been identified as a key factor behind productive remote working [17,18]. However, as a consequence of COVID-19, the number of people working remotely in the United Kingdom has increased to 13.02 million [10]. Thus, there is an urgent need to understand the ramifications of this unprecedented switch in employment type, including resultant well-being and productivity lifestyle changes. Although well-being is a complex and multifactorial state, key facets include diet, exercise (physical health), and mental health [19,20], which are each linked to societal, economic, and mortality issues.

### Well-being and Work Productivity

Mental health disorders account for a significant proportion of the global disease burden; together with worker burnout, it is estimated that they are currently costing the global economy over US \$1 trillion per year and will cost \$16 trillion per year by 2030 [21]. Reports have already been published of physical and emotional burnout, as well as mental health difficulties, among physicians and nurses [22-25] as well as among social carers [26,27], pointing to a clear link between mental health and work productivity [28]. Holmes and colleagues [29] report that major adverse consequences of the COVID-19 pandemic are likely to be social isolation and loneliness; both of these can lead to depression, anxiety, self-harm, and attempted suicide. Social isolation and loneliness are factors that can be exacerbated by remote working, especially where the switch has been rapid and unexpected. Indeed, Holmes et al [29] further suggest that working from home, as a consequence of the pandemic, has abruptly interrupted many social opportunities that are important for physical and psychological health.

Remote working may also allow for greater media consumption, which in turn has been correlated with anxiety and depression amid the current pandemic [30]. Moreover, following the Ebola crisis, media exposure was found to exacerbate stress responses and worries [31], and messaging regarding Ebola risks was found to increase public anxiety [32]. Thus, increased consumption of media during times of crises and pandemics may be a maladaptive coping consequence. For example, Jungmann and Witthöft [33] have reported that both health anxiety and cyberchondria (excessive searching for information

on the web) constitute risk factors for COVID-19 anxiety. However, they further observed that adaptive emotion regulation (in this particular case, using cognitive emotion regulation strategies to cope with negative life events) protected against COVID-19 anxiety. Consistent with this, in a sample of over 5000 Spanish adults surveyed during the Spanish lockdown, Fullana and colleagues [34] found that consuming a healthy diet and avoiding high consumption of COVID-19 news predicted lower reports/symptoms of depression and anxiety, as did taking the opportunity to pursue hobbies and engaging with nature (even if just looking outside).

During the COVID-19 pandemic, people's eating habits have been shown to be unhealthier, particularly those relating to snacks and alcohol consumption [35]. Obesity and its related comorbidities are additionally cited as major risk factors for COVID-19 infection [36,37] and poorer clinical outcomes [38]. Of direct relevance is the recently launched "Better Health" campaign by the UK government, which aims to support actions against COVID-19 and reduce obesity-related costs in the National Health Service (£6 billion [US \$4,334,260] per year [39]). Hence, diet has a crucial role in preserving health and protecting at-risk populations during the COVID-19 pandemic. As such, it is essential to understand how diet has changed as a consequence of COVID-19 work pattern changes, including the potential added factor of sedation (ie, physical inactivity and increased sedentary behaviors).

The World Health Organization (WHO) has classified physical inactivity (6%) as the fourth leading risk factor of global mortality, after hypertension (13%), smoking (9%), and diabetes (6%) [40]. The WHO recommends 60 minutes per day of moderate to vigorous physical activity for youth aged 6-17 years and 75-150 minutes per week of vigorous or moderate physical activity for adults and older persons, respectively, including 3 and 2 days per week each of muscle- and bone-strengthening activities (eg, resistance training) [41]. COVID-19 has had a major impact on physical activity behaviors, due to movement (even leaving one's residence) and self-isolation restrictions for prolonged periods [42]. Ammar and colleagues [35] report that COVID-19 home confinement has negatively affected all physical activity intensities (light, moderate, vigorous, and overall), while sedentary behaviors such as sitting, lying down, or screen use (eg, TV viewing, video game playing) have increased from 5 to 8 hours per day, despite widespread access to web-based physical activity training programs or workouts [43].

Prior to the COVID-19 pandemic, physical inactivity was costly and was recognized as the fourth leading cause of mortality by the WHO [44]. For example, in 2013, it was reported that physical inactivity cost health care systems worldwide US \$53.8 billion [45], with deaths attributable to physical inactivity costing a further \$13.7 billion in productivity losses [46]. Sedentary behaviors (independent of physical inactivity) are further associated with cardiovascular risk factors and increased cardiovascular morbidity and global mortality [47]. Unfortunately, since the start of the COVID-19 crisis, restrictions have removed many opportunities to be physically active and reduce sedentary behaviors. The global ramifications of this are concerning, as individuals who were not active before

COVID-19 are now at even more risk of cardiometabolic abnormalities, sarcopenia, and frailty in older persons [48]. This scenario has been referred to as "two pandemics"—one pandemic being COVID-19, and the second consequential pandemic being physical inactivity [46].

In sum, an individual's ability to maintain a healthy diet, physical activity, and good mental health have likely been impacted by transitioning to remote working. The pandemic has further added several obstacles to the world of work (eg, childcare duties given school closures, which could disproportionately affect women) [49]. Consequently, there is an urgent need to better understand how, for those in employment, the abrupt switch to remote working (and, more generally, remote working during a pandemic) has affected mental and physical health, including general patterns of change in well-being. These findings will also inform our understanding of the public health implications of a long-term or permanent shift to remote working or hybrid arrangements for many people, even after the end of the pandemic. As such, our goals were to explore (1) the relationship between physical activity, mental health, diet, and work productivity during the initial COVID-19 lockdown period; (2) the demographic characteristics associated with varying well-being in this population; and (3) the perceptions remote workers had of their well-being and its influence on work productivity.

## Methods

### Design

A correlational design was employed to investigate associations between standard indices of mental health, physical activity, and productivity and ad hoc measures of changes in physical activity, dietary habits, and smoking habits. Open-ended questions were also posed to further probe diet, and a final question asked remote workers about the perceptions had of their well-being in relation to work productivity.

### Respondents

Following ethical approval by the local university, the survey was circulated to adult residents of the United Kingdom on social media (ie, Facebook and Twitter) and through press releases between May 15 and July 6, 2020. The latter date marked the beginning of the first week during which a number of indoor amenities (eg, museums, places of worship, libraries) and hospitality facilities (cafes, pubs, and restaurants) reopened in England [50].

Between these dates, data were collected from 279 respondents, of whom 207 were remote workers at the time. Of these, 25 respondents did not complete all compulsory aspects and were therefore excluded. This left a final sample of N=184, of whom 167 (90.7%) were not remote workers before the lockdown (ie, before March 23, 2020 in the United Kingdom). Based on power analysis for a correlational design, assuming  $r=0.3$  and with  $\alpha=.005$ , we estimated that N=142 should be sufficient to have 0.8 power to detect such relationships.

## Measures

The survey included quantitative standardized measures of mental health, physical activity, and work productivity as well as an open qualitative question asking respondents to provide any additional information about their lockdown experiences that was not covered by the questionnaire measures and further quantitative items. These further quantitative items were used to probe dietary habits, socialization, and activities used as coping mechanisms to preserve well-being during the lockdown (see specifically *Measures of Diet and Well-being Change During the Lockdown* and *Socialization, News Consumption, and Coping Strategies*).

### Kessler-6 Distress Scale

The Kessler-6 Distress Scale (K6) [51] was administered as a measure of psychological distress. The K6 asks respondents to rate the degree to which, in the past 30 days, they have experienced nervousness, hopelessness, restlessness, depression, and feelings of worthlessness on a Likert scale with responses ranging from 1, all of the time, to 5, none of the time. The scale produces a potential score range between 0 and 24, with scores  $\geq 5$  generally considered markers of moderate distress and scores of  $\geq 13$  considered markers of high psychological distress and serious mental illness [52]. The scale has good internal consistency [51],  $\alpha=.89$ .

### International Physical Activity Questionnaire

The short version of the International Physical Activity Questionnaire (IPAQ) for middle-aged adults [53,54] was used to measure the degree of physical activity or sedentarism. The questionnaire asks respondents to estimate (1) the number of days they spent more than 10 minutes walking or engaging in moderate (eg, cycling, doubles tennis) and vigorous (eg, heavy lifting, fast cycling) exercise over the past 7 days; (2) the number of minutes they spent walking or engaging in these activities during the average day over this period; and (3) the number of hours they spent sitting per average day. Physical activity is categorized by intensity and includes sedentary behaviors, as well as light, moderate, and vigorous physical activity levels. Metabolic equivalents (METs) are then commonly used to express the intensity of the physical activities reported. A MET is defined as the ratio of an individual's working metabolic rate to their resting metabolic rate. A MET equates with the oxygen consumption required at rest/sitting quietly and is assumed to be  $3.5 \text{ mL/O}_2/\text{min} \times \text{kg body weight}$  [55]. In sedentary behavior (as defined above), the energy expenditure is less than 1.5 METs

[56]. It is suggested that compared with sitting quietly, a person's caloric consumption is 3 to 6 times higher when they are moderately active (3-6 METs) and more than 6 times higher when vigorously active ( $>6$  METs). The scale has acceptable internal consistency [57],  $\alpha=.60$ .

### Brief Instrument to Assess Workers' Productivity During a Working Day Scale

Work productivity was assessed using the Brief Instrument to Assess Workers' Productivity During a Working Day (IAPT) [58]. This 10-item instrument asks respondents to rate the degree to which they have felt focused, tired/sleepy, confident, productive, annoyed/upset, satisfied, or affected by physical symptoms such as pain or dizziness over the last two hours of work. Ratings are given on a scale of "not at all" to "extremely," which is scored between 0 and 4. This produces an overall score ranging from 0 to 40 points, with higher scores denoting higher productivity. The scale has good split-half reliability ( $r^2=0.86$ ), good internal consistency ( $\alpha=.80-.91$ ), and high convergent validity ( $r^2=0.86$ ) with longer instruments such as the Health and Work Performance Questionnaire [59].

### Measures of Diet and General Well-being Change During the Lockdown

A total of 9 items were used to assess whether respondents had experienced an increase, decrease, or no change (3 response options) in overall food consumption, which included consumption of fruits, vegetables, snacks, treats, takeaway food, home cooking, soft drinks, and alcoholic drinks. Similarly, 4 items probed whether the time individuals had spent walking, sitting, or engaging in moderate and vigorous physical activity had changed since the lockdown. Respondents were also asked whether they had started or quit smoking since the start of the lockdown, and whether the amount they smoked had increased, decreased, or stayed the same. Lastly, respondents were asked whether the amount they socialized (including virtually) with others had increased, decreased, or stayed the same since the lockdown.

Measures of diet and well-being change during the lockdown were coded as 0 for no change and +1 or 1 for a decrease or increase depending on the item, respectively. The full coding scheme is presented in Table 1. Responses were then aggregated into a well-being change index (WCI) since the start of the lockdown, with scores ranging from -16 to +16, with higher values typically indicating improved overall general well-being.

**Table 1.** Scoring scheme for the questionnaire items directly probing habit changes since the start of the lockdown.

Measure	More than before	No change	Less than before
Overall food intake	-1	0	1
Snacks	-1	0	1
Treats	-1	0	1
Sugar/fizzy drinks	-1	0	1
Alcohol	-1	0	1
Take-away food	-1	0	1
Sitting	-1	0	1
Smoking <sup>a</sup>	-1	0	1
Smoking frequency	-1	0	1
Fruits	1	0	-1
Vegetables	1	0	-1
Cooking/baking	1	0	-1
Walking	1	0	-1
Moderate exercise	1	0	-1
Vigorous exercise	1	0	-1
Socializing	1	0	-1

<sup>a</sup>Smoking initiation (“more than before”) or cessation (“less than before”) since the start of the lockdown.

### Socialization, News Consumption, and Coping Strategies

Respondents were also asked to estimate the average amount of time (in minutes per day) that they spent socializing with individuals within and outside their household, and the amount of time (in minutes per day) they spent consuming news content (in print, on the internet, or on TV/radio). Respondents were further asked to select all the resources and strategies they had engaged in to maintain their physical and mental well-being during the lockdown.

The list of resources and strategies for physical activity included already-owned implements, newly purchased implements, specialized books and magazines, smartphone apps, web pages, TV programs, and advice from friends and family. This yielded a possible range of counts between 0 and 7.

The list of resources and strategies for mental well-being included yoga, meditation, prayer and other spiritual practices, counseling, reading, watching TV, playing video games, and keeping a diary. Respondents were also given the opportunity to list any further mental well-being coping strategies they were employing. These were counted and added to the overall count. This yielded a range of responses between 0 and 13.

### Open-Question Self-reports

Respondents were given the opportunity to enter text (3000 characters maximum) to volunteer additional information on any of the aspects probed by the survey (diet, mental health, exercise, and work productivity) or to mention anything not covered by the survey that they felt was relevant to their experiences of well-being changes during the COVID-19 lockdown.

### Demographics

Lastly, respondents were asked several demographic (age group, gender, educational attainment) and household questions (marital status, whether they had adult or underage children, whether they lived with other adults).

### Procedure

Following informed consent, respondents selected a 6-digit alphanumeric code used to anonymize their data and allow for retrieval. They were then presented with items/questionnaires regarding, in order, work productivity (IAPT), dietary changes, mental health (K6), physical activity (IPAQ), exercise resources, and coping strategies. These were followed by the optional open-ended question and, finally, the demographics questions.

### Data Analysis

Kolmogorov-Smirnov tests of normality were conducted on key measures (IAPT, K6, WCI, METs, and sitting time); all significantly deviated from normality ( $P < .05$ ). Visual inspection of the correlation plots for these measures additionally revealed substantial nonlinearity in the relationships between several of them. For this reason, Kendall  $\tau_b$  correlations were performed to detect statistically significant relationships between psychophysical well-being and productivity. Independent-sample Mann-Whitney  $U$  tests and chi-square analyses were used to test for differences in exercise habits, mental health scores, and productivity between demographics (focusing on gender differences and childcare responsibilities). Missing cases were excluded pairwise to maximize the amount of data available for analysis.

The open-ended question responses were analyzed using conventional content analysis [60], conducted by YATH and



following the eight steps suggested by Zhang and Wildemuth [61], which involved preparing data, coding texts, and making inferences from the meanings of the data. This allowed for the observation of trends in the respondents' opinions. To increase the trustworthiness of the data, triangulation was conducted with the quantitative results, reflexivity was included across data collection and analysis, and peer debriefing was conducted with other members of the research team [62].

### Ethical Considerations

The study was approved by the University of Derby College of Life and Natural Sciences Research Ethics Committee (ETH1920-3136). Participants provided informed consent at the start of the web-based survey.

## Results

### Relationships Between Physical Activity, Dietary and Well-being Changes, Mental Health, and Productivity

Descriptive statistics for standardized measures of productivity (IAPT), mental health (K6), physical activity (IPAQ, expressed in METs), time spent sitting, and well-being change since the lockdown (WCI) are presented in Table 2. Figure 1 shows the distribution of responses for the WCI components.

An initial round of one-tailed correlations (with the  $\alpha$  level set at  $P < .005$ ) was computed between respondents' productivity scores (IAPT), mental health scores (K6), aggregated well-being change scores (WCI), MET measures derived from the IPAQ,

and reported time spent sitting. The results are reported in Table 3 (sections 1-8) and suggest relationships between sedentarism, poorer mental health, a decrease in well-being, and productivity. Namely, the more time respondents reported spending sitting, the worse their mental health scores (K6) and the lower their productivity (IAPT); similarly, a decrease in reported well-being since the start of the lockdown (WCI) was associated with worse productivity and poorer mental health.

Given the observed relationship between physical activity, mental well-being, and productivity, we tested for differences in the above measures between individuals with and without a reported pre-existing mental health diagnosis (45/184, 24.4%, and  $n=137/184$ , 74.5%, respectively, as 2 respondents did not provide this information). The results of the independent-sample Mann-Whitney  $U$  test are reported in Table 4. As expected, respondents with a previous mental health diagnosis reported significantly worse mental health, engaged in significantly less vigorous exercise, and spent more time sitting than those without a pre-existing diagnosis.

Excluding the subset of respondents (45/184) with a pre-existing mental health diagnosis (80% [36/45] of whom had K6 scores  $\geq 5$  and 22.2% [10/45] of whom had K6 scores  $\geq 13$ ), 55.5% (76/137) of the remaining respondents had scores consistent with moderate distress and 12.4% (17/137) had scores consistent with severe distress. For context, a survey of over 50,000 noninstitutionalized Californian adults under nonpandemic conditions [52] yielded incidences of 27.9% with scores  $\geq 5$  and 8.6% with scores  $\geq 13$ .

**Table 2.** Descriptive statistics for the assessed measures of physical activity (IPAQ METs), sitting time (hours per average day), mental health (K6), work productivity (IAPT), and well-being change (WCI).

Measure	Range (IQR)	Mean (SE)	95% CI
IAPT <sup>a</sup>	1 to 39 (11)	21.61 (0.511)	20.60 to 22.62
K6 <sup>b</sup>	0 to 24 (7)	6.94 (0.361)	6.23 to 7.65
WCI <sup>c</sup>	-10 to 12 (7)	-0.28 (0.310)	-0.89 to 0.33
Vigorous METs <sup>d</sup>	0 to 5040 (1440)	827.17 (75.95)	677.31 to 977.04
Moderate METs	0 to 3840 (360)	286.80 (39.90)	208.08 to 365.53
Walking METs	0 to 3465 (610.50)	645.87 (44.19)	558.68 to 733.06
Total METs	0 to 6993 (2033.88)	1759.85 (104.41)	1553.83 to 1965.86
Sitting time	2 to 18.0 (3.0)	8.81 (0.238)	8.34 to 9.28

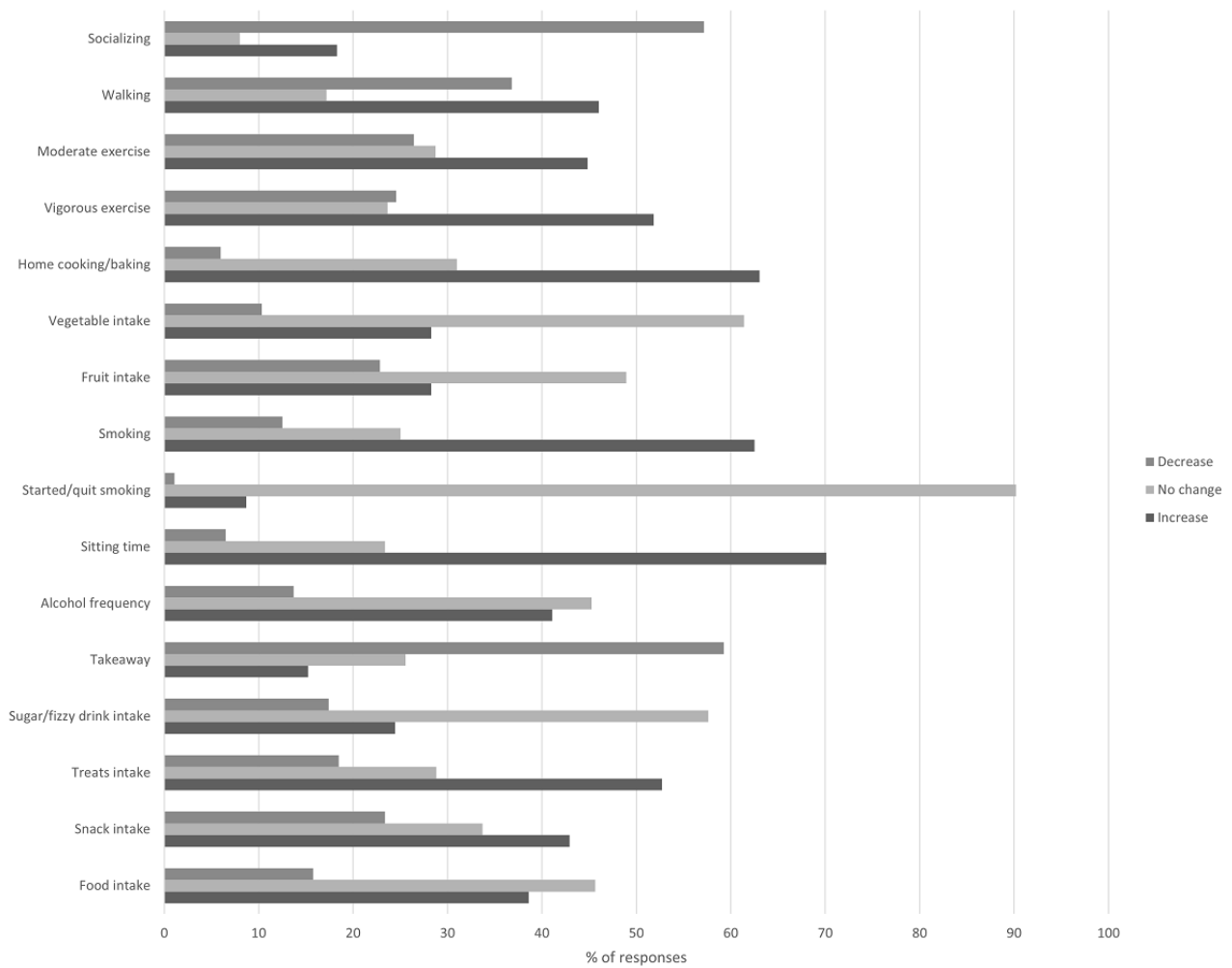
<sup>a</sup>IAPT: Brief Instrument to Assess Workers' Productivity During a Working Day.

<sup>b</sup>K6: Kessler-6 Distress Scale.

<sup>c</sup>WCI: well-being change index.

<sup>d</sup>METs: metabolic equivalents.

**Figure 1.** Respondents' reported changes in dietary habits, physical activity, socialization, and general well-being as a function of lockdown during the COVID-19 pandemic (metrics were computed by following the scheme in Table 1). Bars indicate the percentages of respondents reporting a decrease (top bar in each cluster), increase (bottom bar), or no change (middle bar).



**Table 3.** Results of both rounds of Kendall  $\tau_b$  correlations between productivity (IAPT), mental health (K6), IAPT METs, sitting time, resources for physical activity, and general coping activities. News intake (minutes per average day) and total time spent socializing (within and outside the household) did not produce any significant correlations (at  $P<.005$ ) and were therefore excluded from the table. Italic text indicates significance at  $\alpha=.005$ .

Measure	IAPT <sup>a</sup>	K6 <sup>b</sup>	WCI <sup>c</sup>	Vigorous METs <sup>d</sup>	Moderate METs	Walking METs	Total METs	Sitting time	Exercise resources	Coping activities
<b>IAPT</b>										
$\tau_b$	1	<i>-0.393<sup>e</sup></i>	<i>0.178<sup>e</sup></i>	0.038	0.073	0.108	0.090	-0.107	0.010	-0.074
<i>P</i> value	—	<i>&lt;.001</i>	<i>&lt;.001</i>	.24	.10	.02	.04	.02	.43	.09
<b>K6</b>										
$\tau_b$	<i>-0.393<sup>e</sup></i>	1	<i>-0.148<sup>f</sup></i>	-0.081	-0.108	-0.102	-0.121	<i>0.147<sup>f</sup></i>	0.050	0.089
<i>P</i> value	<i>&lt;.001</i>	—	.003	.07	.03	.03	.009	<i>.003</i>	.19	.054
<b>WCI</b>										
$\tau_b$	<i>0.178<sup>e</sup></i>	<i>-0.148<sup>f</sup></i>	1	0.143	0.001	0.105	0.133	-0.097	0.112	0.028
<i>P</i> value	<i>&lt;.001</i>	<i>.003</i>	—	.005	.50	.02	.005	.04	.03	.31
<b>Vigorous METs</b>										
$\tau_b$	0.038	-0.081	0.143	1	<i>0.224<sup>e</sup></i>	<i>0.057</i>	<i>0.646<sup>e</sup></i>	<i>-0.256<sup>e</sup></i>	<i>0.219<sup>e</sup></i>	0.036
<i>P</i> value	.24	.07	.005	—	<i>&lt;.001</i>	<i>.14</i>	<i>&lt;.001</i>	<i>&lt;.001</i>	<i>&lt;.001</i>	.26
<b>Moderate METs</b>										
$\tau_b$	0.07	-0.108	0.001	<i>0.224<sup>e</sup></i>	1	<i>0.027</i>	<i>0.379<sup>e</sup></i>	<i>-0.180<sup>f</sup></i>	0.157	0.060
<i>P</i> value	.10	.03	.50	<i>&lt;.001</i>	—	<i>.31</i>	<i>&lt;.001</i>	<i>.001</i>	.005	.15
<b>Walking METs</b>										
$\tau_b$	0.108	-0.102	0.001	0.105	0.027	1	<i>0.361<sup>e</sup></i>	-0.134	-0.018	-0.07
<i>P</i> value	.019	.025	.496	.023	.312	—	<i>&lt;.001</i>	.006	.378	.448
<b>Total METs</b>										
$\tau_b$	0.090	-0.121	0.133	<i>0.646<sup>e</sup></i>	<i>0.379<sup>e</sup></i>	<i>0.361<sup>e</sup></i>	1	<i>-0.269<sup>e</sup></i>	<i>0.151<sup>f</sup></i>	0.008
<i>P</i> value	.04	.009	.005	<i>&lt;.001</i>	<i>&lt;.001</i>	<i>&lt;.001</i>	—	<i>&lt;.001</i>	<i>.003</i>	.44
<b>Sitting time</b>										
$\tau_b$	-0.107	<i>0.147<sup>f</sup></i>	-0.097	<i>-0.256<sup>e</sup></i>	<i>-0.180<sup>f</sup></i>	-0.134	<i>-0.269<sup>e</sup></i>	1	-0.139	-0.070
<i>P</i> value	.02	<i>.003</i>	.04	<i>&lt;.001</i>	<i>.001</i>	.006	<i>&lt;.001</i>	—	.008	.11
<b>Exercise resources</b>										
$\tau_b$	0.010	0.050	0.112	<i>0.219<sup>e</sup></i>	0.157	-0.018	<i>0.151<sup>f</sup></i>	-0.139	1	<i>0.240<sup>e</sup></i>
<i>P</i> value	.43	.19	.03	<i>&lt;.001</i>	.005	.38	<i>.003</i>	.008	—	<i>&lt;.001</i>
<b>Coping activities</b>										
$\tau_b$	-0.074	0.089	0.028	0.036	0.060	-0.007	0.008	-0.070	<i>0.240<sup>e</sup></i>	1
<i>P</i> value	.09	.05	.31	.26	.15	.45	.44	.11	<i>&lt;.001</i>	—

<sup>a</sup>IAPT: Brief Instrument to Assess Workers' Productivity During a Working Day.

<sup>b</sup>K6: Kessler-6 Distress Scale.

<sup>c</sup>WCI: well-being change index.

<sup>d</sup>METs: metabolic equivalents.

<sup>e</sup> $P<.001$ .

<sup>f</sup> $P<.005$ .

**Table 4.** Physical activity (IPAQ METs and sitting time), mental well-being (K6), well-being change (WCI), and productivity (IAPT) measures compared between respondents with or without a mental health diagnosis.

Measure	Pre-existing diagnosis		<i>U</i>	<i>z</i>	<i>P</i> value
	Yes (mean rank)	No (mean rank)			
IAPT <sup>a</sup>	78.97	95.62	2518.50	-1.84	.07
K6 <sup>b</sup>	116.10	83.42	1975.50	-3.62	<.001 <sup>c</sup>
WCI <sup>d</sup>	84.03	93.95	2746.50	-1.10	.27
Vigorous METs <sup>e</sup>	71.27	98.15	2172.00	-3.07	.002 <sup>f</sup>
Moderate METs	87.52	92.81	2903.50	-0.63	.53
Walking METs	95.60	90.15	2898.00	-0.60	.55
Total METs	82.99	94.30	2699.50	-1.24	.21
Sitting Time	111.49	84.22	2138.00	-3.05	.002 <sup>f</sup>

<sup>a</sup>IAPT: Brief Instrument to Assess Workers' Productivity During a Working Day.

<sup>b</sup>K6: Kessler-6 Distress Scale.

<sup>c</sup>*P*<.001.

<sup>d</sup>WCI: well-being change index.

<sup>e</sup>METs: metabolic equivalents.

<sup>f</sup>*P*<.005.

## Supplementary Analyses

### Socialization and Coping Strategies

To gain a better understanding of how respondents were affected by lockdown social restrictions and how these are related to coping strategies, including resources individuals employed to maintain physical and mental well-being, we performed a second round of correlations (with the  $\alpha$  level again set at *P*<.005). As such, correlations were computed for the respondents' work productivity and mental health scores, physical activity (MET) scores, and reported sitting times (see Table 2 for descriptive statistics), together with the total number of physical activity resources (median 1, SD 1.15) and general coping activities

(median 3, SD 1.78) that the respondents reported using or engaging in, the total amount of time they reported socializing with people within (mean 192.8 minutes, SE 15.4) and outside (mean 78.9 minutes, SE 6.15) their household, and their news intake (mean 50 minutes, SE 4.04). These results revealed no significant relationships between time spent socializing and any further measures.

Table 5 shows what part of our sample reported engaging in the different coping activities we provided. Respondents also had the option of mentioning activities not included on the list; some of the most frequently provided responses were arts, crafts, and general do-it-yourself activities (35/184, 19%), gardening (16/184, 8.7%), and cooking/baking (13/184, 7.1%).

**Table 5.** Respondents who reported engaging in different coping activities to maintain their psychophysical well-being (N=184).

Activity	Value, n (%)
Yoga	59 (32.1)
Meditation	30 (16.3)
Prayer/spiritual practices	12 (6.5)
Counselling/therapy	12 (6.5)
Reading	113 (61.4)
Watching TV	142 (77.1)
Playing video games	44 (23.9)
Keeping a diary	14 (7.6)
Other	62 (33.6)

### Household and Gender Differences

Next, we aimed to investigate whether key demographic factors influenced respondents' psychophysical and social well-being during the lockdown, as well as their coping strategies.

Here, we used the independent-sample Mann-Whitney *U* test to compare key measures between respondents from households with (n=46) and without (n=136) children under the age of 18 years. The results are reported in Table 6. Adults living in households with children reported, on average, approximately

2 hours less of sitting time and reported resorting to fewer recreational activities to maintain their psychosocial well-being. No other difference (eg, in mental health or productivity scores) achieved significance at the .005  $\alpha$  level.

Comparing the same measures as in Table 6 between men (n=40) and women (n=143) similarly revealed that women reported engaging in more recreational activities than men (mean ranks of 63.06 and 100.09, respectively) to maintain their

psychosocial well-being ( $U=1702$ ;  $z=-3.98$ ;  $P<.001$ ). Women were also significantly more likely than men to report being the main providers of childcare ( $\chi^2_2=17.08$ ;  $\phi_c=0.609$ ;  $P<.001$ ), and homeschooling ( $\chi^2_2=9.21$ ;  $\phi_c=0.458$ ;  $P=.01$ ) in the household. No significant gender differences were found in the total number of physical activity resources that respondents reported using,  $P=.92$ .

**Table 6.** Physical activity, mental well-being, and productivity measures of respondents with and without children under 18 years of age.

Measure	Children aged <18 years in household, mean rank		U	z	P value
	Yes	No			
IAPT <sup>a</sup>	95.26	90.23	2955.00	-0.561	.57
K6 <sup>b</sup>	84.48	93.88	2805.00	-1.04	.29
WCI <sup>c</sup>	92.13	91.29	3099.00	-0.094	.92
Socialization (in)	102.44	82.36	2042.50	-2.23	.02
Socialization (out)	88.48	90.51	2946.50	-0.23	.81
News intake	79.47	92.70	2471.00	-1.48	.13
Coping activities	64.64	100.58	1892.50	-4.07	<.001 <sup>d</sup>
Vigorous METs <sup>e</sup>	80.79	95.12	2635.50	-1.65	.09
Moderate METs	87.61	92.82	2949.00	-0.63	.52
Walking METs	92.58	91.14	3078.50	-0.16	.87
Total METs	79.87	95.46	2589.00	-1.74	.08
Sitting time	64.10	100.17	1867.50	-4.06	<.001 <sup>d</sup>

<sup>a</sup>IAPT: Brief Instrument to Assess Workers' Productivity During a Working Day.

<sup>b</sup>K6: Kessler-6 Distress Scale.

<sup>c</sup>WCI: well-being change index.

<sup>d</sup> $P<.001$ .

<sup>e</sup>METs: metabolic equivalents.

## Qualitative Self-report Data

Three themes emerged from the content data analysis related to different aspects of remote working. These were barriers to remote working and well-being preservation, mixed feelings and attitudes toward remote working, and aids to improve physical and psychosocial well-being. This section presents a narrative analysis of these themes with supporting illustrative respondent extracts.

### Theme 1: Barriers to Remote Working and Well-being Preservation

This theme dealt with aspects of the lockdown that represented limitations to working and maintaining health and well-being at the standards individuals would have liked. Some respondents mentioned childcare responsibilities as a constraint, others mentioned how their eating habits had worsened, and some respondents reported difficulties in engaging with remote working.

Various respondents that were engaged in childcare duties described how stressful and tiring their work responsibilities

were and how challenging it was to take care of themselves (health wise).

*I have struggled to separate work and home learning with children [R9]*

*...but have an 18-month-old also at home full time so productivity goes out the window; we have to organise our diaries at the start of the day so that we can pass her back and forth between us [R23]*

*I have however been very unproductive work-wise, as my husband is still working full time and I have 2 young children to home school [R31]*

*I have a child (3 years old) and having him off nursery [...] dramatic impact on my mental health as I struggle to move from "mum mode" into "work mode" and has an impact about how I feel about my lack of work achievement – this then becomes a cycle of feeling as though I'm not achieving anything along with feeling mum guilt for not being with my son [R51]*

Respondents who reported having teaching and pastoral occupations recorded feeling more tired, stressed, and anxious.

Moreover, there was an overall fear of losing their job and of not being “as productive” as expected if they could not adapt successfully to working from home.

*...my concentration is poor and online teaching is tiring, I feel concerned that I have to perform at even higher level to ensure the student get the best from me [R3]*

*I feel I am working harder to prove myself to my employers as I do not want to lose my job. This has resulted in me becoming run down and ill [...] I did not take any time off during this time. [R4]*

*Yet I believe I am near to cracking trying to do a full day's work with the distraction of the virus is really difficult [R14]*

Furthermore, respondents had an overall negative perception of the change in their eating habits and tended to comment on their consumption of alcohol and sweet foods more than other foods.

*I try not to eat from boredom or comfort eat [sic] but I'm not really succeeding. I also drink more alcohol and fizzy drinks, going from almost never to a couple of times a week. I had cut out snacks and drinks like these almost completely in an attempt to lose weight before lockdown, but I feel like the joy of snacking and drinking is more important than losing weight right now. [R7]*

*My appetite is definitely less. I often go without breakfast and have a very small lunch. However, I can binge eat more than before. For example, when I bake, I will eat all that I have made within a day. [R22]*

Lastly, aspects that were not explored in the survey have emerged as potential barriers to psychological well-being. Some activities that respondents considered beneficial to limit included time spent on news intake and visits to supermarkets. Additionally, lockdown restrictions to exercising were mentioned as problematic.

*I have become increasingly anxious when in shops because people are increasingly forgetting to keep their distance [R1]*

*I find news and [sic] media very worrying and negative. I find that sometimes I feel ok and maybe even positive and then I'll read a bad statistic online or see news headlines and it ruins my mood. [R11]*

*Only being able to exercise once a day was a real issue as it made me feel restricted. My running has reduced due to nervousness about going out and bumping into others as local parks etc have become increasingly busy with other people [R8]*

*I have been confined to my flat, either sitting or lying down most of the times. The restrictions have left me unable to walk as much as I always did before [R10]*

This theme reveals that the lockdown caused various disruptions to the personal lives of those performing their work duties remotely, including the negative effects of balancing childcare,

and their employment fears, which included not performing to “acceptable” standards. Eating habit concerns were also noted, including a report of bingeing and/or “comfort eating.” Furthermore, challenges affecting mental health were described as key well-being antecedents (and vice versa).

### **Theme 2: Mixed Feelings and Attitudes Toward Remote Working**

It was clear that the respondents' attitudes toward remote working depended on their personal circumstances, and a link between physical health and mental states was observed across narrations. This seemed to also influence what respondents recognized as the challenges or advantages of their remote working dynamic. Physical activity needs, as well as mental health struggles, were reported as challenges. Patterns of more tiredness and lack of sleep during the lockdown were major trends reported among respondents. A lack of ergonomic aids or efficient information technology (IT) resources and the “overuse” of technologies were also reported to negatively impact mental health. Some impracticalities of working from home were reported:

*[...] however, everything had to change overnight and that takes time to get right! It has been exhausting, mentally exhausting. I miss the little breaks, walking to a meeting, popping to coffee shop [R5]*

*I am not working as much in the evenings and at weekends. I am behind, though, on my work. In the first couple of weeks of lockdown, I found it difficult to concentrate, adapt, sleep, keep working. I find it hard to mark work online and am fed up of [sic] looking at a computer screen. [...] Work online takes about three times as long [R18]*

*The physical difficulties associated with using a dining table desk set-up without proper office equipment (I have an occupational health assessed ergonomic chair at work) have added another layer of challenge [R63]*

*From a personal point of view, I was doing well with exercise but have had some injuries and felt unwell at times. I've felt more tired than usual regularly too [R37]*

*Sleep worse than before, cannot switch off at night-time. Have switched from listening to radio 4 to go to sleep to Radio 3 as felt it was constantly information about COVID19 [R59]*

For some, the switch to home working provided limited opportunities for physical activity and blurred the line between work and home life. Several respondents, however, pointed out that a more flexible work dynamic and trust from their employers gave them a greater sense of ownership.

*It suits me working more flexibility [sic], my blood pressure is lower, and I have less headaches. [...] [R5]*

*the lockdown has not had a negative impact on mental health and has had a positive impact on physical health as we are doing more exercise [R17]*

*Working from home has allowed me to reclaim a few more hours for myself, now that I'm not commuting, and I've been finding ways to make sure that I'm using that time to create a good work/life balance [R19]*

*I am pleased to say that the quality of my life has significantly improved since the COVID outbreak and consequent lockdown. This is because I can work from home and more flexibly, without having to commute and drive/use public transport between cities. [R57]*

Several respondents further reported some benefits in their physical health and quality of life or work life balance.

In sum, this theme demonstrates that remote working has had both benefits and disadvantages for the work dynamic of the respondents as well as for how they perceive their work-life balance, personal lives, and physical and mental health; all of these factors are key for well-being.

### **Theme 3: Aids to Improve Physical and Psychosocial Well-being**

This theme focused on various activities and aspects that positively benefited the physical and psychosocial well-being of respondents. Gardening and DIY activities were cited as hobbies that helped respondents to cope with the current stressful situation:

*We are still trying to keep active, get fresh air and do DIY at home to balance the body and mind. [R29]*

*Spending more time in the garden which helps to relax, spending more time with pets, learned [sic] new hobbies. [R46]*

*I have tried to keep myself as active as possible, doing work around the house/garden. [R48]*

Some of the most mentioned benefits of going through this unique circumstance were increasing spirituality, having more contact with nature, self-reflection on life goals, valuing family or a partner's physical presence, discovering new skills and hobbies, and positive use of the time and resources saved by not commuting:

*[...] although it has helped me to focus more on myself [sic] and the things that truly matter [R10]*

*I have still found some elements of lockdown beneficial particularly in the slower pace of life, which has made me think that I may want to keep some aspects of my new routine to improve my mental health when things go back to "normal" [R16]*

*I am grateful for the space in our home, for living with my partner, in the countryside and still being able to go outside. I think I appreciate the "small" things more [R34]*

*I can save money on not having to commute, which helps me because I am the only earner in my household [R57]*

In summary, this theme encompasses some stressful situations circumvented by the lockdown that were not considered in the closed questions. It additionally identifies coping strategies that

several respondents had been employing during the lockdown that had positively influenced their psychosocial well-being.

## **Discussion**

### **Principal Findings**

The purpose of the present study was threefold. Firstly, we set out to investigate the relationship between physical and psychosocial well-being and work productivity under lockdown conditions that were imposed as a result of the COVID-19 pandemic. Secondly, we explored whether remote workers with different demographic profiles (eg, gender, parental duties) were differentially affected by lockdown and home-working conditions with respect to their well-being and work productivity. Finally, we aimed to explore remote workers' perceptions of the lockdown—specifically, its effects on their work productivity and well-being. Key results included (1) the observation of significant relationships between sedentary behavior and poorer mental health, which were in turn related to worse work productivity; (2) exacerbation of these relationships as a consequence of poorer mental health; (3) self-reports of childcare responsibilities (particularly for women), unhealthier diets, work-life balance and home-working environment as barriers to remote working productivity and mental health; (4) self-reports of potential aids and benefits during the lockdown, that researchers, employees, policy makers, etc, can learn from when considering home-working practices. These will now be discussed in turn.

Correlational analyses revealed significant relationships between sedentary behavior (ie, time spent sitting, which in turn was negatively correlated with physical activity, expressed as IPAQ METs) and poorer mental health, which was further related to worse work productivity. To expand, we observed associations between work productivity, mental health, and changes in well-being. For example, we found that higher mental distress scores (K6) were correlated with worse work productivity (IAPT) and worsened well-being (WCI) since the start of the UK lockdown. This is consistent with existing evidence associating work performance and productivity with well-being under nonlockdown conditions [18,19] and demonstrates that the links between physical and mental health observed before the pandemic still explain the variations in these measures and work productivity. It also suggests that recommendations to support remote working that have been proposed in light of past research (eg, adequate IT support, clear communication between staff and management regarding outcomes [18]) still have the potential to be applied in the current situation to improve the productivity of remote workers. Similarly, the current circumstances should prompt broader discussion and policy development concerning the uptake of technology to enable the remote provision of mental health care [63].

Notably, the rates of moderate (55%) and severe (12%) psychological distress were substantially higher in respondents without a mental health diagnosis than has been previously observed in large samples during nonpandemic periods [52] and disasters such as nuclear accidents and earthquakes [64]. Although an element of participant self-selection may explain the extremely high rates of psychological distress we observed,

we cannot exclude that the unprecedented magnitude of the ongoing COVID-19 crisis and the prolonged restrictions in many countries, such as the United Kingdom, may be the catalyst for such pronounced reported decreases in psychological well-being.

A further major finding of the current research was that individuals who had received a mental health diagnosis before the lockdown had significantly worse mental health scores, and spent significantly more time sitting, than individuals without a diagnosis. Previous research has identified stress, depression, and anxiety as key predictors of absenteeism (13,800 days lost per annum) in the United Kingdom, resulting in a 6% decrease in productivity [65]. Mental health issues have been reported to affect fundamental aspects of work-life balance [28] and to increase absenteeism and presenteeism [66]. Economic losses as a result of poor mental health have also been documented, further justifying research into cost-effective occupational and psychosocial interventions [67]. Thus, the present findings point to the prevalence of previous and new mental health issues as a crucial consideration of the COVID-19 pandemic, not only for public policy makers when considering management of societal recovery from the pandemic, but also for the private sector to maintain viable working environments. This includes promoting the importance of good well-being and available services that employees can access (without stigma).

Psychological distress and poor mental health, nonetheless, can affect more than just work productivity, and in turn, they can be affected by a variety of environmental stressors. The narrative self-reports revealed that several aspects of respondents' daily lives during the pandemic (eg, changes to shopping habits and lack of contact with relatives and friends) interacted with other sources of stress or anxiety, which individuals related to poorer mental health. Fear, stress, tiredness, and lack of sleep were widely reported across narrations; and news intake appeared to add to worries and stress. This accords with existing research showing that media and risk-elevating message exposure exacerbated stress, worries, and public anxiety [31,32], but also that news intake correlated with poor mental health in the United Kingdom, particularly at the beginning of the pandemic [30]. Interestingly, however, news intake did not appear to produce significant correlations with mental health (K6) scores or overall well-being change (WCI), although it was correlated with work productivity and was represented as a concern across qualitative comments. As such, other aspects of news consumption not probed in the present survey (eg, how many times per day news is watched; preferred news source or news media type) may be more informative in understanding its effects on mental health, as opposed to simply the number of minutes dedicated to viewing news reports during an average day.

The majority of respondents in our sample (70%) also reported spending a greater amount of time sitting compared to before lockdown restrictions came into effect. Decreasing physical activity for various respondents was partly due to the initial restrictions to outdoor exercise. These findings are important, as even before the COVID-19 pandemic, physical inactivity and sedentary behavior were suggested to be pandemic in their own right, with 31% of individuals aged 15 years or older being identified as physically inactive and approximately 3.2 million

deaths per year attributed to these types of behavior [68]. Thus, strategies to circumvent sedation need to be promoted. Encouragingly, however, portions of our sample reported walking more (46%) and engaging in more moderate (45%) and vigorous (52%) exercise.

Similarly, substantial proportions of our sample reported an increase in smoking (63%), alcohol intake (41%), and overall food intake (39%), including sweet treats (53%) and savory snacks (43%); this is consistent with existing research [34] showing more snacking and unhealthy food choices in the general population worldwide during the COVID-19 pandemic. However, we also observed increases in vegetable intake (28%) and home cooking (63%), and a decrease in takeaway use (59%). Our qualitative data suggest that these positive health changes may represent attempts at coping with life and work stressors during the lockdown, a result of more time available, and/or increased awareness of the ill effects of a poor lifestyle, particularly in the context of COVID-19, which have been widely documented during the pandemic [34,38].

Regarding physical activity, our data revealed that some respondents had more time to engage in indoor physical activity than before the lockdown. There is evidence of greater public awareness of the importance of physical activity than ever before [69,70]. Fitness centers have posted free web-based workouts to promote physical activity [43], and information about examples of exercises that can be done at home has been disseminated [71,72]. This includes practical recommendations for aerobic exercise, bodyweight exercises, dance, and active video gaming, as a means to promote physical activity and protect individuals both physically and mentally from COVID-19 [42]. The WHO further highlights how adults and children can achieve the recommended physical activity guidelines at home, with no special equipment and limited space [41]. These recommendations for home-based activities may have been paramount in ensuring that some individuals remained physically active and reduced engagement in sedentary behaviors.

We also explored gender and household characteristics as potential sources of differences in well-being and productivity. Adults living in a household without underage children were significantly more sedentary and, although they engaged in more coping activities, they did not significantly differ on any other metrics as compared to the rest of the sample. More importantly, and consistent with recent research [5], we observed that women were significantly more likely to be the main childcare providers in the household. Although the quantitative analyses did not reveal any significant gender differences in mental health or productivity as a consequence of gender, our qualitative data pointed to childcare duties as a significant challenge for adults—particularly women—who are attempting to maintain their well-being. These childcare responsibilities, which women reported, proved an obstacle to optimal work functioning. However, we did observe that women, compared to men, reported engaging in more recreational activities (eg, cooking/baking, arts and crafts, gardening) in an attempt to preserve their psychological well-being. This could explain why, despite women reporting the challenges of childcare to their psychological health, the quantitative analysis did not



reveal differences in well-being as a function of gender. Notably, given the wealth of evidence for existing gender inequalities [9,73-75], research on psychophysical well-being and employment outcomes in remote workers in the aftermath of the pandemic should consider gender an important factor [76]. To circumvent the negative effects of remote working, some of the recreational activities respondents in our sample resorted to (eg, gardening, or meditation) could be further researched as effective strategies to promote good coping/well-being during lockdowns, such as connecting with nature (for a review, see Richardson and colleagues [77]) or embracing a more self-compassionate mindset (for a meta-analysis, see Wilson and colleagues [78]).

Difficulties with maintaining work-life balance were a recurring theme in our qualitative data; however, a more flexible work dynamic and an improved work-life balance were reported in some narrations. Past research [73] has found that voluntary remote working increases work-life balance, observing that remote working can preserve well-being as long as workers can be flexible about it (which is challenging during a lockdown). Mustajab and colleagues [5] further reported a lack of commuting as an advantage of remote working in their sample of Indonesian workers. These findings accord with some of our narrations. However, some of our respondents reported that they were working more hours despite the time saved by not commuting (see also Béland and colleagues [13]). Additionally, and concerning, respondents in our survey further reported that expectations of productivity levels on the part of their employers were often higher than those required prelockdown. Although flexible employment has previously been found to increase productivity [79], past research did not account for the added stressors of a global pandemic and resulting lockdown (nor autonomy of choice—or lack thereof—to work remotely). An important question leading on from this research is whether the perceived productivity expectation was a requirement of a respondent's role or a self-assumed expectation. Either way, it has important ramifications regarding employer-employment communications in pandemic and remote-working situations, especially as high-pressure, high-performance work cultures can lead to poorer mental health and staff retention issues [73,80].

Finally, although the International Labour Organization [81] has identified remote working as an excellent strategy to mitigate job losses, and it calls for policies aimed at protecting workers by supplementing their income [82] and encouraging flexible work arrangements [3], many of our respondents reported complications regarding technologies, equipment, and the use of living spaces as a new workplace, which affected their attitudes toward work [83] as well as their ability to work. Such findings are again consistent with existing research [5] indicating a breakdown of communication with managers and colleagues as a common complaint during the COVID-19 pandemic. Thus, adjusting to the new realities of remote work—materially, socially, and psychologically—appears to pose challenges across national economies and cultures.

In summary, currently, there is scant evidence in the literature concerning remote workers' perceptions of the lockdown's effects on their physical and psychosocial state and how this

might affect their work productivity. This is especially the case for those who were required to transition to remote work during a global pandemic (many of them without being accustomed to this mode of working [83]). However, our qualitative data highlight a range of concerns on the part of respondents, from childcare to perceived work pressures to the practicalities of physically being able to work effectively from home—all of which map onto employment prospects. Notably, employment prospects have been shown to affect mental health, satisfaction, and sense of identity [84], all of which are pillars of psychological well-being [85]. Given the observed relationship between psychological stress and poor work productivity reported by our participants (but also demonstrated via our quantitative data), the current state of affairs for many remote workers could create a negative feedback loop. To expand, the enforced move to remote working, for many, has created work-related uncertainty and pressures, which can negatively affect mental health. The latter, in turn, could then further affect work productivity, exacerbating work-related concerns and, consequently, mental health. Thus, a downward physical, psychological, and work productivity spiral perpetuates.

## Implications

The present study contributes to a nascent field investigating the well-being of remote workers and how remote working can be enhanced. The pandemic recovery process will likely involve a variable period of flexible work arrangements, as some employers may struggle to adapt their workspaces to comply with continued social distancing regulations [86] and some workers might prefer to continue working remotely or via a hybrid office-home model [87]. Importantly, a study [88] conducted among Chinese workers returning to office-based employment following the lifting of restrictions found that ~10% of respondents reported symptoms consistent with a diagnosis of posttraumatic stress disorder. The study found that the incidence of psychiatric symptoms were, among others, the presence of physical symptoms, poor physical health, and a negative perception of a return to the workplace. However, the study also found that the implementation of workplace hygiene and prevention measures (eg, mask-wearing policies) on the part of employers was related to less severe psychiatric symptoms. In light of this, employers, institutional policies, and governments must address the issue affecting workers—both those returning to the workplace, with the perceived vulnerabilities/anxieties this might pose to employees, and those who will continue to work remotely for the foreseeable future. For all modes of working (be it office-based, home-based, or hybrid), all technological and ergonomic aids should be already in place for remote workers to work as closely as possible to their original conditions [83]. Where this is not occurring or cannot be expedited, support structures must be put into place, with employers recognizing that work productivity, rather than increasing, may decrease in the first instance.

Second, childcare responsibilities need greater consideration. Various guidelines have been published to deal with childcare responsibilities [89,90], and calls have been made to support working parents (especially women) in remaining in employment [91]. Current strategies worldwide, however, prioritize changes to individual behaviors without considering

the potential impact that employers and working conditions have on worker well-being or the personal circumstances of employees. In light of the relationship between well-being and productivity, it is in the best interest of both workers and employers to consider systemic obstacles to well-being and systemic solutions to them. Expectations of high productivity imposed on workers trying to juggle parental as well as teaching duties while remote working during a time of ongoing or potential school closures can dramatically worsen gender inequalities [91]. Employers should acknowledge the considerable physical and psychological burden on primary child carers (overwhelmingly women) who are balancing remote working with childcare (including home tutoring) responsibilities and implement strategies accordingly.

Dietary recommendations in light of the COVID-19 pandemic [92,93] and particularly for people in lockdown have not been widely formulated and disseminated. Our data revealed increases in overall food intake, specifically the increased consumption of sweet treats and savory snacks and increased frequency of alcohol consumption. However, respondents also reported decreases in takeaway use and increases in home cooking, suggesting there is potential to make remote working a sustainable and healthy lifestyle provided individual and systemic obstacles are investigated and tackled. For example, recent evidence has favored the idea of promoting immunonutrition, rather than only healthy eating, during the current pandemic [94,95]. Although the Better Health campaign in the UK attempts to tackle some systemic barriers, tailoring information that encourages sustainability of a healthy diet across society by guaranteeing access to essential nutrients through healthy eating and/or vitamin supplements is still needed.

Finally, our data point to a clear mental health crisis unfolding in remote workers, which may engender and be engendered by sedentarism and poor nutrition, and in turn may negatively affect work productivity. Public health guidelines for clear and effective actions are needed to improve psychophysical well-being and promote health, thereby also potentially increasing work productivity in the home-working population. There is no shortage of published research to inform such policies in the context of improved nutrition [96,97], exercise [41], mental health [98-100], and work productivity [101,102]. However, evidence-based public health guidelines are only as good as their implementation, which will likely be a function of the material resources both public and private organizations are willing to invest. Future research should continue to promote workers' physical and psychological well-being, not only as a fundamental goal of public governance but also as a strategic priority for private enterprises and the continued health/wealth of such companies [102].

### Limitations and Future Directions

While the results of our study reveal many findings which could pose important implications for private businesses and public policy, there are important caveats to consider. It should be noted that the survey was distributed via the web. Web-based surveys always include uncertainties about the validity of the data, especially where the survey is self-report and if there are

no published studies with a similar or same population to compare to [103]. Nonetheless, web-based surveys have advantages such as decreasing respondents' inhibitions, offering higher anonymity and increasing the gender, sexual orientation, and diversity of a sample [104].

In attempting to quantify the quality of well-being changes since the start of the lockdown, we could not rely on a standardized, validated measure that probed changes to diet, exercise, and lifestyle. Therefore, we opted to compute an aggregate score (WCI) of distinct questionnaire items on a decrease-increase scale. Despite the lack of formal validation of this scale, the observation of significant correlations between it and standardized measures of productivity (IAPT) and psychological distress (K6) is indicative of both construct and criterion validity. Future work should explore and improve the psychometric properties of this instrument.

In terms of statistical power, our study had a sufficient sample size to detect correlations of  $\tau_b > 0.3$  with 0.8 power at an  $\alpha$  of .005 but may have had less power to detect true effects for our smaller correlations at the same  $\alpha$  level. We nevertheless opted to adopt this more stringent  $\alpha$  level given the number of correlational tests we conducted. While even the smaller correlations we observed were interpretable in light of the existing literature (and additional correlations were significant at lower  $\alpha$  levels), future research should aim for larger samples to achieve greater statistical power and to possibly enable the analysis of individual differences. Indeed, in recruiting larger samples, future studies should seek to differentiate the type of remote worker occupation enabling fuller analysis of the particular struggles of different worker groups [8]. In addition, adding focus group or semistructured interview methods would add to the robustness, richness, and depth of any findings [105,106], especially concerning a novel topic such as this. Indeed, to our knowledge, this is the first study that considers a comprehensive overview of well-being and its effects on remote-working productivity in a UK population.

### Conclusion

The mass switch to working remotely during COVID-19 lockdown, and the many worries stemming from the pandemic, have been argued to adversely affect the physical and mental well-being of workforces globally. The results of the current study demonstrate that well-being, which has a significant impact on productivity, is at stake when it comes to working remotely during a pandemic. The main findings of the current study were a relationship between sedentary behavior and poorer mental health, with negative effects on work productivity; moreover, challenges to productive remote working ranging from IT provisions to parental obligations were observed. Therefore, policies that promote physical activity, reduce psychological distress, address gender gaps, and support balancing childcare/home schooling while working remotely are urgent. It is also essential that employers monitor workers' well-being and implement systemic guidelines and practices to maintain worker well-being (eg, encouraging physically active breaks, providing more logistic support) while also promoting individual lifestyle changes (eg, meditation, healthy cooking), as well as policy related to reasonable adjustments in the "new"

workplace and clear productivity expectations. Targeted strategies such as these to support people working remotely as a consequence of COVID-19 may help to thwart, or at least attenuate, an international public health crisis. To this end, findings from well-being research also need to be made easily accessible to remote workers and companies.

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## Conflicts of Interest

None declared.

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## Abbreviations

**IAPT:** Brief Instrument to Assess Workers' Productivity During a Working Day

**IPAQ:** International Physical Activity Questionnaire

**IT:** information technology

**K6:** Kessler-6 Distress Scale

**MET:** metabolic equivalent

**WCI:** well-being change index

**WHO:** World Health Organization

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Review

# Machine Learning and Medication Adherence: Scoping Review

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## Abstract

**Background:** This is the first scoping review to focus broadly on the topics of machine learning and medication adherence.

**Objective:** This review aims to categorize, summarize, and analyze literature focused on using machine learning for actions related to medication adherence.

**Methods:** PubMed, Scopus, ACM Digital Library, IEEE, and Web of Science were searched to find works that meet the inclusion criteria. After full-text review, 43 works were included in the final analysis. Information of interest was systematically charted before inclusion in the final draft. Studies were placed into natural categories for additional analysis dependent upon the combination of actions related to medication adherence. The protocol for this scoping review was created using the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) guidelines.

**Results:** Publications focused on predicting medication adherence have uncovered 20 strong predictors that were significant in two or more studies. A total of 13 studies that predicted medication adherence used either self-reported questionnaires or pharmacy claims data to determine medication adherence status. In addition, 13 studies that predicted medication adherence did so using either logistic regression, artificial neural networks, random forest, or support vector machines. Of the 15 studies that predicted medication adherence, 6 reported predictor accuracy, the lowest of which was 77.6%. Of 13 monitoring systems, 12 determined medication administration using medication container sensors or sensors in consumer electronics, like smartwatches or smartphones. A total of 11 monitoring systems used logistic regression, artificial neural networks, support vector machines, or random forest algorithms to determine medication administration. The 4 systems that monitored inhaler administration reported a classification accuracy of 93.75% or higher. The 2 systems that monitored medication status in patients with Parkinson disease reported a classification accuracy of 78% or higher. A total of 3 studies monitored medication administration using only smartwatch sensors and reported a classification accuracy of 78.6% or higher. Two systems that provided context-aware medication reminders helped patients to achieve an adherence level of 92% or higher. Two conversational artificial intelligence reminder systems significantly improved adherence rates when compared against traditional reminder systems.

**Conclusions:** Creation of systems that accurately predict medication adherence across multiple data sets may be possible due to predictors remaining strong across multiple studies. Higher quality measures of adherence should be adopted when possible

so that prediction algorithms are based on accurate information. Currently, medication adherence can be predicted with a good level of accuracy, potentially allowing for the development of interventions aimed at preventing nonadherence. Monitoring systems that track inhaler use currently classify inhaler-related actions with an excellent level of accuracy, allowing for tracking of adherence and potentially proper inhaler technique. Systems that monitor medication states in patients with Parkinson disease can currently achieve a good level of classification accuracy and have the potential to inform medication therapy changes in the future. Medication administration monitoring systems that only use motion sensors in smartwatches can currently achieve a good level of classification accuracy but only when differentiating between a small number of possible activities. Context-aware reminder systems can help patients achieve high levels of medication adherence but are also intrusive, which may not be acceptable to users. Conversational artificial intelligence reminder systems can significantly improve adherence.

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## KEYWORDS

machine learning; medication adherence; adherence monitoring; adherence prediction; medication compliance; health technology

## Introduction

Health care costs will continue to rise into the foreseeable future unless technology is implemented that substantially increases the efficiency of care delivery. Machine learning is a technology with the potential to automate many health care processes, including actions that impact medication adherence. Medication adherence is an important issue because approximately 50% of patients with chronic disease are not adherent to their medications, thus increasing medical costs and avoidable human suffering [1].

Recently, reviews were published that discuss the effectiveness of using machine learning to improve medication adherence. Awan et al [2] investigated the use of machine learning to improve the care of patients with heart failure. Two of the studies mentioned in this review used machine learning to predict medication adherence. Another review, written by Cresswell et al [3], investigated the use of data-driven artificial intelligence (AI) in computerized systems that support health and social care. Of the articles mentioned, 2 of them focused on using machine learning to improve medication adherence. One used neural networks and computer vision to enhance outpatient adherence to anticoagulant medications. The other adherence study discussed using an AI system to provide personalized support to patients taking warfarin.

In contrast to previous works, this review is focused more generally on the use of machine learning within the confines of medication adherence. By using a broader perspective, this paper provides high-level insight into this area of study, which is not possible with more narrowly focused examinations. Medication adherence is a complex problem that can be engaged from multiple angles using machine learning. This paper serves as a way to quickly learn about different approaches, their current level of development, and obstacles that need to be overcome to use machine learning more effectively toward improving medication adherence.

This review also categorizes and summarizes how machine learning has been used to execute actions related to medication adherence in academic literature. Within each category, common themes will be explored to find gaps and opportunities for future work.

## Methods

### Eligibility Criteria

The eligibility criteria were developed through collaboration between authors AB and JM. Papers included in this review carried out at least one action related to machine learning and medication adherence. Studies also had to test out their application of machine learning to medication adherence using either real patients, research participants, or simulations. The ABC taxonomy was used to define medication adherence for this study. This taxonomy defines medication adherence as “the process by which patients take their medications as prescribed, composed of initiation, implementation and discontinuation” [4].

### Information Sources

The following databases were searched to identify relevant papers: PubMed, Scopus, IEEE, ACM Digital Library, and Web of Science. These databases were selected by the Laboratory of Applied Informatics Research (LAIR) team as representing the largest and most extensive coverage of studies that investigate applying machine learning to medication adherence.

### Search Query

Search queries for this paper were created with the help of Rebecca Carlson and Fei Yu, both of whom are experienced research librarians. Search terms were selected by reviewing exhaustive term lists provided by the research librarians on the topics of machine learning and medication adherence. The same keywords were selected for all five databases by combining the lists of machine learning and medication adherence terms using an AND operator. The final search was conducted on April 30, 2020. When searching PubMed, Medical Subject Headings (MeSH) terms were incorporated to provide broad coverage of related vocabulary. Following PubMed, this same query strategy was used to search Scopus but with Emtree Terms in place of the MeSH terms. For IEEE, ACM Digital Library, and Web of Science, the keywords were used exclusively to discover relevant papers. Examples of the search queries are provided in section A of [Multimedia Appendix 1](#).

### Selection of Evidence Sources

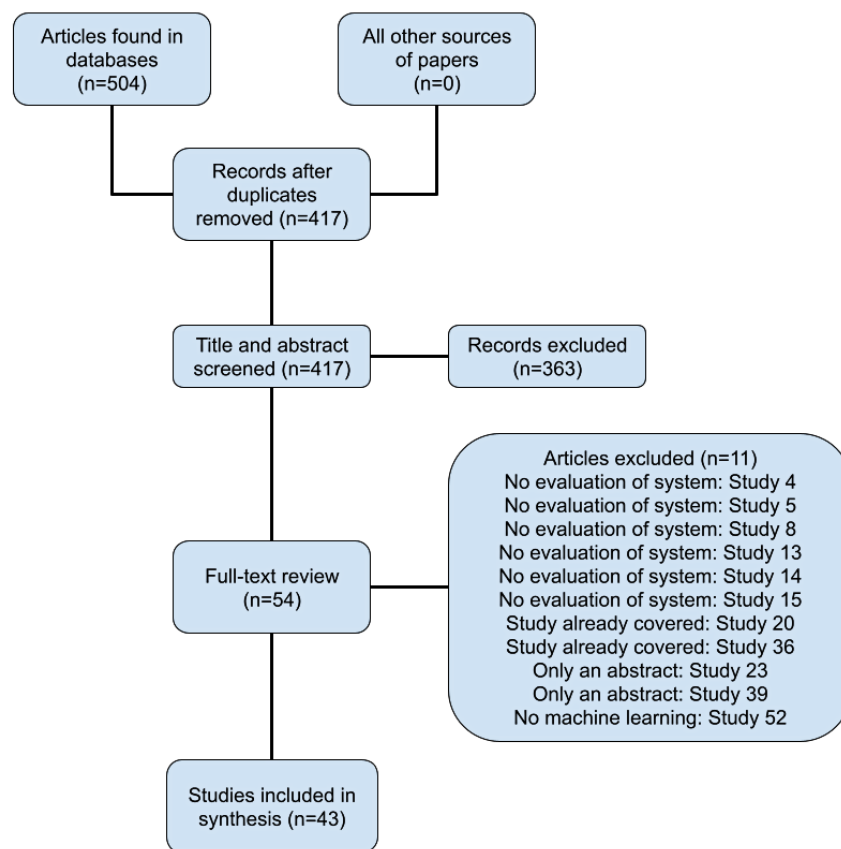
The search queries found 504 studies that contain both machine learning and medication adherence terms. After removing

duplicate studies, 417 papers were identified for review. The title and abstract review were conducted using a two-person team consisting of authors AB and MK. The title and abstract evaluation reduced the total number of relevant papers to 54. Next, a sample of 20 articles was screened. This initial screening was done to ensure that information was collected in a consistent manner using a data charting template. This template was developed through collaboration with the LAIR team and the primary author of this work. After finalization of the data charting template, all 43 papers were reviewed in full by AB and MK. Studies that passed the full-text review focused on both medication adherence and machine learning. A focus on medication adherence and machine learning was essential to

reduce the number of studies to a manageable list of highly relevant works. Included works also evaluated the use of machine learning for medication adherence actions using either patients, research participants, or simulations. This testing requirement was used to exclude studies that are still in the early development stages and to make sure that included works contained all of the relevant data charting elements. Next, the results were grouped into natural categories and analyzed according to the combination of medication adherence actions in each study. This grouping of related studies was carried out by AB, JM, and MK.

Figure 1 shows the article review process and provides reasons why specific studies were excluded during the full-text review.

Figure 1. Article review process.



## Data Charting Process

A data charting form was created and updated throughout the review process as needed. This form was used to guide the selection of relevant information throughout the review process and was tested to ensure consistency across different articles during the sample screening. The items included in the data charting template are listed in the next section.

## Data Items

Data charted for this review includes the article title, publication date, study number, study goals, main study results, disease states, predictors of medication adherence, types of machine learning used, number of participants, data collection methods, actions related to medication adherence, adherence measurements, limitations, and inclusion or exclusion status.

## Categorization of Studies

Following data charting, actions related to medication adherence were determined for each study. Next, articles were grouped for further analysis according to the combinations of medication adherence actions included in each work. AB, JM, and MK conducted the categorization process, and disagreements were discussed until a consensus was reached. Following categorization, the data charting documents for these works were reviewed to find relevant themes. A general analysis was also conducted before categorization in terms of the number of publications per year, articles per disease state, and publications per database type.

## Results

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### Results of Individual Sources of Evidence

This paper includes the analysis of 43 studies selected for inclusion. The main results of this review are listed in [Tables 1-3](#). More detailed data charting tables are also available in section B of [Multimedia Appendix 1](#).

**Table 1.** Summary of studies that predict medication adherence.

Study	Year	Data collection	Algorithms	Disease states	Strong predictors of adherence <sup>a</sup>	Adherence metric predicted	Main outcome metric <sup>b</sup>
Walczak and Okuboyejo [5]	2017	Self-reported questionnaire	ANNs <sup>c</sup>	General	Variable strength not discussed in detail	Self-reported reasons for medication adherence status	79.3% accuracy when predicting reasons for poor adherence
Son et al [6]	2010	Self-reported questionnaire	SVM <sup>d</sup>	Heart failure	Disease severity classification, medication knowledge, gender, daily medication frequency, marital status	Self-reported medication adherence status	77.6% accuracy when predicting medication adherence
Aziz et al [7]	2020	Self-reported questionnaire	ANNs, RF <sup>e</sup> , SVM	Hypertension	Education level, marital status, general overuse, monthly income, specific concern	Self-reported medication adherence status	79% accuracy when predicting medication adherence
Aznar-Lou et al [8]	2018	Pharmacy claims data	LR <sup>f</sup>	General	Medication cost for low-income individuals	Filling a medication within 2 months of issuance	Statistically significant association between medication cost and medication adherence in low-income group
Zhang and Meltzer [9]	2016	Self-reported questionnaire	LR	General	Time between social security check arrival and filling prescriptions, age, specific chronic conditions	Self-reported adherence status	Statistically significant association between medication adherence and time difference between receiving social security check and filling drugs
Aznar-Lou et al [10]	2017	Pharmacy claims data	LR	High-cost diseases	Age, nationality, number of chronic conditions, active disease, being treated by primary care provider	Patient filling their medication within 1 month of issuance	Statistically significant association between medication adherence and age, nationality, number of chronic conditions, specific active diseases, type of care provider
Haas et al [11]	2019	Self-reported questionnaire	RF	Fibromyalgia	Type of medication, years of treatment, dosage, age, gender, region of residence	Self-reported adherence status on a health forum	67.8% accuracy when predicting medication adherence
Lu et al [12]	2005	Self-reported questionnaire	ANNs, SVM	HIV	Viral load, drug abuse, alcohol abuse, psychiatric diagnosis, missed clinic visits, housing, HIV-related inpatient medical care	Self-reported adherence class ranging from class one to four	100% accuracy when predicting adherence class but sample size of only 33
Franklin et al [13]	2016	Pharmacy claims data	LR	High cholesterol	Age, sex, race, specific statin medication, count of health services score, cardiovascular disease status, cardiovascular procedure status, comorbidities, initial statin fill behavior	Proportion of days covered of 0.8 or higher	84.2% accuracy when predicting medication adherence

Study	Year	Data collection	Algorithms	Disease states	Strong predictors of adherence <sup>a</sup>	Adherence metric predicted	Main outcome metric <sup>b</sup>
Karanasiou et al [14]	2016	Clinical estimation	ANNs, SVM, RF, J48, random tree, logistic tree, classification tree, rotation forest, radial basis function, Bayesian network, Naive Bayes	Heart failure	Specific medical conditions, specific medications, medication dose, medication frequency	Provider determined adherence status to medications and lifestyle changes	91% sensitivity when predicting medication adherence
Bourdès et al [15]	2011	Self-reported questionnaire	ANNs, LR	ACS <sup>g</sup>	Coronary artery bypass graft status, overweight with BMI between 25 and 30, hypercholesterolemia, education level	Self-reported concurrent use of an ace inhibitor or angiotensin receptor blocker, beta blocker, statin, and a blood thinning agent	0.80 AUC <sup>h</sup> when predicting medication adherence
Kim et al [16]	2019	Self-reported questionnaire	Classification tree	Smoking cessation	Belief in medication safety, taste and sensory properties, exposure to others smoking, quitting confidence	Self-reported adherence during a phone interview	2.22 importance score for belief in medication safety, 1.84 importance score for taste and sensory properties, 1.67 importance score for exposure to other smokers, 1.15 importance score for quitting confidence
Kardas et al [17]	2020	Pharmacy claims data	LR	Chronic disease	Age, medication cost, medication class	Not picking up a medication within 1 month of issuance	Statistically significant association found between age and medication adherence
Desai et al [18]	2019	Pharmacy claims data	LR	Fibromyalgia	Gender, age, race, comorbidity score, medication type, health coverage, emergency room visits	Medication possession ratio of 80% or higher	AUC of 0.6224 when predicting medication adherence
Elahinia et al [19]	2017	Discharge summaries	Natural language processing	General	Keywords frequently found in the discharge summaries of nonadherent patients	Adherence status based on professional interpretation of discharge summaries	Statistically significant association between category 1, 2, and 3 keywords with medication adherence

<sup>a</sup>Predictor strength was based on individual study results.

<sup>b</sup>Main outcome metric based on judgement of the research team after careful consideration of all results presented in the individual study.

<sup>c</sup>ANN: artificial neural network.

<sup>d</sup>SVM: support vector machine.

<sup>e</sup>RF: random forest.

<sup>f</sup>LR: logistic regression.

<sup>g</sup>ACS: acute coronary syndrome.

<sup>h</sup>AUC: area under the curve.

**Table 2.** Summary of studies that monitor medication adherence.

Study	Year	Algorithms	Sensors	Diseases	Data analyzed using machine learning to determine adherence	Main outcome metric <sup>a</sup>
Hezar-jaribi et al [20]	2016	Classification tree	Body worn	Chronic disease	Smartwatch movement data collected during one of five tasks: drinking water, taking a pill while sitting, taking a pill while standing, writing, eating	78.6% detection accuracy using only smartwatch sensors
Fozoon-mayeh et al [21]	2020	RF <sup>b</sup> , LR <sup>c</sup> , SVM <sup>d</sup> , boosted tree	Body worn	General	Smartwatch movement data collected during medication ingestion or other predetermined tasks	98.3% detection accuracy using smartwatch sensors
Aldeer et al [22]	2019	RF, SVM	Smart pill bottle	General	Medication bottle movement and cap sensor data collected during medication ingestion or other predetermined tasks	90% accuracy when using all smart bottle sensors
Ntalianis et al [23]	2019	ANNs <sup>e</sup>	Audio recording device	Asthma/COPD <sup>f</sup>	Sound recordings of inhaler use broken down into different inhaler use actions like breathing in, actuation, and breathing out	95.86% classification accuracy using audio files
Tucker et al [24]	2015	NB <sup>g</sup> , IBk <sup>h</sup> , SVM, J48, RF	Kinect	Parkinson disease	3D movement scans of patients with Parkinson disease in different adherence states	97% classification accuracy when determining medication status for a single patient, 78% classification accuracy when determining medication status of multiple patients
Ma et al [25]	2018	RF	Body worn	General	Movement data collected using a smartwatch during six predefined activities: medication intake with nondominant hand, medication intake with dominant hand, walking, texting, writing with a pen, drinking water	Recall of 1.00 with a precision of 0.80 for medication intake classification using smartwatch sensors
Nousias et al [26]	2016	SVM, RF, Adaboost	Audio recording device	Asthma/COPD	Audio recordings of inhaler use, breathing in, breathing out, and noise not related to medication use	97.59% classification accuracy using audio recordings
Bilodeau and Ammouri [27]	2011	Petri net	Camera	General	Video footage of people taking medications in which the head, hands, and medication bottle are clearly visible	Correctly identified medication taking 9 out of 12 times
Aldeer et al [28]	2019	SVM, RF	Smart pill bottle	General	Patient-specific movement profile data collected using pill bottle movement and cap sensors	91% accuracy identifying the movement patterns of a specific patient
Zhang et al [29]	2019	ANNs	Body worn	Parkinson disease	Movement data of patients with Parkinson disease collected using a smartphone	83.4% classification accuracy using body worn sensors
Pettas et al [30]	2019	ANNs, RF	Audio recording device	Asthma/COPD	Audio recordings of sounds related to inhaler use or recordings of non-inhaler-related sounds	Classification accuracy of 93.75% using audio recordings
Moldovan et al [31]	2018	ANNs, LR, RF, decision tree	Body worn	Dementia	Movement data of patients with dementia during medication ingestion and other predetermined tasks collected using four body worn motion sensors	Classification precision of 0.91 using body worn sensors
Kikidis et al [32]	2015	ANNs	Audio recording device	Asthma/COPD	Audio recordings that contain either an inhaler actuation or a non-inhaler-related sound	99.5% classification accuracy using audio recordings

<sup>a</sup>Main outcome metric based on judgement of the research team after careful consideration of all results presented in the individual study.

<sup>b</sup>RF: random forest.

<sup>c</sup>LR: logistic regression.

<sup>d</sup>SVM: support vector machine.

<sup>e</sup>ANN: artificial neural network.

<sup>f</sup>COPD: chronic obstructive pulmonary disease.

<sup>g</sup>NB: Naive Bayes.

<sup>h</sup>IBk: instance-based classifier with parameter k.

**Table 3.** Summary of studies that monitor and attempt to improve medication adherence.

Study	Year	Sensors	Adherence intervention	Disease states	Algorithms	Data analyzed using machine learning to determine adherence	Main outcome metric <sup>a</sup>
da Silva et al [33]	2019	Smart medication cabinet, cameras, movement sensors, light sensors, thermostat, smart TV sensors, smartphone sensors, smartwatch sensors, door sensors, blood pressure sensors	Context-aware medication reminder prompts	Hypertension	C4.5, random tree, RepTree	Medication ingestion confirmed by medication cabinet using door sensors, RFID <sup>b</sup> tags, video recording, patient daily patterns monitored using motion sensors in house, light sensors, thermometer sensors, smart TV sensors, smartphone sensors, home door sensors, blood pressure sensors	95.10% medication adherence level for people using the system
Lundell et al [34]	2007	Smart medication cabinet, motion sensors, refrigerator sensors, smartphone sensors, smartwatch sensors, bed sensors, front door sensors	Context-aware medication reminder prompts	General	Dynamic Bayesian network	Medication ingestion confirmed using pill tray lid sensors, patient daily patterns tracked using motion sensors in house, refrigerator sensors, smartphone sensors, smartwatch sensors, bed sensors, front door sensors	92% medication adherence for people using the system
Silva et al [35]	2018	Smart medication cabinet, computer sensors, tablets sensors, TV sensors, smartwatch sensors, smartphone sensors	Context-aware medication reminder prompts	Hypertension	J48, RF <sup>c</sup> , Rep-Tree, random tree	Medication ingestion determined by smart drug cabinet that uses RFID tags and door sensors, patient daily patterns tracked using computer sensors, tablet sensors, smart TV sensors, smartphone sensors, smartwatch sensors	95.2% classification accuracy using all available sensors
Silva et al [36]	2016	Smart medication cabinet, motion sensors, lighting sensors, cameras, smartphone sensors, TV sensors	Context-aware medication reminder prompts	General	J48, RepTree, random tree	Medication ingestion determined using smart medication cabinet with RFID tags and camera system, patient daily activity tracked using motion sensors in home, light sensors, surveillance cameras, smartphone sensors, smart TV sensors	Testing of a prototype system was conducted but no statistical results were presented
Nousias et al [37]	2018	Microphone	Visualization of inhaler use process	Asthma, COPD <sup>d</sup>	GMM <sup>e</sup> , SVM <sup>f</sup> , RF, AdaBoost	Audio recordings of inhalation, exhalation, inhaler actuation, and background noise	98% classification accuracy using audio recordings
Persell et al [38]	2020	None	Conversational AI <sup>g</sup> adherence coaching	Hypertension	Not discussed in detail	Blood pressure, weight, self-reported adherence, number of medications, number of dose increases or substitutions, compliance with: diet, exercise, sleep duration	No significant differences in adherence when comparing patients using smartphone coaching app vs those not using the app
Brar Prayaga et al [39]	2018	None	Conversational AI refill reminder system	Chronic disease	Not discussed in detail	Medication names, gender, number of refills processed using the system, patient responses using keypad or unstructured verbal responses	Text messaging reminder system improved adherence significantly with 14.07% more refills than the control group receiving traditional reminders



Study	Year	Sensors	Adherence intervention	Disease states	Algorithms	Data analyzed using machine learning to determine adherence	Main outcome metric <sup>a</sup>
Chaix et al [40]	2019	None	Conversational AI medication reminder system	Breast cancer	Not discussed in detail	Patient verbal responses to medication reminder: “yes I took it,” “no i didn’t take it,” “send me a message in 15 minutes”	Average compliance improved significantly in the chatbot group with 20% higher adherence levels when compared to the control group
Curci et al [41]	2017	Smart pill bottle	Medication reminder, nonadherence messaging to provider	General	RF, RIPPER, Bayesian networks, SVM, ANNs <sup>h</sup>	Movement sensor data recorded by pill bottle, patient response via cell phone app answering if they took the medication when medication ingestion is suggested by movement data, patient response to scheduled reminders indicating if the medication was taken or not	90% classification accuracy using medication bottle movement sensors
Labovitz et al [42]	2017	Camera	Medication reminder, adherence history visualization	Ischemic stroke	Not discussed in detail	Video recordings of medication ingestion using a smartphone and pill counts for patients in group one, blood concentration of medication and pill counts for patients in group two	Patient adherence using the AI platform was 90.5% compared with 100% using blood samples to measure drug levels

<sup>a</sup>Main outcome metric based on judgement of the research team after careful consideration of all results presented in the individual study.

<sup>b</sup>RFID: radio-frequency identification.

<sup>c</sup>RF: random forest.

<sup>d</sup>COPD: chronic obstructive pulmonary disease.

<sup>e</sup>GMM: Gaussian mixture model.

<sup>f</sup>SVM: support vector machine.

<sup>g</sup>AI: artificial intelligence.

<sup>h</sup>ANN: artificial neural network.

## Synthesis of Results

Before dividing the studies into categories, they were examined as a whole to determine the distribution of articles concerning time, disease states, and database type.

Table 4 displays the number of publications per year that apply machine learning to medication adherence. For the past few

years, this topic has generated a growing number of publications, indicating that there is interest building around this topic.

Table 5 illustrates the distribution of different disease states within the included articles. The largest group in this graph is general and consists of 12 studies. General indicates that these studies did not focus on any specific disease or group of diseases. The remaining 32 papers, except a single study focused on high-cost medications, looked at chronic diseases.

**Table 4.** Number of included studies per year.

Year of publication	Studies included, n
2005	1
2007	1
2010	1
2011	2
2013	1
2015	2
2016	6
2017	7
2018	6
2019	12
2020	4

**Table 5.** Number of included studies per disease group.

Disease groups	Studies included, n
Nonspecific	12
Cardiovascular diseases	10
Pulmonary diseases	5
General chronic diseases	4
Diseases of aging	3
Psychiatric diseases	2
Infectious diseases	2
Chronic pain	2
Smoking cessation	1
Cancer	1
Diseases with expensive medications	1

### Analysis of Natural Categories

Following the general analysis, actions related to medication adherence were determined. The three identified actions were prediction of adherence, adherence monitoring, and adherence interventions. Next, studies were grouped into natural categories for further analysis according to the combination of medication adherence actions that they contain. The following natural groups were identified: prediction of adherence only, monitoring of adherence only, monitoring with an intervention to improve adherence, all three medication adherence actions simultaneously, and prediction with monitoring.

### Studies That Predict, Monitor, and Intervene to Improve Medication Adherence

The fourth group contained 3 articles that predicted adherence, monitored adherence, and intervened to improve medication adherence [43-45].

The first of these studies allowed patients to request medication refills using a conversational AI SMS text messaging system [43]. The system would prompt the user when they needed to request a refill for their medication. The predictors used within

this study were age, gender, spoken language, address (used to determine social determinants of health), race, ethnicity, and patient response via either structured response or using free-text entry. This study used an artificial neural network to predict if the patient would use this system to request a medication refill. Machine learning was also used for conversational AI, but the specifics were not discussed within the article. This system was not restricted to any specific disease state and was tested using approximately 99,000 patients. The limitations are that data was only collected over 3 months and that 8% of free-text responses were not correctly understood by the conversational AI.

The next work used data from the 99DOTS (Directly Observed Treatment Short Course) program, which monitors medication adherence of patients with tuberculosis [44]. Patients in this program used a phone to enter a random code for each dose of the medication they took. Other data collected for 99DOTS included: demographic data (age, weight, gender, treatment center ID), treatment start date, treatment end date, adherence string, and treatment outcome if applicable. This data was manipulated to create both static and time series predictors. Random forest, linear regression, and support vector machine

(SVM) were applied to the static predictors to determine daily nonadherence risk, treatment success, and how to best allocate limited resources. A deep network called LEAP, which is capable of using time series predictors, was also used to predict these same outcomes. LEAP had the best prediction accuracy of the machine learning methods used. This system was tested using the monitoring data of about 17,000 people.

The next paper used face recognition software and computer vision to monitor medication adherence of 53 patients that had schizophrenia [45]. Patients in this study used a smartphone camera to record medication ingestion and submitted those recordings to the research team. Face recognition and computer vision techniques were then used to flag patients engaging in suspicious behavior, which indicated that long-term adherence was unlikely. This system also reminded patients to take their medications at a specific time each day. The main limitation was that patients were allowed to choose either direct in-person observation or monitoring via the app thus introducing bias into the study.

### Studies That Predict and Monitor Medication Adherence

The next group had 2 articles that predicted and monitored medication adherence but did not introduce any medication adherence intervention [46,47].

The first of these articles used data collected during hospital stays to generate predictors. Of these predictors, disease severity and biomarkers (breath, saliva, blood) had the largest impact on the model's accuracy [46]. The overall goals of this study were to predict the adherence risk of a given patient with heart failure and to monitor their ongoing adherence. Nine different classifiers were tested for this study, including random forest, logistic model trees, J48, simple classification/regression tree-CART, rotation forest, radial basis function network, SVM, Bayesian network, and Naive Bayes. Of all of these methods, random forest performed the best in terms of classification accuracy. The data of 29 patients was used to create this system.

The second paper used interactive voice response assessments to predict future adherence and to monitor current medication adherence in patients with depression [47]. The data used for this study was collected using interactive voice response assessments of 208 patients. These assessments were then used to create predictors. Of these predictors, the following added to the power of the model: past medication adherence, age, and physical functioning at baseline. Only logistic regression was used to predict future medication adherence.

## Discussion

### General Discussion

This is the first review to focus broadly on applying machine learning to medication adherence. This study provides a general summary of the topic and categorizes literature according to the combination of medication adherence actions. Within each category, common themes were explored and opportunities for future work were identified.

The application of machine learning to medication adherence is a topic still in its infancy that has become more prevalent over the last few years. This technology is typically being applied to patients with chronic diseases that require long-term medication use. In fact, 29 of the 43 studies looked at using machine learning to impact medication adherence within the context of chronic disease [6,7,11-15,17,18,20,23,24,26,29-33,35,37-40,42-47]. This is not surprising, since patients with chronic diseases often have a high medication burden and poor medication adherence over an extended period of time.

### Discussion of Studies That Predicted Medication Adherence

Twenty predictors of medication adherence were found to be important across two or more independent studies [6-19]. These predictors included: education level, marital status, income, gender, geographic location, emergency care interventions, age, race, ethnicity, disease severity, comorbidities, medication cost, insurance coverage, substance abuse, medication beliefs, medication knowledge, medication dose, medication frequency, initial medication adherence, and current medications. This suggests that it may be possible to build models that maintain a high level of accuracy even when applied to a different set of patients. In fact, 1 study in this review applied an established algorithm developed using the MEPS data set to a new data set pulled from a social health forum. This study managed to achieve a modest prediction accuracy of 67.8%, despite being trained on a completely different data set. However, this required careful manipulation of the input data to ensure it was formatted appropriately for the established prediction algorithm. In addition, two predictor variables were discarded to improve prediction accuracy. One limitation of several studies that predicted medication adherence is that they did not take socioeconomic factors into consideration [16,18]. Socioeconomic factors were determined to be strong predictors of adherence by multiple studies within this review and should be included when possible [7-9,17].

Similar methods of data collection were also used in works that solely predicted medication adherence. The most popular method of data collection and determining adherence was self-reported questionnaires. In fact, 8 of the 15 studies in this group determined medication adherence using self-reported questionnaires [5-7,9,11,12,15,16]. Although collecting data with questionnaires is attractive due to its simplicity and low cost, it typically overestimates adherence when compared to other data collection methods. When a questionnaire is used, a validated self-adherence measure is preferred, and efforts should be made to reduce negative social pressures associated with reporting nonadherence [48]. Pharmacy claims data was also used by one-third of these studies for both patient information and to determine adherence [8,10,13,17,18]. Pharmacy claims data is generally considered more reliable than self-reported questionnaires but still may overestimate adherence since it does not actively investigate whether the patient is taking the medication or not.

Additionally, studies that only predicted medication adherence used many of the same algorithms. Of 15 studies, 13 in this group used either logistic regression, artificial neural network,

SVM, or random forest algorithms. Some of these works compared the different types of algorithms to determine which was the most accurate [7,12,14,15]. However, more publications need to be generated before any type of consensus can be reached on this issue.

Furthermore, 13 of the 15 studies that attempted to predict medication adherence used either a self-reported adherence metric or medication filling data to train their models [5-13,15-18]. This adherence metric along with predictor variables was provided during the training of each algorithm. Following model training, the adherence metric was not provided to the model and instead was predicted based only on the predictor variables. Of the 6 studies that provided prediction accuracy, 5 of them reported accuracy of 77.6% or higher [5-7,12,13]. This level of accuracy is impressive, and this data could potentially be leveraged to prevent medication adherence issues before they occur. However, the specificity of the algorithm in question would need to be carefully investigated to ensure that it is not overpredicting poor medication adherence, potentially wasting resources directed at preventative measures. Within this group, 5 other studies reported a statistically significant association between predictor variables and medication adherence as their main result [8-10,17,19]. One study found that both nationality and provider type are significant predictors of medication adherence [10]. These two predictors should be investigated in follow-up studies to determine if they remain significant across multiple investigations. Another study within this review found a significant association between specific keywords and medication adherence, which can be used to predict medication adherence based on free-text discharge summaries [19]. More studies should be conducted to find keywords associated with medication adherence since a large amount of medical documentation is stored as free text. This is especially useful in analyzing data from less sophisticated clinical systems with less structured documentation.

### Discussion of Studies That Monitored Medication Adherence

Machine learning was also used to monitor medication adherence. The main purpose of all 13 studies within this group was to develop new ways of monitoring medication adherence with the aid of sensors and machine learning. One popular approach, used in 6 of these 13 studies, was to attach sensors to the container holding the patient's medication [22,23,26,28,30,32]. Four of these studies attached a microphone to an inhaler, and the other 2 used a smart pill bottle to track medication adherence. Direct attachment of sensors to medication holding devices is an established method of tracking medication adherence since the opening or activation of the medication holding device can be directly recorded. However, this form of data collection still has some major drawbacks outside of smaller deployments because it requires copious hardware to scale. This hardware would also likely be disposable unless additional effort was required on the part of the patient to load the medication or medication container into a reusable device.

Another popular approach was to use portable smart devices to track medication adherence. Of these studies, 6 used portable sensors found in common consumer electronics like smartwatches or smartphones [20,21,25,27,29,31]. One of these studies required users to actively record ingestion using a smartphone camera, and the other 5 recorded movement data using smartwatch sensors. Having patients track their medication ingestion with a camera every time they take a dose is accurate since the act of ingestion is being directly observed. However, it is unclear if patients would actually use the system and might find this level of observation overly intrusive.

Studies that only monitored medication adherence used many of the same machine learning algorithms. Of the 13 studies, 11 in this group used logistic regression, artificial neural network, SVM, or random forest algorithms [21-26,28-32]. Several studies compared the accuracy of these different algorithms, but this was not enough to generate any meaningful conclusions [22,26,28,30].

Moreover, works that only monitored medication adherence often built systems that classified user activities based on data provided by sensors. Several studies attempted to monitor the use of inhalers by analyzing audio recordings of inhaler use [23,26,30,31]. All 4 of these studies were able to classify sounds of inhaler use with an accuracy of 93.75% or higher. This is especially impressive when one considers that 3 of the studies also introduced background noise samples to make the evaluation more comparable to real-world environments [26,30,31]. All four systems also classified different parts of inhaler use such as inhalation, actuation of the inhaler, and exhalation. This allows these systems to track both medication adherence and proper inhaler technique simultaneously. Patients using a device like this could be coached in real time using an app or could be flagged for inhaler use training by a health care professional at a later time. In addition, since these systems are only using audio samples, similar results could probably be obtained using a smartwatch with a microphone.

Two other studies observed the movement patterns of patients with Parkinson disease [24,29]. Both of these systems were able to classify the medication status of the patient with an accuracy of 78% or higher, one using body worn sensors and the other using a stationary sensor mounted in a room. This level of accuracy is impressive and has potential that goes beyond simple medication adherence. Systems like this could be used to help inform clinicians of when a patient's medications need to be adjusted. This is helpful for patients in more advanced stages of degenerative diseases who may have difficulty communicating their current status to care providers. Three systems also classified medication administration using only movement sensors in a smartwatch. These studies were able to achieve a classification accuracy of 78.6%, which is impressive, but this was in a controlled setting with the number of possible activities restricted to a small list [20,21,25]. Determination of medication administration using only movement sensors in a smartphone is an attractive option since it allows tracking with devices that many patients are already using. However, this technology still requires more testing in realistic environments before it can be trusted to accurately determine administration.

## Discussion of Studies That Monitored and Intervened to Improve Adherence

A total of 10 studies also monitored medication adherence and introduced an intervention to improve it [33-42]. Some of the works within this group used many sensors in conjunction with alerts to provide context-aware reminders [33-36]. Two systems using context-aware reminder systems were able to keep patients at an adherence level of 92% or higher [33,34]. This is an impressive level of adherence, but these systems were intrusive and required the use of a large number of sensors throughout the living spaces of the user. Additionally, only 1 of these studies compared its results against a traditional reminder system, and they did so with the results of only a single patient [34]. Furthermore, none of these studies mentioned any effort to establish if users were comfortable with the level of monitoring required to produce a context-aware reminder system. This is potentially an oversight since these systems require the use of multiple sensors throughout a person's home. The companies creating smart devices would also need to be open to data sharing with their competitors if systems like this are going to be possible in the future. Other works that included medication monitoring with an intervention used conversational AI to communicate with patients [38-40]. All of the conversational systems included reminders and were able to interpret free-text responses provided by patients. Additionally, all of the conversational AI systems were compared against a control group to show if they improved adherence. Two of the three conversational AI systems significantly improved adherence over more traditional reminder systems. One of the conversational AI systems improved refill rates by 14.07% and the other improved average adherence by more than 20% over the study's duration [39,40]. However, the third conversational AI system did not significantly improve medication adherence when compared to a more traditional system [38]. In general, conversational AI systems are further along in development, allowing the authors to focus more on comparing their systems to more traditional solutions.

## Conclusions

### *Conclusions About Studies That Predicted Medication Adherence*

Machine learning also has the potential to substantially improve medication adherence. However, the development of this technology must be well guided to ensure optimal outcomes. The information presented in this review indicates that some predictors remain significant across multiple studies. The creation of more generalizable models that can be quickly adapted to new data sets may make prediction of medication adherence a less time-consuming endeavor in the future. Higher quality measures of adherence status should also be adopted, when possible, to ensure that predictions are based on accurate data. Currently, machine learning has the ability to predict medication adherence with a good level of accuracy. These predictions should be paired with targeted interventions to help prevent medication adherence issues before they occur.

However, careful evaluation of models is still paramount to avoid wasting resources on systems that overpredict medication nonadherence. More work also needs to be done to identify predictors of medication adherence in free-text documents. Currently, a lot of medical data is in a free-text format, and this is especially the case for less advanced systems with less structured documentation.

### *Conclusions About Studies That Monitored Medication Adherence*

Moreover, systems that monitor medication adherence can accurately classify inhaler use actions, even in the presence of background noise. This technology can be used to track inhaler adherence but can also be taken a step further, allowing for directed interventions aimed at improving inhaler use technique. Adherence monitoring systems are also currently capable of accurately determining the medication status of patients with Parkinson disease using movement data. This information could be used beyond mere adherence by providing clinicians with information that could be used to guide dosage adjustments. This is particularly helpful in a population that is likely to have difficulty communicating their struggles to providers. Systems are also being developed to track medication administration using only smartwatch movement sensors. However, these systems are still in the early development phase and are only being asked to differentiate between a small handful of different activities. These systems need to maintain a good level of classification accuracy in real-world environments before they can offer any clinical utility. However, if these systems are able to achieve this feat they will be highly attractive since they allow for unobtrusive monitoring with common devices that many patients already wear.

### *Conclusions About Studies That Monitored and Intervened to Improve Adherence*

Context-aware reminder systems have shown that they can help patients to achieve a high level of adherence but do so in an intrusive fashion. Studies need to be conducted to evaluate the acceptability and desirability of systems like this. These systems should also be compared against traditional reminder systems to make sure they are actually improving adherence. Conversational AI systems aimed at improving medication adherence are already starting to be deployed, and a few have significantly improved adherence over traditional reminder systems. One advantage of these systems is that people can interact with them using the spoken word, so they may be more usable for people who have difficulty interacting with systems requiring the ability to use a computer or smartphone.

## Limitations

The analysis of this topic was limited to five important databases, and some relevant articles from other sources may have been missed. Different grouping strategies might have also added additional insights but were not attempted since they are outside the scope of this paper.

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## Conflicts of Interest

None declared.

Multimedia Appendix 1  
Supplementary material.

[[PDF File \(Adobe PDF File\), 276 KB - xmed\\_v2i4e26993\\_app1.pdf](#)]

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## Abbreviations

**AI:** artificial intelligence

**LAIR:** Laboratory of Applied Informatics Research

**MeSH:** Medical Subject Headings

**PRISMA-ScR:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews

**SVM:** support vector machine

**99DOTS:** Directly Observed Treatment Short Course



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Original Paper

# A Local Community-Based Social Network for Mental Health and Well-being (Quokka): Exploratory Feasibility Study

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## Abstract

**Background:** Developing healthy habits and maintaining prolonged behavior changes are often difficult tasks. Mental health is one of the largest health concerns globally, including for college students.

**Objective:** Our aim was to conduct an exploratory feasibility study of local community-based interventions by developing Quokka, a web platform promoting well-being activity on university campuses. We evaluated the intervention's potential for promotion of local, social, and unfamiliar activities pertaining to healthy habits.

**Methods:** To evaluate this framework's potential for increased participation in healthy habits, we conducted a 6-to-8-week feasibility study via a "challenge" across 4 university campuses with a total of 277 participants. We chose a different well-being theme each week, and we conducted weekly surveys to (1) gauge factors that motivated users to complete or not complete the weekly challenge, (2) identify participation trends, and (3) evaluate the feasibility of the intervention to promote local, social, and novel well-being activities. We tested the hypotheses that Quokka participants would self-report participation in more local activities than remote activities for all challenges (Hypothesis H1), more social activities than individual activities (Hypothesis H2), and new rather than familiar activities (Hypothesis H3).

**Results:** After Bonferroni correction using a Clopper-Pearson binomial proportion confidence interval for one test, we found that there was a strong preference for local activities for all challenge themes. Similarly, users significantly preferred group activities over individual activities ( $P < .001$  for most challenge themes). For most challenge themes, there were not enough data to significantly distinguish a preference toward familiar or new activities ( $P < .001$  for a subset of challenge themes in some schools).

**Conclusions:** We find that local community-based well-being interventions such as Quokka can facilitate positive behaviors. We discuss these findings and their implications for the research and design of location-based digital communities for well-being promotion.

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## KEYWORDS

local social network; community health; wellbeing; digital health; consumer health

## Introduction

It is not an exaggeration to say that mental health is one of the most significant issues of our time, and wellness has never been more topical than it is today. Mental health conditions account for one-third of adult health conditions, and suicide is the leading cause of death among people 15-29 years of age [1]. With the continuing shortage of mental health professionals [2-7], it is becoming increasingly clear that the current model of treating mental illness does not sufficiently address the scale and severity of the mental health crisis [1]. It is worth considering how we can augment the traditional medical model of treating mental health conditions with solutions that integrate preventive methods and exploit the ubiquity of technology in positive ways.

Current digital solutions to address behavioral and mental health concerns are often initiated by the individual, such as meditation apps [8,9], fitness apps [10,11], apps providing therapies for developmental delays [12-15], and wearable therapeutics [16-24]). Digital interventions initiated by the individual often require at-home use. When digital solutions are not involved, treatments for behavioral and mental health require repeated in-person visits with a health professional. Although these approaches are helpful, they either do not address the individual's true needs or are inaccessible to the broader population due to cost and time constraints [25].

Although individuals know that physical activity, nutrition, and sleep, for example, are fundamental components of a healthy lifestyle, this knowledge does not necessarily mean that healthy habits are easy to maintain. Behavior change, particularly as it pertains to health, requires understanding of *why* a change must be made and *how* to actually make the change [26]. Education, knowledge, and awareness are only a few necessary components to encourage behavior change. It is essential to understand how to design and implement behavioral programs and interventions that go beyond these factors to empower individuals to adopt and maintain healthier lifestyles.

Theories of behavior change, termed behavior change theories (BCTs), suggest that intervention effectiveness may be increased through the incorporation of social and cultural factors that also influence behavior [27-29]. These theories targeting lifestyle focus on learning and decision-making to drive action and reflection; however, understanding other factors, such as individual beliefs, motivations, and the environment, are

important for continued maintenance of health as well [30,31]. Examples of BCTs that examine these additional factors as applied to health outcomes include the health belief model (ie, behavior change is posited on barriers, benefits, self-efficacy, and threat) and the theory of planned behavior (ie, actions are driven by behavioral intent, subjective norms, and perceived behavioral control) [31-33]. Several of these theories have been studied in the university setting, which is especially pertinent given the Quokka setting. Quokka builds upon prior works by incorporating social, cultural, and local environmental elements into its framework and examining the effects of these community factors on individual action and reflection. Furthermore, Quokka uses several digital intervention techniques (including option-based, attribute-based, and goal-based techniques) that build upon these theories to drive further habit formation and maintenance [30].

There is a strong, well-researched connection among social influence, social media, and health and wellness [34,35]. Health habits are influenced by peers and within social networks. College student health and wellness occupies a particularly interesting and pressing niche, partly due to the prevalence of mental illness in the college population [36-38] and partly due to the unique confluence of communities, resources, and types of development represented during this formational stage of life [39]. College students are uniquely bound to their local and social communities, and their health is largely influenced by both these pivotal factors during their time as students and by the experience of caring for their health independently (eg, determining their own course of physical activity and diet without the aid of others). Committing to change habits as part of a group, such as one's college peers, can increase the odds of success due to the communal experience and accountability that comes with social pressures. Because of the consistent and ubiquitous prevalence of mental health and other wellness issues across school campuses [40,41], we were interested in exploring the potential of social technologies for behavior change specifically within networks of college students.

Social technologies, both existing platforms and domain-specific technologies, have been used to advance behavior change related to health. A Social-Local-Mobile (So-Lo-Mo) app has been developed to help addicts quit smoking [42]. Twitter has been considered and studied as a platform to disseminate public health information and has successfully changed the attitudes of tweet recipients [43], which is the first step toward successful behavior

change. Social influence has been documented to drive engagement in web-based health applications [44]. For example, community programs hosted on digital platforms have facilitated behavior change to increase walking [45] and self-manage diabetes [46].

The idea of digital interventions that feature an online community to aid behavioral change outcomes is not novel. Examples include the AFFIRM Online program [47], Facebook groups for connecting populations [48], and targeted messaging on social media platforms [49]. There are also existing digital interventions that use a local community and local resources to facilitate behavior change. Examples include the Atmiyata intervention approach [50], SocialNet [51], and the +Connect intervention [52]. These prior social technologies do not incorporate a local community aspect into the online social community.

In contrast to these prior works, we test the feasibility of a mental health digital intervention that leverages both local health opportunities and community-based programming to drive behavior change in a single social network. Toward this end, we developed a web platform, Quokka, that promotes an interventional program, the Quokka Challenge. The challenge capitalizes on the established success of community-based social programs for behavior change via a digital intervention. We expand upon the successes of prior literature by exploring the incorporation of the physically local community into a social digital intervention. We note that the primary goal of this study is not to provide a controlled trial or to claim that Quokka has been fully evaluated as an intervention. Instead, our goal is to test the feasibility of such a system by verifying that study participants engage in the behaviors suggested by Quokka for the duration of the program.

The Quokka system was used during the Quokka Challenge, which took place during the fall academic quarter/semester of 2017 and served as a feasibility study for digital well-being programs focused on local, social, and novel experiences. We provide a description of the challenge themes provided each week and describe a longitudinal 6-to-8-week remote pilot feasibility study we ran on 4 independent college campuses. We analyze user retention and participation and code responses to free-form surveys administered to participants at the end of each challenge week. We end with a discussion of the effects of social connectivity, importance of community, limitations of the study, and future directions.

## The Quokka Platform and Challenge

### Overview

We designed the Quokka Challenge, hosted on the Quokka web platform that we designed and developed, as a new program in the fall academic quarter/semester of 2017 to promote healthier habits in the university setting. The design and implementation

of the program were influenced by prior research in the field, although it was uniquely created for the university setting. This manuscript highlights Quokka's first pilot programs, evaluating its framework's potential for increasing participation in healthy habits.

Three social elements are fundamental to Quokka's program: culture, competition, and community. The goal of the program is to change health behaviors by making habit-building easier, more fun, and more social. To do this, the program uses (1) network tools (eg, existing cultures, clubs/social groups) to leverage social influence, (2) gamification (eg, competition, trophies) for intrinsic motivation, and (3) events and external rewards (from local businesses, resources, and student clubs) to further motivate participation and create a sense of confluence for users within communities that are practicing the same habits at once.

The Quokka Challenge follows the same series of user flows and prompts, regardless of where the program is run. Each week, users receive a "Challenge of the Week" email in their inbox. Included is the challenge itself, scientific research supporting the habit, and a list of suggested resources, both remote and local.

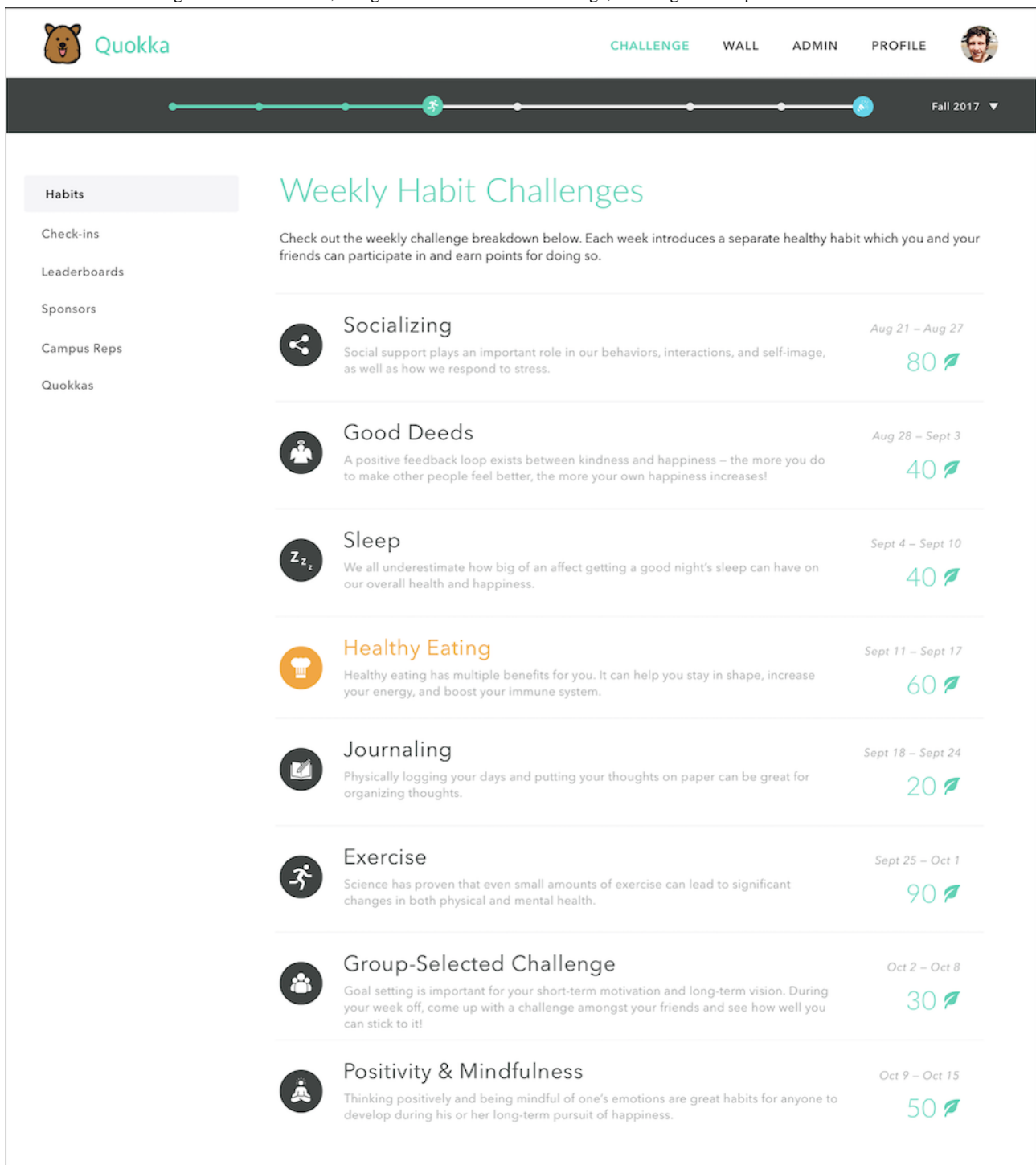
### Quokka System

The Quokka system consists of a website that provides information about challenge themes through a new community-based social network. On the Quokka website, users see a progress bar at the top of the page visualizing their challenge progress (Figure 1). Weekly challenge habits for the entire challenge are shown to users along with the dates of the challenge, allowing users to plan ahead. Users can read an overview of the challenge, including further research details, the exact challenge, the prizes awarded for completing the challenge, suggestions for particular activities to complete the challenge, and instructions for providing feedback (Figure 2).

An additional aspect to the Quokka system is the option for participation by sharing photos on a community Facebook page hosted by a club at their university (Figure 3). This encourages social participation and is relevant as another program component facilitating the local and social drivers of the program.

Toward the end of the week, users are prompted, via an email notification, to submit a check-in by answering a set of provided questions. Users who answer the set of check-in questions are then entered into a pool of participants eligible to win a prize. Prize winners each week are randomly selected from this pool. Optionally, users can attend (in-person) events that are related to the week's theme. These events are often hosted in partnership with university health resources, student clubs, and local sponsors.

**Figure 1.** Example user view of weekly challenges. Users see a progress bar at the top of the page visualizing challenge progress. Weekly challenge habits for the entire challenge are shown to users, along with the dates of the challenge, allowing users to plan ahead.



**Figure 2.** Example user view of a particular challenge, in this case "Healthy Eating." An overview of the challenge (including further research details), the exact challenge, the prizes awarded for completing the challenge, suggestions for particular activities to complete the challenge, and instructions for providing study feedback are displayed.

**Quokka** CHALLENGE WALL ADMIN PROFILE

**Healthy Eating**  
WEEK 4 - SEPT 11 - SEPT 17

SLEEP JOURNALING

### Habit Overview

Over the past few weeks, you've been learning a lot about what you can do to improve your well-being. This week is an opportunity for you to do some research on your own! The focus of this week is on how foods can affect how we feel, both physically and emotionally. Besides helping you stay in shape, healthy foods can help you increase your energy, boost your immune system, minimize inflammation, promote muscle building, and more. [Learn more about the science behind healthy eating.](#)

**Challenge** 60

Take the first day of this week to check out the Harvard School of Public Health's [Healthy Eating Plate Guide](#) on how to make better food decisions. Pick what will be an improvement for your health and then stick to it for every day this week.

### Prizes

Participants of this week's challenge will earn **60 Quokka points** and be eligible for the following prizes:

- Reversible Yoga Mat  
Lululemon
- \$20 Gift Card  
Tender Greens
- Wind Trainer  
The North Face

### Suggestions

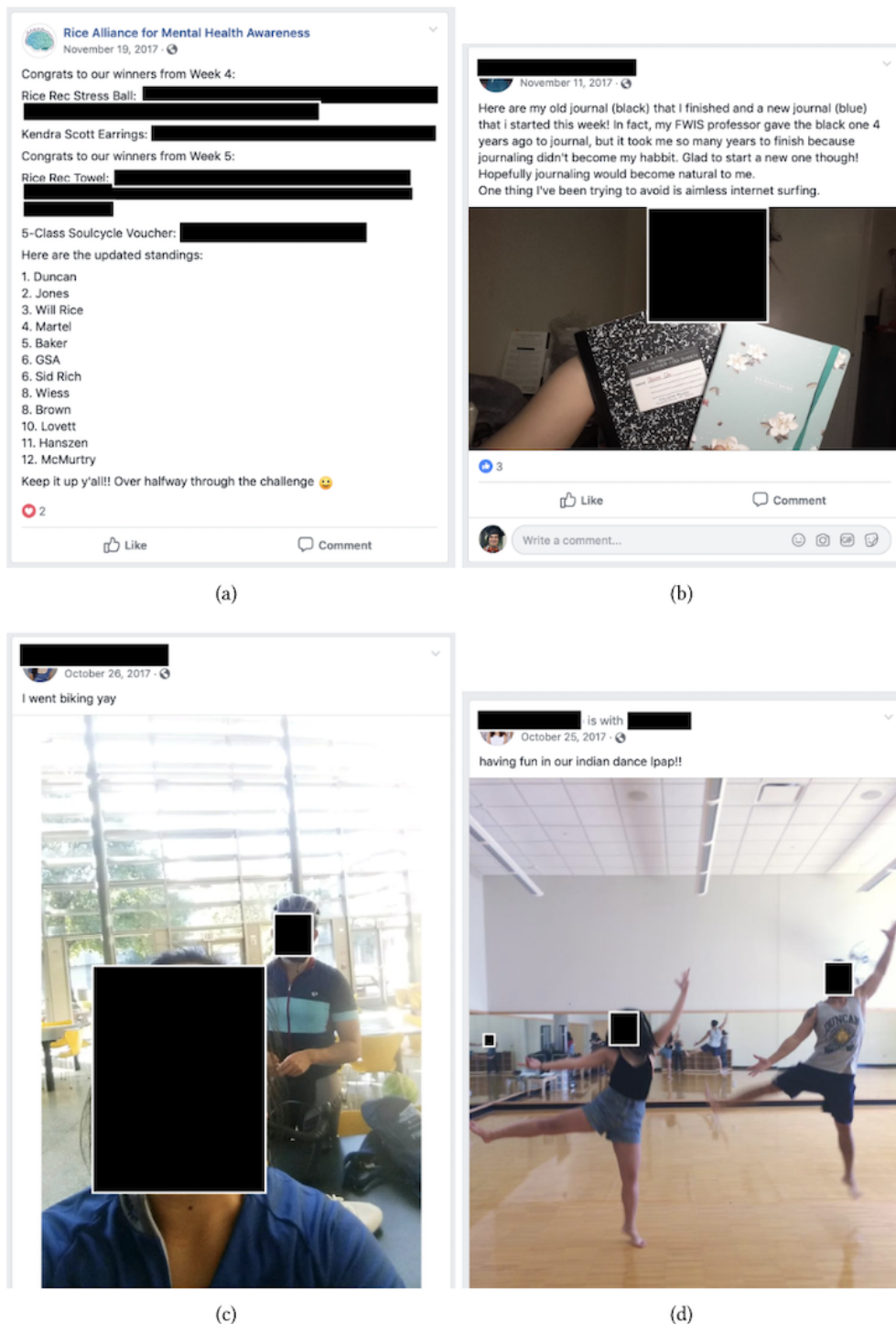
Need a few ideas or suggestions to help get you started?

- Consider eating bigger breakfasts, more protein, greater amounts of fiber, or meals with all food groups.
- Try drinking the full recommended amount of water per day.
- Look ahead to the [online menu](#) to pick what you'll eat before you hit the dining hall – you'll be more likely to stick to your decision if you know what you're eating beforehand.
- Learn more about the [portion sizes](#) of Stanford's dishware to become more aware of how much you're eating.

### Check-In

Don't forget to submit your Check-in this week by Sunday, September 17th! Check-ins help you earn Quokka points, provide us with feedback, and make you eligible for this week's prizes. [Take me to my Week 4 Check-in.](#)

**Figure 3.** Each university program created Facebook event pages for participants to share their experiences with peers. (a) The coordinator from the university posts regular updates to the Facebook page, including university-specific prizes and rankings. (b) Individual users share updates on the Facebook event page, often garnering reactions from other challenge participants. (c) and (d) Friends can participate in activities together and share on the event page.



### Challenge Themes

It is critical to provide health-related educational information to motivate behavior change. We hypothesized that the more that people understand the reasons why a behavior is generally considered healthy, the more motivated they will be to engage in that healthy behavior. Each recommendation made to participants from the challenges was supported by documented research and resources to connect students to more information

about health that provides knowledge and motivation regarding the challenge and overall wellness. This scientific research (the “why”) supplemented the challenges (the “what”) as well as the set of resources and tools (the “how”) that could be used to help users successfully complete each challenge.

Each local program selected their weekly “challenge themes” from a set of eight options, with different language provided to users for each theme (Table 1).

**Table 1.** Weekly challenge themes for the eight challenges of the Quokka program and accompanying messages.

Theme	Message
Socialize	“Take 3 purposeful study breaks this week to talk to friends. Schedule a call with someone you haven’t talked to in a while, put away your phone during meals with others, or invite friends to join the Challenge and keep you on track.”
Exercise	“1. Try 3 different types of exercise this week. 2. Move More! Sit less, walk or bike instead of driving, and take stairs over elevators.”
Good Deeds	“Pick a good deed to do or help a person every day this week. Doing something nice, like buying someone coffee or bringing soup to a sick friend, might encourage them to spread the cheer, too!”
Healthy Eating	“1. Add More (of the ‘good’ things) – more water, more fruits and vegetables, and more whole grains to your meals. 2. Be more mindful – of how much you’re eating and when you’re full, of when you’re mindlessly snacking, or of how you feel after you eat different foods.”
Journaling	“Pick a time to journal every day this week – right when you wake up, as an afternoon study break, or before you head to bed. Be consistent, even if it’s just for a few minutes every day.”
Sleep	“Get a full night’s sleep every day this week. Try to keep a consistent schedule and log how many hours you actually sleep and how you felt as a result.”
Positivity/Mindfulness	“1. Practice positive thinking and be kind to yourself and to your peers. To wrap up this week, make a purposeful effort to give out positive comments and compliments to your friends-verbally or written. 2. Acknowledge negative thoughts, but don’t dwell. See how you can reframe your perspective whenever you experience a negative thought this week.”
Campus-Selected Theme	Each campus had the option to select one of the following messages: <ul style="list-style-type: none"> <li>• Giving Thanks: “1. Write thank-you notes. Think of people around you who you don’t stop to thank enough. Perhaps it’s close friends who look out for you/have your back, or perhaps it’s people who play a smaller role in your life – dining hall staff, administrators, people who open doors for you... 2. Keep a gratitude journal. Write down a few things you’re thankful for every day. If it’s a loved one, choose to share and let them know.”</li> <li>• Self-Care: “1. Every day, take at least 30 minutes to do an activity that you love! Pick something that makes you feel good, and that you don’t usually make time for! It can be watching an episode of your favorite TV show, reading a book while drinking tea, drawing, or painting a picture. 2. Work on an important relationship at least once this week. Let someone in your life know what you need from/in your relationship with them. Let someone know why you are thankful for them. 3. At least once this week, talk to a friend about how you are coping with work and life demands.”</li> </ul>

## Methods

### Recruitment

We reached out to over 15 US colleges and universities and met with several administrative health services and student health club staff members to discuss the possibility of running a program on their campuses. Because this was an early pilot, we chose a small subset of schools (Duke University, University of North Carolina at Chapel Hill [UNC], Rice University, and Tufts University) to coordinate programs based on their overall interest and availability to dedicate time and effort toward participating. Typically, one student health club or group per campus would become the designated “host” while working with other school resources and groups to customize their programs.

Coordinators at each university were responsible for the enrollment of participants in the 2-week period leading up to the Quokka Challenge start date. Coordinators used school email listservs, Facebook event pages, and on-campus recruiting efforts to garner interest.

### Study Design

Of the eight potential challenge themes, university coordinators chose the subject and order of each week for their respective challenges. While the Duke University and UNC coordinators organized 6-week Quokka Challenge programs, the Rice University and Tufts University coordinators opted to include

2 additional weeks, for a total of 8 weeks. The challenge theme order for each university was as follows:

- Duke University (6 weeks): Socializing, Healthy Eating, Exercise, Good Deeds, Sleep, Self-Care
- UNC (6 weeks): Healthy Eating, Exercise, Socializing, Self-Care, Sleep, Positivity/Mindfulness
- Rice University (8 weeks): Healthy Eating, Exercise, Good Deeds, Journaling, Sleep, Give Thanks, Socializing, Positivity/Mindfulness
- Tufts University (8 weeks): Socializing, Exercise, Good Deeds, Healthy Eating, Journaling, Self-Care, Sleep, Positivity/Mindfulness

The program focused on one habit per week, although participants were encouraged to adhere to whichever habits they found to be the most effective throughout the duration of the program. A final survey was sent to participants at the end of each program to collect input and feedback from them, and respondents were asked to cite which habits they had continued and were planning to continue from then on, although this was not further assessed after the program completion.

Every week, we sent a check-in email to all study participants toward the end of the weekly challenge. These check-ins consistently asked the same set of questions: (1) “What’d you do to complete this week’s challenge?” (2) “Tell us about your experience. Did you enjoy it or notice anything different about



yourself?” (3) “Any additional comments (about the week or the overall challenge)?”

For this study, we tested the following hypotheses:

- H1: Quokka participants will self-report participation in more local activities than remote activities for all challenges.
- H2: Quokka participants will prefer social activities over individual activities for all challenges.
- H3: Quokka participants will prefer new activities over familiar activities.

We note that we present a feasibility study of social community-based wellness interventions, and the above hypotheses are therefore exploratory in nature.

### Facebook Event Page

Each university program had its own Facebook event page where participants could post shared experiences with others. We used Facebook in lieu of reimplementing a social network within the Quokka interface to maximize the reach of coordinator messages. [Figure 3](#) shows example posts from one of the Facebook event pages.

### Role of Coordinators

Volunteer coordinators at each campus had responsibilities that included (1) enrolling participants in the program, (2) meeting with their self-organized committees regularly, (3) customizing and sending emails through our website, (4) organizing and hosting related challenge events, (5) establishing relationships with local businesses and resources, and (6) securing and distributing prizes to weekly challenge winners. Although the same program content was shared with all the coordinators, they were responsible for the tailoring of their own prizes, events, and outreach.

### Question Coding

To understand the impact of the challenge theme on behavior and to tease apart differences in effects between schools, we qualitatively coded all weekly check-in responses from all study participants into the following categories: (1) whether the challenge for that week resulted in activities that were local or remote, (2) whether the challenge resulted in group or individual activities, (3) whether the challenge created a familiar or new habit, and (4) whether the challenge resulted in a positive, negative, or neutral experience. Coding of questions was performed by 3 independent raters recruited on Upwork, a popular web-based freelancing platform that connects workers to job providers. To reach the final category, a majority-rules consensus was taken for the categorical labels provided by

raters. In cases where all 3 raters disagreed, the authors provided the final rating. Protected user data were anonymized when provided to Upwork workers.

### Statistical Tests

To perform statistical testing for H1-H3, we conducted a binomial proportion test in which we used the proportion of local (H1), social (H2), and new (H3) self-reported activities per week. The null hypothesis was that the proportion would be 0.5 (equal numbers of local and remote, social and individual, as well as new and familiar activities). The goal was to determine if the increased rates of local, social, and new self-reported activities were statistically significant. We calculated a Clopper-Pearson binomial proportion confidence interval for one test; this method leverages the cumulative probabilities of the binomial distribution.

## Results

### User Statistics

Across the 4 schools, a total of 1038 people signed up during the 2-week enrollment period leading up to the challenge. Of that total, 277 users completed a week 1 check-in survey; this constitutes the total number of participants who were evaluated during this study. While the Duke University and UNC coordinators organized 6-week Quokka Challenge programs, Rice University and Tufts University opted to include 2 additional weeks for a total of 8 weeks. Due to the differences in duration, we have listed the total number of users who submitted a check-in during their respective “final” weeks, which occurred at either the 6- or 8-week mark ([Table 2](#)).

According to the US Census [53], typical demographics of college students in the United States follow an approximate equal split of women and men (with women holding a slight majority). The vast majority of these students are between 18 and 24 years of age (87.5% in 2017, when this study took place). By ethnicity, the US undergraduate college student population in 2017 was approximately 53% non-Hispanic White, 21% Hispanic, 15% Black, 8% Asian, and 3% non-Hispanic “other.”

For the 4 universities included in this study, the typical demographics of their undergraduate college students followed a similar pattern to the national statistics: approximately equal split between women and men, age primarily between 18 and 24 years, and predominantly identifying as non-Hispanic White, with varying distributions of students identifying as Hispanic, Black, Asian, or “other.”

**Table 2.** User retention across the 4 universities participating in the study, according to the respective 6- or 8-week durations of the program.

School	Program duration (weeks)	Users who initially signed up, n	Users who completed week 1 check-in, n	Users who completed final check-in, n	Retention (%)
Duke University	6	144	36	17	47.2
Rice University	8	491	125	28	22.4
Tufts University	8	153	61	13	21.3
University of North Carolina at Chapel Hill	6	250	55	11	20

## Evaluation Outcomes

All 3 hypotheses were confirmed: significantly more local than remote (H1, [Table 3](#)), group than individual (H2, [Table 4](#)), and familiar than new (H3, [Table 5](#)) activities were reported by participants across all challenges. P values from a Clopper-Pearson binomial proportion confidence interval for one test are included in the tables. After Bonferroni correction, we rejected the null hypothesis that similar proportions of users would participate in local and remote activities during the challenges ([Table 3](#)). Instead, there was a strong preference for local activities for all challenge themes. Similarly, users significantly preferred group activities over individual activities ([Table 4](#)). For most challenge themes, there were not enough data to significantly distinguish preferences toward familiar or new activities ([Table 5](#)).

The challenge theme had a noticeable effect on the count of users who reported whether the week's challenge included local versus remote activities ([Table 3](#)), individual versus group

activities ([Table 4](#)), and familiar versus new activities ([Table 5](#)). This indicates that the challenge theme had a strong effect on the engagement of the participants. Interestingly, the participants' school did not have a noticeable effect, validating the influence of the challenge theme on the type of behavior regardless of the environment of the participant.

According to the qualitative analysis performed on each school's complete set of responses, 95.1% of survey responses from Rice University over the course of the challenge exhibited positive sentiment, 92.2% of Duke University survey responses exhibited a positive sentiment, 96.4% of Tufts University survey responses exhibited a positive sentiment, and 92.1% of UNC survey responses exhibited a positive sentiment. Of all 6 possible pairs of schools, a paired Welch *t* test between every survey response between all participants in both schools in the pair showed that there was no statistically significant difference between any pair of schools in the sentiment of participating students (all  $P > .04$ ) after accounting for multiple hypothesis testing using Bonferroni correction.

**Table 3.** Counts of users who reported local and remote activities across the challenges for all schools. All P values are significant after Bonferroni correction.

School and values	Challenges								
	Socialize	Exercise	Good Deeds	Healthy Eating	Journaling	Give Thanks	Sleep	Positivity and Mindfulness	Self-Care
<b>Duke University</b>									
Local, n	81	36	23	66	N/A <sup>a</sup>	N/A	38	N/A	41
Remote, n	16	1	1	0	N/A	N/A	0	N/A	1
P value	<.001	<.001	<.001	<.001	N/A	N/A	<.001	N/A	<.001
<b>Rice University</b>									
Local, n	72	158	88	269	94	71	86	58	N/A
Remote, n	12	0	0	5	0	1	1	0	N/A
P value	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001
<b>Tufts University</b>									
Local, n	143	91	48	62	36	N/A	30	28	27
Remote, n	21	0	1	0	8	N/A	1	0	2
P value	<.001	<.001	<.001	<.001	<.001	N/A	<.001	<.001	<.001
<b>University of North Carolina at Chapel Hill</b>									
Local, n	40	46	N/A	122	N/A	N/A	26	21	31
Remote, n	7	2	N/A	0	N/A	N/A	1	0	1
P value	<.001	<.001	N/A	<.001	N/A	N/A	<.001	<.001	<.001

<sup>a</sup>N/A: not applicable.

**Table 4.** Counts of users who reported individual and group activities across the challenges for all schools.

School and values	Challenges								
	Socialize	Exercise	Good Deeds	Healthy Eating	Journaling	Give Thanks	Sleep	Positivity and Mindfulness	Self-Care
<b>Duke University</b>									
Individual, n	29	30	18	65	N/A <sup>a</sup>	N/A	41	N/A	40
Group, n	71	5	7	2	N/A	N/A	1	N/A	8
P value	<.001 <sup>b</sup>	<.001 <sup>b</sup>	.03	<.001 <sup>b</sup>	N/A	N/A	<.001 <sup>b</sup>	N/A	<.001 <sup>b</sup>
<b>Rice University</b>									
Individual, n	105	163	86	302	99	76	108	68	N/A
Group, n	43	9	25	0	0	13	0	8	N/A
P value	<.001 <sup>b</sup>	<.001 <sup>b</sup>	<.001 <sup>b</sup>	<.001 <sup>b</sup>	<.001 <sup>b</sup>	<.001 <sup>b</sup>	<.001 <sup>b</sup>	<.001 <sup>b</sup>	N/A
<b>Tufts University</b>									
Individual, n	85	98	22	65	48	N/A	34	30	29
Group, n	98	10	41	3	3	N/A	0	1	11
P value	.34	<.001 <sup>b</sup>	.02	<.001 <sup>b</sup>	<.001 <sup>b</sup>	N/A	<.001 <sup>b</sup>	<.001 <sup>b</sup>	.004
<b>University of North Carolina at Chapel Hill</b>									
Individual, n	28	50	N/A	136	N/A	N/A	31	21	34
Group, n	20	1	N/A	0	N/A	N/A	0	3	3
P value	.25	<.001 <sup>b</sup>	N/A	<.001 <sup>b</sup>	N/A	N/A	<.001 <sup>b</sup>	<.001 <sup>b</sup>	<.001 <sup>b</sup>

<sup>a</sup>N/A: not applicable.<sup>b</sup>Significant after Bonferroni correction.

**Table 5.** Counts of users who reported familiar and new activities across the challenges for all schools.

School and values	Challenges								
	Socialize	Exercise	Good Deeds	Healthy Eating	Journaling	Give Thanks	Sleep	Positivity and Mindfulness	Self-Care
<b>Duke University</b>									
Familiar, n	91	30	17	48	N/A <sup>a</sup>	N/A	39	N/A	40
New, n	3	6	6	24	N/A	N/A	2	N/A	2
P value	<.001 <sup>b</sup>	<.001 <sup>b</sup>	.02	.005	N/A	N/A	<.001 <sup>b</sup>	N/A	<.001 <sup>b</sup>
<b>Rice University</b>									
Familiar, n	43	34	27	4	3	32	2	18	N/A
New, n	13	31	13	3	4	2	0	2	N/A
P value	<.001 <sup>b</sup>	.71	.03	.71	.71	<.001 <sup>b</sup>	.16	<.001 <sup>b</sup>	N/A
<b>Tufts University</b>									
Familiar, n	68	17	19	3	14	N/A	1	0	10
New, n	6	12	1	0	0	N/A	0	0	1
P value	<.001 <sup>b</sup>	.35	<.001 <sup>b</sup>	.08	<.001 <sup>b</sup>	N/A	N/A	N/A	.007
<b>University of North Carolina at Chapel Hill</b>									
Familiar, n	29	20	N/A	68	N/A	N/A	15	12	17
New, n	13	17	N/A	39	N/A	N/A	8	6	10
P value	.01	.62	N/A	.005	N/A	N/A	.14	.16	.18

<sup>a</sup>N/A: not applicable.

<sup>b</sup>Significant after Bonferroni correction.

### Participation Due to Localized Social Influence

Although many of the challenges were focused on individual execution and adherence (ie, did not require interactions with others in order to “complete” the challenge), many users cited the importance of the simultaneous participation of the broader community. Acknowledging that others at the university were fulfilling the same challenges at the same time, users noted that this phenomenon created “positive peer pressure,” encouraging them to complete each week. Additionally, some users noted that the opportunity to participate with others meant they could also share their own lessons more broadly. For example, a user from Rice during the Healthy Eating week stated, “I take a nutrition/health course that teaches me a lot about physical exercise and the importance of dieting so it was great to be able to find other people doing the Quokka Challenge and help them make better food choices.”

### Shared Experiences

The communal experience among users within the same community offered reminders and nudges, encouraging continued participation. Examples of contributions to these shared experiences were unified event offerings, photo sharing on the Facebook pages, and built-in university and friend networks. For example, one user from Rice University during the Healthy Eating week commented:

*Seeing the Color My Plate [activity on Facebook] inspired me to eat healthier because other people*

*were doing it! I am better at sticking to good habits if I know people around me care as well.*

The shared experience of the Quokka Challenge also prompted users to cite feeling more connected as a result, with one user from Tufts University during the Socializing week stating:

*I had a wonderful experience completing this week’s challenge! I have felt more positive and connected as a result of prioritizing time for relationships.*

### Local Community-Supported Resources

Every challenge included a set of community-supported resources for participants to learn more about. These recommendations were tailored for the local community and featured information and tips on using resources such as university programs, student clubs, and nearby businesses. Some programs also included external resources (eg, podcasts, apps) to supplement them. For example, participants could learn more about group fitness classes, fitness assessments, or personal training programs offered at the campus recreation center during the Exercise week. In turn, some users stated plans to continue to use new resources they discovered through the challenge, as exemplified by one user at Rice University who stated, “I discovered more ways to enjoy the good weather and all of the resources offered through the Rec center (spin classes, borrowing equipment, etc.) and know that I’ll try to incorporate them more into my weekly exercise routines!”

## User Reflection

Throughout the challenge, users commented on the effects and impact that participating in the Quokka Challenge had on them. The program encouraged users to practice weekly wellness habits, focusing on simple and manageable ways to engage in behavior change. This helped prepare them for a longer-term commitment to being mindful and extending these behaviors beyond the challenge duration. One Rice user during the Exercise week said:

*I was really forced to re-examine my health and exercise routine that I had settled into after 2 months into college. This challenge has inspired me to make small changes to see big results in my health and fitness.*

Beyond learning more research and facts about the individual habits highlighted in each week's challenge, users noted other lessons and outlooks they learned in the process. Users at Rice University, for example, reported that the Quokka Challenge helped them reflect more on the benefits of engaging in well-being-promoting activities. Some of these personal learnings also led to further goal setting and commitments to future self-care, as demonstrated by a Rice user stating:

*It made me reflect on my life choices and be more mindful of many of the things I do. It made me change my behavior for the better and be more considerate, both with myself and others.*

## Discussion

### Principal Results

Here, we discuss Quokka, a local community-based social network designed to encourage and promote health awareness and behavior change by hosting well-being "challenges" across different college campuses. Participants were encouraged to engage in different behaviors, such as drinking more water, exercising, and journaling, to improve overall wellness. Students were also provided implicit social incentives to participate via the social integration of the challenges, as "challenge coordinators" encouraged participants to engage with one another through email and social media.

By encouraging networks of friends to promote healthy behaviors on campus through Quokka challenges, we aimed to create a positive impact that permeated throughout the entire social network within these communities. We customized the Quokka program to each campus and personalized the program's components to increase the familiarity, comfort, and connections for participants. We tailored health communications with the goal of helping people feel more motivated by their localized resources and thus more likely to make decisions that will help them achieve their health goals. We further encouraged participation in these resources with incentives, such as prizes and praise. By focusing on short-term, attainable goals (eg, focusing on one healthy habit per week), we compartmentalized healthy habits for busy students to focus their efforts and see results on a small yet consistent scale.

After Bonferroni correction, we rejected the null hypothesis that similar proportions of users would participate in local and

remote activities during the challenges (Table 3). Instead, there was a strong preference for local activities for all challenge themes. Similarly, users significantly preferred group activities over individual activities (Table 4). For most challenge themes, there were not enough data to significantly distinguish preference toward familiar or new activities (Table 5).

The retention rate per school ranged from 20% to 47%, with a median retention of 21.5% (Table 2). Two of the schools had a 6-week (42-day) challenge, and two had an 8-week (56-day) challenge. These retention numbers are significantly greater than the average retention rates of 93 well-being apps evaluated in a systematic study, which had a median 15-day retention rate of 3.9% and 30-day retention rate of 3.3% [54]. This suggests that the combination of social community and tailored local experiences created by the Quokka experience created a unique environment that promoted high levels of engagement and retention. A future controlled study is needed to determine whether the tailored local experiences, the social community, or a synergistic combination of these aspects drove the high engagement rates.

### Importance of Community

The community of local businesses can also play a substantial role in contributing to the "health community." For example, affluent areas with gyms, health food restaurants, yoga studios, etc, are often stereotyped to be "healthier" [55]. Social marketing has been proven to be especially effective in promoting health and igniting healthy behavioral change [56-58], and Quokka capitalizes upon this by partnering with local businesses to offer prizes such as free yoga classes and coupons for healthier food vendors to engage in popular health marketing. This practice also encourages a sense of comfort and familiarity for users in their local environment by connecting them to their health community beyond campus.

While Quokka simultaneously hosts challenges on multiple college campuses, it customizes each program to be catered to each university's student body and local environment. This is achieved through partnerships with local mental health resources and services available on each particular campus and with local businesses or school-affiliated groups. Research suggests that the environment in which students participate in such challenges can greatly affect their performance and their continuation of these habits beyond the challenges if supported by community health directives and resources [59-62]. A strong community provides an excellent foundation for building health at a macro level [62,63]. The demand for community resources among college students is growing [64-66], and students are sometimes not even aware of these resources, forgoing possible improvements in health and wellness because of a lack of visibility. Quokka highlights these resources for students participating in challenges, which are particular to each campus and local health department per program.

Based on the analysis, across all 4 schools, Quokka's challenge themes were largely grounded in being local (vs remote), individual (vs in a group), and based on familiar habits (vs new habits). While users were participating in the Quokka Challenge individually, they were immersed in their local environment, used local resources, and were still surrounded by a broader

community of fellow challenge participants. They were also primarily building upon fundamental or familiar habits, while some users reported having “new habit” experiences.

### **Achieving Balance of Prescriptive and Suggestive Activities**

While many health and well-being–related behavior change apps follow a purely *suggestive* model that only recommends potential healthy activities, others follow a fully *prescriptive* model of requiring users to participate in specific activities at specific times. Quokka attempts to leverage the benefits of both paradigms by following a *balanced* model, removing the need for participants to identify their own initial steps to action and enabling them to instead follow a baseline set of activities to participate in the habit and challenge. We note that Quokka is prescriptive with respect to the type of health activity and not the specific activity to follow (eg, a challenge will recommend exercising and request that users attempt to exercise several times within a week, but it will not explicitly state what exercises users should perform or how or when they should exercise). When the barriers to entry for starting activities are lowered or removed (with suggested local activities or resources), participants feel increased motivation.

### **Localized Social Challenges Drive Personalization**

The community aspect of the Quokka paradigm enables personalization, which, in turn, drives behavior change. Personalization for this program was not based on the individual or on data collected from the individual; rather, personalization was achieved at the local, in-person environment, and community level. This level of personalization enables a higher degree of user privacy, a concern increasingly at the forefront of public attention in technological health care interventions [67].

### **Limitations: Quokka System**

Despite the many strengths of this study, it has several limitations. The program used “prebuilt communities” by using the existing college culture and environment and focused its participation recruitment on college-aged students, which are factors that could decrease the generalizability of our results. Because the Quokka Challenge was established around the college context, the time of the study was confounded by differing academic calendars (eg, differences in quarter vs semester calendars).

Quokka attempts to use users’ social networks by allowing them to opt into inclusive, school-specific Facebook groups particular to the Quokka Challenge. This method does not directly exploit friend connections already made on the Facebook platform, however, and thus may not necessarily maximize the primary social connections that users have established prior to participating in Quokka Challenges. Another key design obstacle in harnessing social networks for health and wellness purposes is that users often desire different degrees of privacy. This perhaps requires a more meticulous solution in which users are able to be more selective about which people from their overarching social networks are privy to information a user chooses to share about their own goals and progress [68]. Quokka currently allows users to preserve the privacy of their

successes and failures. However, this means that Quokka does not yet employ full accountability. Users can curate which successes to share with their network; thus, they can easily hide their failures.

An overwhelming majority of users (>90% for all schools) found the experience to be positive, indicating that the Quokka Challenge is enjoyable for most users. However, we did not gather baseline data on the participants’ sentiments prior to the challenge. Further studies should evaluate the sentiment of participants using a Likert scale in a controlled fashion.

Further research is needed to determine the effect of increased social interactions and accountability on building healthy habits. Potential future enhancements to the program include shifting to a mobile-based application and conducting more holistic, technical evaluations of health as opposed to strictly using self-reported evaluations (eg, using firmware trackers or implementing tracking features within a mobile app). The research could also be extended to evaluate behaviors prior to, during, and after the Quokka Challenge to assess the extent of behavioral change and habit-forming as a result.

### **Limitations: Study Design**

Our knowledge about Quokka’s ability to increase social, local, or new activities is limited. Because no control condition was provided, we only know that when participating in the Quokka Challenge, users are more likely to engage in social, local, or new activities than individual, remote, or familiar activities, by a large and statistically significant margin.

In addition, our study analysis consisted of a quantitative analysis on coded qualitative data. Although the purpose of this analysis was to fully understand the extent of the participants’ well-being activities without collapsing their responses into static categories, a more ideal data collection pipeline would include a combination of multiple-choice selection options in addition to the free response component.

### **Comparison With Prior Work**

To identify prior studies discussed here and in the Introduction, we searched for “digital mental health intervention local community,” “digital mental health intervention online community,” “mental health social network,” and “digital mental health intervention local social network” on Google Scholar as well as the *Journal of Medical Internet Research* search page. We selected articles published after January 2015. We found several digital interventions that feature an online community to aid in the behavioral change outcome. Examples include the AFFIRM Online program [47], Facebook groups for connecting populations [48], and targeted messaging on social media platforms [49]. We also found digital interventions that use a local community and local resources to facilitate behavior changes. Examples include the Atmiyata intervention approach [50], SocialNet [51], and the +Connect intervention [52].

In contrast to these prior works, we explored a mental health digital intervention that leverages local health opportunities and community-based programming to drive behavior change. To our knowledge, no digital mental health intervention has incorporated elements of a hyperlocal community and a social

network to ground the intervention via recurring and targeted challenges.

### Opportunities for Future Work

Interventions such as Quokka provide a mechanism for eliciting behavior change from distributed participants. To optimize the provided interventions, direct measurement of behavior changes via machine learning [69-76] along with self-reported questionnaires can generate useful multimodal data sets. Feature selection approaches could be applied to such data streams to identify salient behavioral markers [77-81] of mental health, and classifiers for these could be realized via trustworthy and reliable crowdsourced labeling of the incoming data [82-87]. Privacy-preserving methods are crucial for behavioral data collected from interventions such as Quokka that contain easily identifiable protected health information [67]. We envision the

presented feasibility study of Quokka as the first step toward a local community-based precision health care approach [88-92] to mental health.

### Conclusions

We present Quokka, a social network that encourages participation in well-being-promoting activities through weekly local, community-based challenges. We hosted organized challenges to the undergraduate population at 4 universities, presenting weekly well-being challenges organized by challenge coordinators. We find that participation in the Quokka Challenge coincides with positive experiences for participants and promotes self-reported well-being activity. The Quokka paradigm presents a promising sociotechnical methodology for motivating communities to collectively practice health and well-being.

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### Conflicts of Interest

CS was the founder of Quokka. At the time of manuscript writing, this company was developing digital mental health solutions. All other authors declare no competing interests.

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## Abbreviations

**BCT:** behavior change theory

**So-Lo-Mo:** Social-Local-Mobile

**UNC:** University of North Carolina at Chapel Hill

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Original Paper

# Offenders With Personality Disorder Who Fail to Progress: A Case-Control Study Using Partial Least Squares Structural Equation Modeling Path Analysis

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## Abstract

**Background:** Offenders with personality disorder can be challenging to engage and retain in treatment. The UK Offender Personality Disorder (OPD) pathway aims to proactively and responsively identify and engage offenders with personality disorder. However, a subpopulation of offenders on the pathway have been found to not be accepted into any OPD service and therefore fail to progress.

**Objective:** This study aims to identify and describe offenders on the OPD pathway who fail to progress and to understand the causal drivers by which individuals fail to progress in the pathway.

**Methods:** A sample of 50 offenders on the OPD pathway who had been refused from at least two OPD services (nonprogression group) were compared to 100 offenders accepted into OPD services (control group). Partial least squares structural equation modeling was used to model the causal factors involved in not being accepted into OPD services.

**Results:** The path coefficients in the structural model showed that the most influential factor in nonprogression was attitude toward treatment ( $\beta=.41$ ;  $P<.001$ ;  $f^2=0.25$ ) alongside those with psychopathology ( $\beta=.41$ ;  $P<.001$ ;  $f^2=0.25$ ), specifically, psychopathy, psychosis, and co-occurring personality disorder.

**Conclusions:** The findings of the study provide a basis of how to work with this population in the future to increase the likelihood of acceptance into OPD services.

**KEYWORDS**

offender; personality disorder; progression; prison; PLS-SEM; partial least squares structural equation modeling; mental health; OPD; offender personality disorder; proactive diagnosis; psychopathy; psychosis; mental health services; health services

## Introduction

### Personality Disorder

Personality disorder is an enduring mental disorder in which the individual's pattern of inner experience and behavior deviates markedly from the expectations of their culture. It is associated with significant psychological distress, comorbid mental illness, difficulties with interpersonal relationships, premature mortality [1], and in some cases increased risk to others [2]. The Diagnostic and Statistical Manual of Mental Disorders classification system groups the 10 subtypes of personality disorder into three clusters based on some shared characteristics. Cluster A contains odd and eccentric personalities; cluster B dramatic, impulsive, and emotional personalities; and cluster C fearful and anxious personalities. Psychopathy is a particularly extreme form of personality disorder, characterized by antisocial behavior combined with a callous lack of empathy and the absence of guilt; psychopathic individuals show little concern for the suffering of others. The overall community prevalence of personality disorder in the United Kingdom is around 4.5% [2], while psychopathy is a relatively rare condition affecting around 0.6% of the household population [3].

The subtypes of personality disorder most commonly associated with offending are antisocial (in which criminal behavior and aggressiveness form part of the definition), borderline, narcissistic, and paranoid. Individuals in the community with cluster B personality disorders are more likely to have had a criminal conviction and to have served a prison sentence [2]. People with any personality disorder are also twice as likely to report being a victim of violence [2]. A systematic review of 62 surveys found a prevalence of personality disorder among prisoners of 65% [4] while that of psychopathy is nearly 8% of male UK prisoners [5].

It has long since been recognized that offenders with personality disorder can be challenging to engage with treatment [6]. The importance of doing so is underscored by the fact that these offenders have poor criminal justice outcomes [7], including increased risk of violence [8] and increased odds of repeat offending [9]. Subsequently, the implementation of interventions and treatment for offenders with personality disorder receives a lot of attention [10,11].

### Engagement With Treatment

Factors associated with offenders with personality disorder not engaging with treatment include personal characteristics such as young age [12], low education level [13], low occupation level and unemployment [13,14], juvenile convictions [15], and childhood emotional neglect [16]. Psychological need factors have also been identified and include having several personality disorder diagnoses [17], low levels of persistence [18], high levels of avoidance [19], and poor ego structure [18]. Lastly,

there are some environmental factors, for example, less previous service use [12] and poor therapeutic alliance [20].

For those offenders who do begin treatment, the likelihood of dropping out is high. A systematic review identified the attrition rate for offenders with personality disorder to be 37% [18], with other estimates as high as 73% [21]. Reoffending outcomes are worse for offenders who do not complete treatment, compared to those who do not engage with any treatment, even when the initial risk of reoffending is similar [22]. Young offenders with lower education and occupation levels, poor social problem solving, low levels of persistence, and greater avoidance coping styles have been found to be more likely to drop out of treatment [18], which are similar characteristics related to nonengagement.

### The Offender Personality Disorder Pathway

Given these complexities, since the early 2000s, UK Government policy has focused on developing a more informed approach to the assessment, risk management, and treatment of this complex offender group. The Offender Personality Disorder (OPD) pathway was developed in 2011 following consultation on the earlier Dangerous and Severe Personality Disorder Programme [23]. The *pathway* is jointly managed through National Health Service (NHS) England and the Ministry of Justice, and aims to adopt a proactive and responsive approach to identifying and engaging offenders with personality disorder. As part of this approach, probation staff and NHS clinicians work together to identify offenders with a likely diagnosis of personality disorder early in their sentence using a screening algorithm [24]. The screening tool helps identify people with a likely diagnosis of personality disorder or those with personality disorder traits and considers risk factors such as the type of sentence, sexual or violent offending, and risk of harm alongside indicators of personality disorder including childhood difficulties, mental health difficulties, self-harm or suicide attempts, and challenging behavior. A case formulation is then developed and used to inform sentence planning. Within secure environments, services available to those on the OPD pathway include specialist prison-based therapeutic services and therapeutic communities (TCs), and psychologically informed planned environments (PIPEs) [25]. Those whose needs cannot be met within the criminal justice system (CJS) can be transferred to a specialist secure psychiatric hospital for treatment.

The OPD approach, although in its early years, has seen broadly encouraging results. A considerable proportion of cases screened in as eligible have either been referred to a specialist service or have made a progressive move. A progressive move would include acceptance into an OPD service, a step down in security category, or release into the community. Over 36,000 offenders have been identified as suitable, and as of 2017, a total of 3400 had engaged with pathway interventions [26].

However, several of the authors are clinicians working within the London Pathways Partnership (LPP), a consortium of NHS trusts delivering services within the OPD pathway, and are aware of several individuals that no OPD service, in prison or the NHS, is prepared to accept. Anecdotally, this seems to be for several reasons, for example, the nature or degree of risk posed; disagreement about diagnosis; the offender's unwillingness to engage in a therapeutic intervention; or, linked to this, a perception of being *untreatable* [27] or *difficult* [28], both psychosocial labels with a complex causality. The nonacceptance of offenders into OPD services on the OPD pathway is likely related to issues of engaging high-risk offenders [5] and overcoming obstacles to treatment readiness [29].

Given that one of the key stated purposes of the OPD pathway is to “manage breakdown and failure...to support future progression” [30], it is important to understand why some offenders are not progressing to learn how pathway plans can adapt. The OPD pathway is informed from the “What Works?” literature [31], the risk needs responsivity (RNR) principles [32] and the Good Lives Model [29]. However, the RNR model has been criticized for not providing clear guidance for therapists for engaging offenders lacking in treatment readiness [33]. The responsivity principle of the RNR model may not currently be effectively implemented in the OPD pathway and contributing to the problem of offenders being referred but not accepted to numerous OPD services.

Furthermore, there are costs associated with the OPD pathway. For example, an OPD prison bed was costed at £50,000 (US \$68,812) [34] at the program's launch, compared to £37,000 (US \$50,920) for a standard prison bed at the same time point [35]. Offenders who are screened into the OPD pathway need to be treated cost-effectively, and nonprogression is likely to be costly. Aside from the acute costs of the OPD pathway, engaging and treating offenders with personality disorder is intended to reduce recidivism [36], and subsequently overall criminal justice spending.

It is clear, that despite its successes with many, the pathway approach is not meeting the needs of a group of individuals. For clinicians to be more responsive to this subpopulation of offenders on the OPD pathway, the characteristics of this group and the reasons why they are not being accepted into treatment need to be better understood. Much about the characteristics of this specific group is unknown, making it difficult to rectify this situation. For the OPD pathway to be meeting the aim of working with the most complex and stuck cases in the CJS, a refined understanding of the potential causal drivers of a failure to progress through services is sorely needed.

## Aims

The aim of this study is to identify and review the characteristics of individuals who have been screened into the OPD pathway but failed to progress and for whom no clear pathway can be established. Four objectives were identified to achieve the aim:

1. Identify a sample of offenders that have not progressed on the OPD pathway from routine data sets

2. Describe the failure to progress (nonprogression) sample cases' demographic, offending, and clinical characteristics alongside referral information to identify common features of this group
3. Use a complex regression model (partial least squares structural equation modeling [PLS-SEM]) to understand the causal drivers by which individual offenders and ex-offenders identified for entry into the OPD pathway fail to progress within the pathway
4. Suggest possible approaches to meeting the criminogenic and psychological needs of the nonprogression sample

## Methods

### Sample and Procedure

All participants in the study were under the supervision of the London area of the National Probation Service (NPS). The nonprogression sample was purposive and consisted of 50 male offenders, identified through professionals such as Offender Managers, LPP psychologists, and LPP forensic psychiatrists. Emails explaining the rationale and aims of the study requested names of offenders who had been declined from at least two OPD services. Cases discussed at the NPS London Division IPP Complex Case Panel were also included in the nonprogression group when they met the inclusion criteria. A case-control design, where cases (nonprogression sample) were compared to a random sample of controls (progression sample), was used. The broader caseload comparison group consisted of male offenders identified from the LPP case database through random selection (every 10th case). Based on suggested sample sizes for PLS-SEM models with at least 10 cases per path in the *busiest* exogenous variable [37,38], we oversampled the comparison group at a ratio of 2:1 (100 cases) to obtain a total sample size of 150, allowing for up to 15 paths per node.

The demographics of the nonprogression and comparison samples are discussed in detail in the Results section, as this addresses the second aim of the research to understand common characteristics of the nonprogression sample. The random selection of the control group should ensure this is representative of the broader LPP caseload. The nonprogression sample should be representative of offenders not being accepted into OPD services, as these cases were identified through a variety of professionals working with these offenders and a case panel designed to discuss offenders who were not progressing through the OPD pathway.

Once cases were identified, the electronic records of the offender were accessed. A specifically designed research schedule containing information on demographics, offending, institutional behavior, psychopathology, risk measures, previous treatments, current attitudes toward treatment, and referrals to OPD services was applied by trained research assistants to systematically collect the relevant data from probation record systems (nDelius and the Offender Assessment System [OASys]) [39]. OASys is designed to assess likelihood of reoffending, classify offending-related needs, identify risk of harm to the individual and others, link assessment to the supervision plan, measure change during the supervision period, and indicate needs for further specialist assessment. nDelius is a browser-based NPS

case management system containing offender-related information.

Gathering data from secondary data sources could have led to errors in recording; however, each research schedule was completed and checked over to ensure errors were identified. The measures identified are all routinely recorded information and are used throughout the CJS to assess offender characteristics and risk.

The same research schedule was used for the nonprogression and control group. The data sets generated and analyzed during this study are not publicly available due to confidentiality agreements with the NPS.

### **Ethics**

Ethical approval for this research was granted by the NPS London Division.

### **Measures**

#### ***Demographics***

Demographic data included date of birth, ethnicity, and current marital status, and was recorded from OASys.

#### ***Offending***

To measure offending, the following variables were recorded: most serious index offence (and, if applicable, secondary and tertiary index offences), the victim of the index offence, previous offending, current sentence type, and security category and recall history. All variables were categorical and obtained from OASys.

#### ***Institutional Behavior***

Institutional behavior was measured by recording the number of adjudications the offender had during their current or most recent prison sentence, if they had ever previously escaped, absconded, been in long-term or repeated segregation, or displayed institutional violence or misbehavior (eg, having contraband, drug use, or not following the prison regime). All variables were measured as “yes” or “no” and collected from nDelius and OASys.

#### ***Psychopathology***

Psychopathology was measured by identifying any previous diagnosis or significant traits of personality disorder, psychopathy (a score of over 25 on the Psychopathy Checklist-Revised [40]), psychosis, learning difficulty, autism spectrum disorder, organic brain disorder, depression, substance misuse, posttraumatic stress disorder, and self-harm. This information was found in OASys and was recorded as “yes” or “no.”

#### ***Risk***

Risk measures included OASys severe personality disorder screen score, the Offender Group Reconviction Scale (OGRS), and OASys Violence Predictor (OVP) 2-year score were recorded from the most recent OASys assessment, the Risk Matrix 2000 (RM2000) [41], and Historical Clinical Risk (HCR-20) [42]. The OASys severe personality screen score comprises 10 items, with a score of 7 or above triggering a

further assessment of personality disorder. The OGRS is a static, actuarial risk assessment providing an estimate of the probability that offenders will be reconvicted within 2 years of release [43]. The OVP is an actuarial violence predictor combining static and dynamic risk factors [39]. The RM2000 [41] is a risk assessment for sexual offenders created to classify sexual recidivism and risk of reconviction for sexual or nonsexual assaults and was recorded if available. Out of the sample that had a sexual conviction (n=21), all had data for this variable. The HCR-20 is a structured professional judgement measure for violence risk; 83 people did not have an HCR-20 assessment on record (n=24, 48% missing in the nonprogression group and n=61, 40% in the progression sample).

#### ***Previous Treatment***

To measure previous treatment, any historical engagement with treatment including offender behavior programs (OBPs), prison TCs, high secure OPD prison service, PIPEs, high secure or medium secure health, and community-based treatments were recorded. For the nonprogression group, it was recorded whether the participant has previously refused, completed, dropped out of treatment, or a combination of the aforementioned (eg, completing one OBP but refusing another). This information was obtained through the nDelius contact log and OASys section 11.

#### ***Attitudes Toward Treatment***

Finally, the nonprogression group sample had their current attitude toward engaging with treatment recorded. This was identified from the OASys section, which discusses treatment motivation, and was categorized into refusing treatment, refusing treatment in a chosen service, refusing treatment in an available service, or unable to engage (with reasons).

#### ***Analysis Plan***

The first objective of the study was to describe the common features of the nonprogression group. To achieve this, summary tables displaying descriptive statistics of the sample were produced, and tests of differences (chi-square or *t* tests) between the nonprogression group and the control group were run.

To understand the causal drivers by which individual offenders identified for entry into the OPD pathway fail to progress, PLS-SEM analysis was used to model the factors involved in not being accepted into OPD services. PLS-SEM is a form of structural equation modeling (SEM) that estimates path coefficients or relationships between several latent variables using a probabilistic algorithm known as maximum likelihood estimation, as opposed to the covariance-based approach adopted in standard SEM. PLS-SEM was chosen because the method can cope with formative constructs, which enhances the understanding of the linear relationships in failing to progress on the OPD pathway and can accept noncontinuous variables. It was predicted that pathways to nonprogression would be complex, with many variables impacting the relationship, so PLS-SEM was chosen over a simpler regression model.

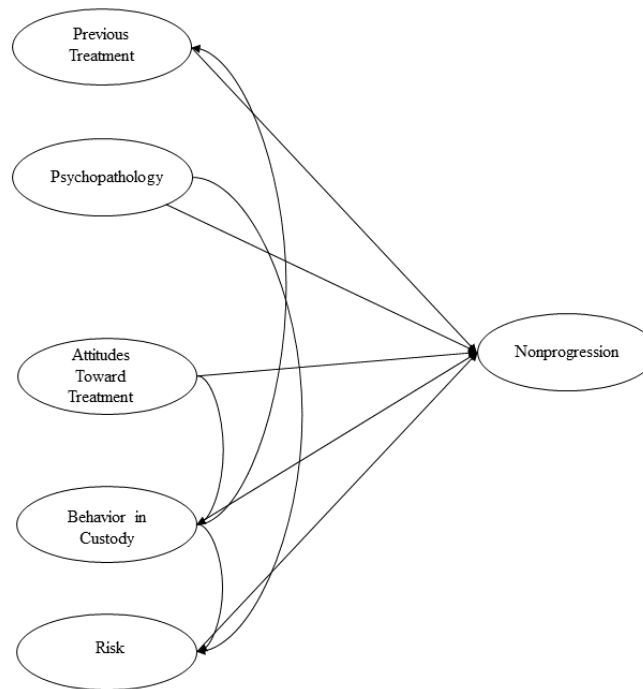
The model was built using the plspm package [44] in the R statistical programming environment (R Foundation for Statistical Computing) [45]. The observed exogenous variables

(see [Multimedia Appendix 1](#) for the outer model) previously described were assessed for their loading onto six latent variables (psychopathology, risk, previous treatment, previous behavior in prison, attitudes toward treatment, and nonprogression). The latent variables create the inner model, and the variables were connected using clinical knowledge and theory ([Figure 1](#)). For example, risk models used in OPD services understand attitudes toward treatment are linked to risk, but attitudes toward treatment are also linked to likelihood of engaging in treatment. A conceptual decision was made to

treat both *psychopathology* and *attitudes toward treatment* as exogenous concepts although the two are undoubtedly related [46]. However, the SEM approach enforces directionality of relationships (eg, personality must either inform attitudes or vice versa), which was not deemed appropriate here, so the link was omitted. [Figure 2](#) outlines the analysis plan visually.

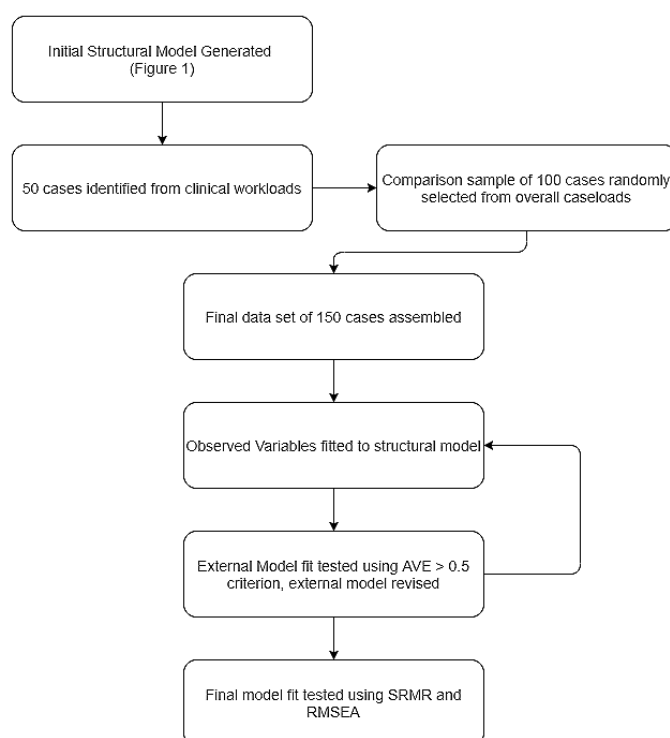
Based on the coefficients observed from the PLS-SEM model, we considered possible approaches to addressing risk factors identified as most important in predicting failure to progress in the Discussion section.

**Figure 1.** Proposed latent structure of factors predicting failure to progress.





**Figure 2.** Visualization of data analysis plan. AVE: average variance extracted; RMSEA: root mean square error of approximation; SRMR: standardized root mean square residual.



## Results

### Characteristics of Nonprogression Group Versus Control Group

An objective of the study was to describe the nonprogression sample's demographic, offending, and clinical characteristics alongside referral information to identify common features of the group. To do this, the nonprogression group was compared

to the control group using chi-square tests of difference (or  $t$  tests where appropriate) to understand the key differences across the samples. Unadjusted  $P$  values are reported throughout; however, following Bonferroni correction, a "true" significance threshold of  $P < .05 / Y = 46 = P < .001$  could be considered. [Table 1](#) presents some key demographic information about age, ethnicity, relationship status, and index offences across the sample. Supplementary descriptive summary Tables were also created (Tables S1-S5 in [Multimedia Appendix 1](#)).

**Table 1.** Descriptive statistics according to nonprogression and control group.

Demographics	Nonprogression (n=50)	Control cases (n=100)	$t$ test ( $df$ )	Chi-square ( $df$ )	$P$ value
Age (years), mean (SD)	41.66 (11.12)	40.73 (11.20)	-0.48 (148)	N/A <sup>a</sup>	.63
<b>Ethnicity, n (%)</b>			N/A	3.42 (4)	.49
White	25 (50)	55 (55)			
Non-White	25 (50)	45 (45)			
<b>Relationship status, n (%)</b>			N/A	14.34 (4)	.006
Single	43 (86)	71 (71)			
Other	7 (14)	29 (29)			
<b>Index offence, n (%)</b>			N/A	17.88 (7)	.01
Violent offence	32 (64)	70 (70)			
Sexual offence <sup>b</sup>	13 (26)	8 (8)			
Other	5 (10)	22 (22)			

<sup>a</sup>N/A: not applicable.

<sup>b</sup>This combines adult and child sexual offences.

### Demographics and Offending

Overall, the nonprogression group was similar to the control group in ethnicity. The groups differed in marital status, with a slightly higher proportion of singleness (43/50, 86% vs 71/100, 71%) in the control group ( $\chi^2_{4,150}=14.34$ ;  $P=.006$ ). The nonprogression group had committed more adult sexual offences (11/50, 22% vs 5/100, 5%), was given more indeterminate sentences for public protection (IPP;  $\chi^2_{5,150}=18.90$ ;  $P=.001$ ), and was detained in category B security prisons more frequently than the control group ( $\chi^2_{6,150}=40.59$ ;  $P<.001$ ; Table S1 in [Multimedia Appendix 1](#)).

### Attitude Toward Treatment and Behavior in Custody

There was a significant difference in the number of adjudications between the control group (mean 7.52, SD 14.43) and the nonprogression group (mean 15.88, SD 22.58;  $U=1537.5$ ;  $P=.003$ ). The groups also significantly differed in the frequency of time spent in long-term segregation ( $\chi^2_{1,150}=10.34$ ;  $P=.002$ ), with the nonprogression group being in long-term segregation more. The nonprogression group was also more likely to misbehave during their sentence (eg, having contraband;  $\chi^2_{1,150}=8.68$ ;  $P=.004$ ) and commit a further offence while in custody than the control group ( $\chi^2_{6,150}=15.73$ ;  $P=.006$ ). The control group was significantly more motivated toward treatment than the nonprogression group ( $\chi^2_{1,150}=30.92$ ;  $P<.001$ ), whereas the nonprogression group displayed more attitudes of having no hope ( $\chi^2_{1,150}=8.29$ ;  $P=.007$ ; Table S2 in [Multimedia Appendix 1](#)).

### Psychopathology and Risk

The nonprogression group had significantly higher levels of diagnosis or traits of antisocial ( $\chi^2_{1,150}=7.09$ ;  $P=.009$ ) and borderline ( $\chi^2_{1,150}=3.73$ ;  $P=.04$ ) personality disorders as well as psychopathy ( $\chi^2_{1,150}=16.05$ ;  $P<.001$ ) and learning difficulties ( $\chi^2_{1,150}=8.29$ ;  $P=.007$ ). The nonprogression group was more likely to be rated as “high risk” on the OGRS ( $\chi^2_{3,150}=8.46$ ;  $P=.03$ ) and scored higher on the HCR-20 (control mean 24.44, SD 5.08; nonprogression mean 28.29, SD 4.68;  $t_{65}=-3.161$ ;  $P=.002$ ), suggesting the nonprogression group displays greater risk (Tables S3-S4 in [Multimedia Appendix 1](#)).

### Previous Treatment and Refusal to OPD Services

The nonprogression group had historically engaged with little treatment aside from offending behaviour programs. Nearly half the nonprogression group had been referred to an OPD medium secure unit or a PIPE and been refused. Around one-third of the sample had been referred to a prison TC and been refused.

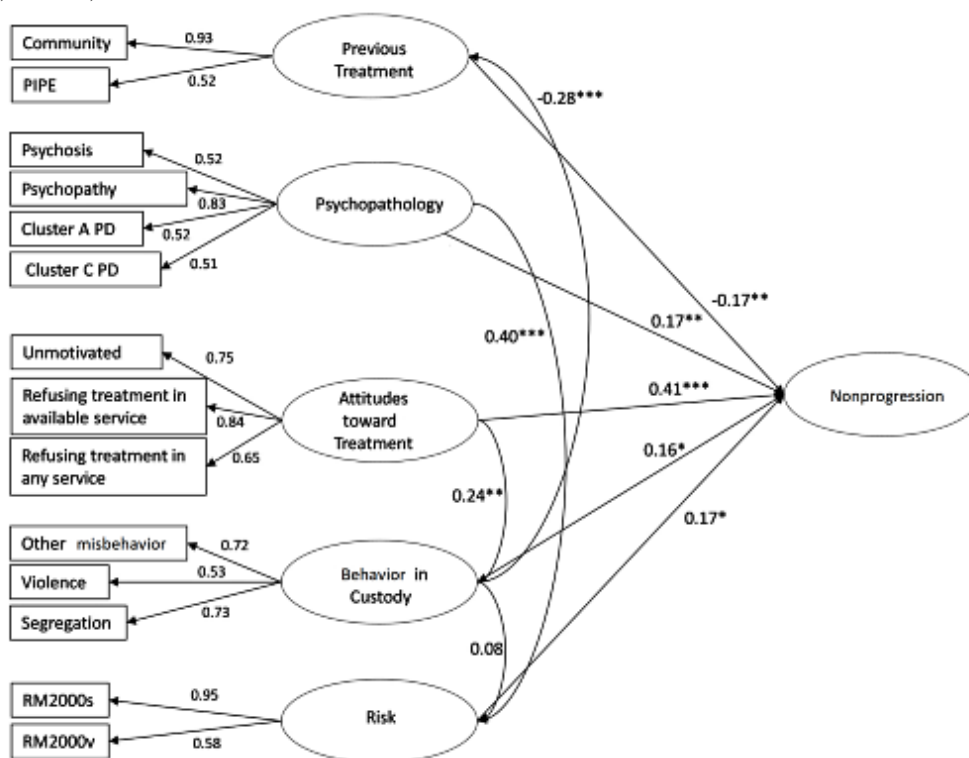
### Predicting Refusal by OPD Services (PLS-SEM)

The next objective of the study was to develop a causal model of service refusal using a SEM method. To do this, we followed a formative approach, proceeding from a theoretical model of likely causal drivers for nonprogression ([Figure 1](#)) that we then operationalized with observed variables taken from the available OPD data ([Figure 3](#)). For example, the *psychopathology* latent construct was formed from the observable variables of psychopathy; psychotic disorder; and cluster A, B, and C personality disorders.

First, the overall model fit of the estimated model was assessed using the standardized root mean square residual (SRMR). The SRMR value of 0.1 showed an adequate fit of the model [47]. Next, indicator loadings for observed variables on latent constructs were assessed. For indicator loadings to be at an accepted level across the model, some individual indicators were grouped (*cluster A personality disorder* was created by combining paranoid, schizoid, and schizotypal personality disorder, and *cluster C personality disorder* was created from avoidant, dependent, and obsessive-compulsive personality disorder). The loadings in the model were all reviewed, and accepted loading coefficients all fell above 0.5. Observed variables removed due to insufficient indicator loadings included ethnicity, marital status, learning difficulty, denial of offence, no hope toward treatment, abscond or escape, serious further offence in custody, previous treatment in medium secure health, TCs or offender programs, OASys personality disorder screen number, or OGRS and OVP risk scores.

Next, the internal consistency was assessed through the composite reliability of observed variables within each latent construct. All variables fell near or above the recommended threshold of 0.7 ([Table 2](#)). Average variance extracted values over 0.5 indicate the construct explains at least 50% of the variance of its items.

**Figure 3.** Path diagram showing coefficients of the inner and outer structural model. PD: personality disorder; PIPE: psychologically informed planned environment. \* $P < .05$ ; \*\* $P < .01$ ; \*\*\* $P < .001$ .



**Table 2.** Reflective constructs assessment of composite reliability and convergent validity according to each latent construct.

Reflective constructs	Composite reliability	Average variance extracted
Psychopathology	0.69	0.37
Attitudes	0.88	0.65
Behavior in custody	0.70	0.44
Previous treatment	0.71	0.57
Risk	0.76	0.62

Finally, the discriminant validity was investigated to understand the extent to which the constructs are empirically distinct from other constructs in the model. To assess this, cross-loadings of observed variables on all latent constructs were reviewed. All the cross loadings were higher in value on their relative latent variable, compared to the other latent constructs, meaning there was no issue of discriminant validity. Table S5 in [Multimedia Appendix 1](#) displays the cross-loadings for the discriminant validity check.

The structural model assessment looks at the exogenous and endogenous latent variables through evaluation of the  $R^2$ . The  $R^2$  value represents the coefficient of determination and shows the amount of variance of endogenous latent variables explained by the model. The model testing nonacceptance to OPD services (ie, nonprogression) had an  $R^2$  value of 0.45. Cohen et al [48] suggest a good model should have an  $R^2$  value greater than 0.26, which is met and shows the model provides a substantial amount of explained variance in the pathway of nonprogression. The remaining models of risk, previous treatment, and behavior in custody fell below the recommended  $R^2$  threshold (0.18, 0.08,

and 0.06, respectively) and therefore should be interpreted with caution.

All specified path coefficients between latent variables were inferred from the  $\beta$  value.  $\beta$  shows the strength of an effect from the exogenous to the endogenous latent variables. Higher  $\beta$  values show stronger effects. The  $\beta$  value is then tested for significance through the  $t$  test. Effect sizes of individual latent variables were calculated using Cohen  $f^2$  [49], which indicates the relative influence of the variable within the overall SEM model.

Table 3 shows the structural model assessments. The most influential factor in nonprogression was attitude toward treatment ( $\beta=.41$ ;  $P<.001$ ;  $f^2=0.25$ ). A negative attitude toward treatment, such as refusing treatment in an available service or being unmotivated, was predictive of not progressing with a moderately strong effect size. Behavior in custody ( $\beta=.16$ ;  $P=.02$ ;  $f^2=0.04$ ), previous treatment ( $\beta=-.17$ ;  $P<.001$ ;  $f^2=0.05$ ), risk ( $\beta=.17$ ;  $P=.02$ ;  $f^2=0.04$ ), and psychopathology ( $\beta=.17$ ;  $P=.01$ ;  $f^2=0.04$ ) provided significant prediction of nonprogression, however, with weak effect sizes.

The remaining model assessments show psychopathology significantly predicted the level of risk with a moderate effect size ( $\beta=.40$ ;  $P<.001$ ;  $f^2=0.19$ ); however, behavior in custody did not predict level of risk ( $\beta=.08$ ;  $P=.24$ ;  $f^2=0.01$ ). Behavior in custody significantly predicted previous treatment with a weak effect ( $\beta=-0.28$ ;  $P<.001$ ;  $f^2=0.09$ ; ie, more *poor behavior* being related to less prison treatment). Finally, attitudes toward treatment significantly predicted behavior in custody ( $\beta=.24$ ;

$P=.01$ ;  $f^2=0.06$ ) but with a weak effect size. Due to the small  $R^2$  sizes of the risk, previous treatment, and behavior in custody models, only a small proportion of variance was explained.

Figure 3 displays the overall model including measured and latent variables with the coefficients and the significant pathways highlighted. The figure shows how the measured variables load onto the latent variables and the strength of effect the latent variables have in explaining nonprogression.

**Table 3.** Structural model assessment.

Model	Overall model $R^2$	Path coefficient ( $\beta$ )	$P$ value	$f^2^a$
<b>Nonprogression</b>	0.45			
Behavior in custody		.16	.02	0.04
Previous treatment		-.17	.001	0.05
Risk		.17	.02	0.04
Psychopathology		.17	.01	0.04
Attitudes		.41	.001	0.25
<b>Risk</b>	0.18			
Psychopathology		.40	.001	0.19
Behavior in custody		.08	.24	0.01
<b>Previous treatment</b>	0.08			
Behavior in custody		-.28	.001	0.09
<b>Behavior in custody</b>	0.06			
Attitudes		.24	.01	0.06

<sup>a</sup>Suggested interpretation of  $f^2$  effect sizes.

## Discussion

### Principal Findings

In this paper, we identified and described a sample of offenders who had not progressed on the OPD pathway to understand the common features of this group. The nonprogression group had more sexual offences, were more likely to be on an IPP sentence and in a category B prison, received more adjudications, spent more time in segregation, had more general misbehavior, were assessed as being high risk, had more traits of antisocial and borderline personality disorder as well as psychopathy, were less likely to have engaged with treatment previously, and displayed more attitudes of hopelessness toward treatment.

The features of this group correspond to the literature that has identified factors related to nonengagement with treatment. For example, several personality disorder diagnoses [17], low persistence [18], less previous treatment [12], and being assessed as high risk [5]. Furthermore, the sample of offenders not progressing on the OPD pathway are also characterized by their sexual offending history, IPP sentence type, and prison security category.

Following this, we built a complex regression model to understand the causal drivers by which individual offenders and ex-offenders identified for entry into the UK OPD pathway fail to progress within the pathway. The model showed that, aside from static factors such as risk not amenable to intervention;

negative attitudes to treatment; and psychopathology including psychopathy, psychosis, and co-occurring personality disorders were the main significant drivers of failure to progress. Completing a treatment program previously, either in the community or a PIPE was negatively associated with nonprogression.

The regression analyses indicated that limited motivation for treatment was the principal driver of being refused from OPD services. Lacking motivation for treatment, a factor already identified as a problem within populations with a likely diagnosis of personality disorder [50,51], remains a problem within the OPD pathway. Various programs offered to offender populations have attempted to address this issue of low motivation through a psychoeducational approach [52,53]; however, this approach can be resource-intensive and has not been subject to rigorous evaluation.

First, low treatment motivation also predicted problematic institutional behavior, including more custodial adjudications and having spent protracted periods in segregation, and this behavior in turn also predicted service refusal. It is likely that presenting in this way would increase the likelihood of cases struggling to meet behavioral stability criteria to enter many services. Although the relationship between problematic custodial behavior and service refusal was not strong, the results still emphasize that services aiming to support individuals on the OPD pathway need to be able to receive men with patterns

of challenging behavior and contain and manage ongoing episodes, without this resulting in treatment termination.

Second, the outer loadings within the SEM model suggest that the single most influential factor was psychopathy or psychopathic disorder, which has long been acknowledged as a limiting factor for treatment and rehabilitation [54]. It could be argued that psychopathic offenders are not best served on a pathway that caters for offenders with personality disorder in the broader sense of the diagnosis, as their needs are known to be different [55]. Treatment programs for this group may therefore need to use more flexible models, which work hard to sustain engagement and rely less on prosocial motivation. An emphasis on promoting positive lifestyle changes in areas of criminogenic need may also be more successful than using traditional therapeutic approaches, which focus on the treatment of maladaptive personality traits [56].

Finally, our results suggest some reasons for cautious optimism. The final finding that treatment completion was negatively associated with nonprogression suggests that nonprogression is a single “hurdle,” and once overcome, that is to say, once an offender successfully engages with a rehabilitative program, they are less likely to become stuck in the future. A possible conclusion from this is that multiple light-touch efforts to engage offenders in rehabilitation programs from an early stage might be a better approach than a single *high stakes* pathway where failure is an *end point*. Some previous treatment approaches for offenders at high risk of reconviction have adopted this approach, with repetition of short duration intensive treatments viewed as a necessary part of progression for some offenders [57].

### Strengths and Limitations

This paper has two key strengths. First, we adopted an uncommon modeling approach that has the potential to show not just predictive associations but also causal links between variables. Causal models are crucial in understanding and managing risk [58], as they can distinguish between predictive associations that are of academic interest but essentially uninformative to the intervention (eg, age or gender) and causal associations where an intervention could potentially be targeted (eg, attitudes to treatment). The PLS-SEM approach allows the use of latent variable modeling to separate confounding or static variables from the model and focus on associations that have clinical meaning. By constructing this model, we have suggested that, in this case, the most important factor in avoiding progression failure is a dynamic risk factor (attitudes to treatment), which has shown amenability to treatment in previous studies.

Second, the sample size identified was more than acceptable for this kind of analysis; Hair et al [37] suggest at least 10 cases per regression estimate in the *busiest* latent variable, which in this case would suggest 70 cases based on the *behavior in custody* variable, which has four endogenous and three exogenous links. In PLS-SEM, larger sample sizes provide important additional generalizability of the models beyond local contexts, which we are claiming here.

However, there were limitations to this paper. First, although the fit statistics for our analysis, which indicate how well our model reflected the structure of the data, were mostly acceptable, they were not unequivocal in their support of the model. For example, an SRMR of less than 0.08 is generally considered a *good fit* [59], but our model did not reach this threshold, although it was close (SRMR=0.1), and statisticians encourage some flexibility in interpretation of these statistics (eg, Hair et al [60] suggest a threshold of 0.12). Second, although the model was able to account for some heterogeneity in demography, psychopathology, and risk between the nonprogression and comparison groups within our sample, the number of differences between the two groups was large and included complex categorical variables such as index offence. Only a larger study using a matching approach (eg, propensity score matching) would truly be able to account for these differences and establish a generalizable model. Third, there was a large amount of missing data for some variables within the model, specifically risk as measured by the HCR-20, which is a standard risk assessment for forensic clients within health settings but is completed by only a small number of prison settings. As the PLS-SEM approach does not allow missing data, this measure was not included in the final model, and therefore, some latent constructs such as *risk* may not be as well specified as we would have hoped.

### Clinical and Practical Implications

The findings of the study are informative about those at the more extreme end of the spectrum of the OPD strategy’s target group, certainly in terms of severity of personality disturbance and risk to others—both in custody and in the community. These results point to the need for a more particular focus on this group in a number of possible ways. First, efforts should be made to identify and target these individuals early in their sentence, before antiauthoritarian attitudes and hopelessness have become entrenched. Second, it could be beneficial to develop a small number of OPD pathway services specifically focused on developing more sophisticated approaches to addressing low treatment motivation. This is known, clinically, to be multifactorial, involving a lack of self-belief, lack of trust, and high levels of distress [61]. Additionally, the role of high epistemic vigilance, or these individuals’ profound reluctance to consider new knowledge and experiences—gained, crucially, through relating to others—as safe and trustworthy, is likely to be relevant let alone worth integrating into their lives [62]. Such services could usefully rely on creative approaches that seem to reduce interpersonal and internal-based threat in the therapeutic encounter, such as art psychotherapy [63]. Peer mentors, especially those who have themselves succeeded in progressing after long years in segregation or otherwise in a state of protest, would also provide a credible means of accessing and addressing ambivalence. Finally, such services will need the flexibility to “weather” periods of disengagement and defiance without rushing to deselect.

### Future Perspectives

This study provides useful information to ensure the OPD pathway is adequately providing for those who need its services. A recommendation from this study would be for the OPD

pathway to consistently use pretreatment motivation interventions to effectively engage more offenders. However, these interventions also need evaluation to understand their effectiveness and utility. The study also highlights the difficulty that psychopathic disorder presents in the OPD pathway. Future research should focus on this subsample within the OPD pathway to understand their specific treatment needs and whether they are best served with the pathway approach.

### Conclusion

In this study, we identified a group of individuals for whom the pathway approach was not working due to their refusal into any

OPD service, despite referrals to these services. The characteristics of this group were compared to a broader caseload (who have been accepted into OPD services), and PLS-SEM was used to understand causal drivers for nonprogression on the OPD pathway. Previously unknown characteristics of offenders on the OPD pathway who are not progressing have now been described. Furthermore, causally modeling factors involved in nonprogression has shown the current OPD pathway struggles to account for those who are lacking in motivation toward treatment alongside those with psychosis, psychopathy, and co-occurring personality disorder.

### Conflicts of Interest

None declared.

Multimedia Appendix 1

Supplementary materials.

[DOCX File, 72 KB - [xmed\\_v2i4e27907\\_app1.docx](#)]

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## Abbreviations

- CJS:** criminal justice system
- HCR-20:** Historical Clinical Risk
- IPP:** indeterminate sentences for public protection
- LPP:** London Pathways Partnership
- NHS:** National Health Service
- NPS:** National Probation Service
- OASys:** Offender Assessment System



**OBP:** offender behavior program  
**OGRS:** Offender Group Reconviction Scale  
**OPD:** Offender Personality Disorder  
**OVP:** OASys Violence Predictor  
**PIPE:** psychologically informed planned environment  
**PLS-SEM:** partial least squares structural equation modeling  
**RM2000:** Risk Matrix 2000  
**RNR:** risk needs responsivity  
**SEM:** structural equation modeling  
**SRMR:** standardized root mean square residual  
**TC:** therapeutic community

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Original Paper

# Machine Learning–Based Prediction of COVID-19 Mortality With Limited Attributes to Expedite Patient Prognosis and Triage: Retrospective Observational Study

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## Abstract

**Background:** The onset and development of the COVID-19 pandemic have placed pressure on hospital resources and staff worldwide. The integration of more streamlined predictive modeling in prognosis and triage–related decision-making can partly ease this pressure.

**Objective:** The objective of this study is to assess the performance impact of dimensionality reduction on COVID-19 mortality prediction models, demonstrating the high impact of a limited number of features to limit the need for complex variable gathering before reaching meaningful risk labelling in clinical settings.

**Methods:** Standard machine learning classifiers were employed to predict an outcome of either death or recovery using 25 patient-level variables, spanning symptoms, comorbidities, and demographic information, from a geographically diverse sample representing 17 countries. The effects of feature reduction on the data were tested by running classifiers on a high-quality data set of 212 patients with populated entries for all 25 available features. The full data set was compared to two reduced variations with 7 features and 1 feature, respectively, extracted using univariate mutual information and chi-square testing. Classifier performance on each data set was then assessed on the basis of accuracy, sensitivity, specificity, and received operating characteristic–derived area under the curve metrics to quantify benefit or loss from reduction.

**Results:** The performance of the classifiers on the 212-patient sample resulted in strong mortality detection, with the highest performing model achieving specificity of 90.7% (95% CI 89.1%-92.3%) and sensitivity of 92.0% (95% CI 91.0%-92.9%). Dimensionality reduction provided strong benefits for performance. The baseline accuracy of a random forest classifier increased from 89.2% (95% CI 88.0%-90.4%) to 92.5% (95% CI 91.9%-93.0%) when training on 7 chi-square–extracted features and to 90.8% (95% CI 89.8%-91.7%) when training on 7 mutual information–extracted features. Reduction impact on a separate logistic classifier was mixed; however, when present, losses were marginal compared to the extent of feature reduction, altogether showing

that reduction either improves performance or can reduce the variable-sourcing burden at hospital admission with little performance loss. Extreme feature reduction to a single most salient feature, often age, demonstrated large standalone explanatory power, with the best-performing model achieving an accuracy of 81.6% (95% CI 81.1%-82.1%); this demonstrates the relatively marginal improvement that additional variables bring to the tested models.

**Conclusions:** Predictive statistical models have promising performance in early prediction of death among patients with COVID-19. Strong dimensionality reduction was shown to further improve baseline performance on selected classifiers and only marginally reduce it in others, highlighting the importance of feature reduction in future model construction and the feasibility of deprioritizing large, hard-to-source, and nonessential feature sets in real world settings.

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## KEYWORDS

COVID-19; coronavirus; medical informatics; machine learning; artificial intelligence; dimensionality reduction; automation; model development; prediction; hospital; resource management; mortality; prognosis; triage; comorbidities; public data; epidemiology; pre-existing conditions

## Introduction

Prior to the COVID-19 pandemic, hospitals in several countries were already experiencing difficulty in managing scarce resources and staff dissatisfaction.

In the United Kingdom, occupancy rates have steadily increased for a decade, with general bed occupancy rising from 84.3% in 2010 to 89.4% in 2019 (92% for general and acute care beds) [1]; meanwhile, overall bed stock across the European Union declined by 2.5% between 2013 and 2018 [2].

In several countries, such as Italy, Greece, and Portugal, this decrease in occupancy rates is set against a financial backdrop of decreasing public health spend, with each listed country registering a decrease in per capita government health care expenditure between 2010 and 2018 [3]. In addition to geographically localized reductions in funding, overall spend has been edging away from acute care and hospital services, with expenditure on inpatient care across Organisation for Economic Co-operation and Development countries growing 14% slower than expenditure on outpatient care and 23% slower than expenditure on long term care between 2013 and 2017 [4].

Staff satisfaction and supply have also proved troublesome. In a cross-sectional US study that was performed shortly prior to the onset of the COVID-19 pandemic, 70% of nurses across hundreds of surveyed institutions stated they would not recommend their hospital; half experienced high burnout, and one-fourth stated they planned to leave the profession within a year [5].

The increased demands imposed by the spread of COVID-19 have in many cases exacerbated the above areas of concern. Lack of resource management protocols and stock limitations led to a shortage of hospital beds [6] and ventilators [7,8] in the early stages of the pandemic, while in some cases, contraction of the virus by medical staff has as much as doubled sickness absence rates [9], further straining staff availability and supply.

These shortcomings have direct adverse consequences for patient care, with a study of 4453 hospitals in the United States from the early phase of the pandemic finding that lower numbers of intensive care unit beds, nurses, and general medicine beds per

COVID-19 case were significantly associated with a higher rate of death [10].

To improve use of equipment and better manage physician and nurse supply, increased focus has been brought to information technology. Of particular interest to this paper are computational models that are capable of predicting mortality using real-time patient data. Such models aim to reduce hospital burden by providing efficient patient triage, allowing for preallocation or local hospital transfer of lifesaving equipment, quantifying the need for further diagnostics or early treatment, and directing limited staff attention and resources toward the patients at highest risk.

Several such models have now entered the academic literature, but with varying degrees of usability. Many suffer from mild to severe flaws, such as training on alternative diseases such as pneumonia as a proxy for COVID-19 [11], depending on less immediately available data from blood tests and other monitoring equipment [12-15], and unrepresentative population samples—often older skewing [16] or monolocalized [17]; these flaws result either in low performance or, more worryingly, in excessively optimistic expectations of performance that overfit to a certain facet of the population.

Although all predictive models will inevitably suffer from issues surrounding quality of data or population reproducibility, many of them still generate valuable findings that can materially aid in patient profiling and optimization of treatment and have been adopted on a supportive level by hospitals.

In this study, we aim to further the utility of existing models by exploring the impact of dimensionality reduction on the predictive accuracy of patient outcomes, providing a use case for reduction of costly or slowly available patient attributes, such as laboratory or imaging results, in favor of simple patient history and demographics.

## Methods

### Data Set

Data for this study were obtained from a continuously updated repository [18] containing anonymized patient level information on 2,676,311 COVID-19-positive individuals across 146 countries. The results represent data sourced on February 18,

2021, encompassing entries up to and including the date in question.

### Variable Extraction and Data Preprocessing

Symptoms and comorbidities in the data set were parsed and one-hot encoded into fixed variable names. [Textbox 1](#) shows all the patient variables used in the study.

**Textbox 1.** Features employed as predictors of mortality by category.

<p><b>Symptoms</b></p> <ul style="list-style-type: none"><li>• Cough</li><li>• Fever</li><li>• Runny nose</li><li>• Fatigue</li><li>• Headache</li><li>• Diarrhea</li><li>• Sore throat</li><li>• Chest symptoms</li><li>• Chills</li><li>• Difficulty breathing</li><li>• Acute respiratory distress syndrome</li><li>• Pneumonia</li></ul> <p><b>Pre-existing conditions</b></p> <ul style="list-style-type: none"><li>• Benign prostatic hyperplasia and other prostate conditions</li><li>• Coronary heart disease or other cardiac condition</li><li>• Chronic kidney disease and other kidney conditions</li><li>• Hypertension</li><li>• Diabetes</li><li>• Pulmonary conditions</li><li>• Asthma</li><li>• Bronchitis</li><li>• Conditions affecting the arteries</li><li>• Cancer</li></ul> <p><b>Demographic attributes</b></p> <ul style="list-style-type: none"><li>• Age</li><li>• Sex</li></ul> <p><b>Derived attributes</b></p> <ul style="list-style-type: none"><li>• Number of pre-existing conditions</li></ul>
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Of the original 2,676,311 patients, only 212 patients had fully populated fields for all the above variables; these patients were retained in the study.

### Dimensionality Reduction

Dimensionality reduction was applied to compare a full 25-feature data set to 7-feature and 1-feature reduced variations. Feature selection was performed, first through mutual information and second through chi-square tests, to compare the selection impact of different approaches.

Both frameworks were executed in Python using the *mutual\_info\_classif* and *chi2* methods in scikit-learn's *feature\_selection* module [19]. The only continuous variable in the data set, age, was discretized through bins in the chi-square method and through a *k*-nearest neighbors approach in the mutual information method; a more comprehensive definition of the latter can be found in the relevant cited work [20].

Features were extracted using the extent of  $P$  value significance in the chi-square framework and mutual information in the alternative method, where the latter can be broadly defined as [21]:



where  $X$  is a predictor feature in the data and  $Y$  is an outcome of death or recovery.

### Predictive Models and Evaluation Criteria

Random forest and logistic regression were employed as primary classifiers to be trained on ex ante balanced data and tested on unprocessed imbalanced data.

Model performance was evaluated based on accuracy, area under the curve (AUC), sensitivity, and specificity. Sensitivity measures the proportion of deaths correctly identified by the model, expressed as:



Where death is a positive outcome and recovery is a negative outcome. Specificity measures the proportion of recoveries correctly identified, expressed as:



All metrics were derived from aggregation during 3-fold cross-validation.

## Results

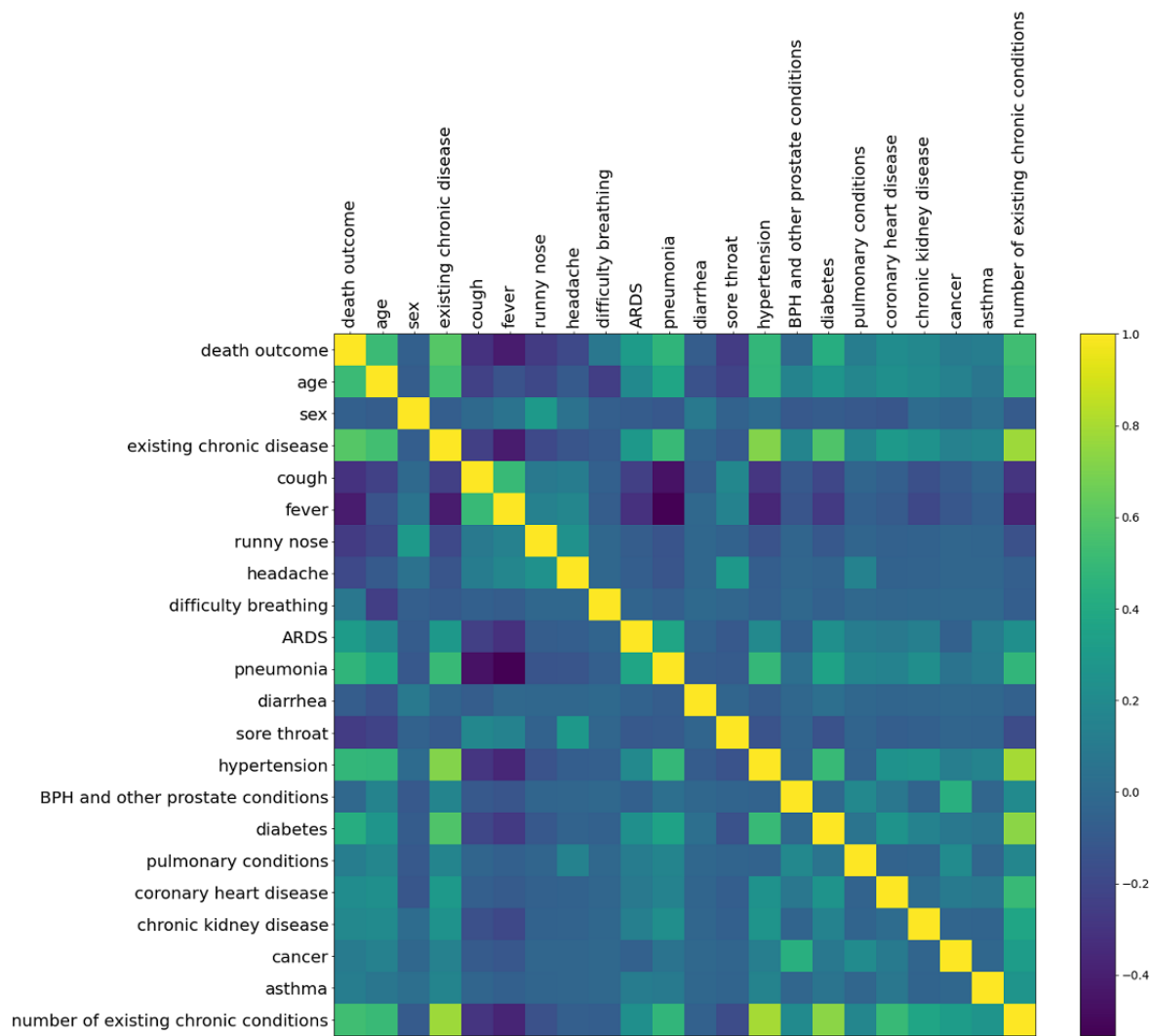
### Sample Baseline Characteristics

The fully populated data set contains full entries for each category mentioned in the methodology, resulting in a sample of 212 patients. The data are geographically diverse, with representation from 17 countries, although 62/212 patients (29.2%) originate from China alone. The mean age in the sample is 55.9 (SD 21.8) years. The mean age of patients who died of COVID-19 is significantly higher than that of those who did not, at 64.1 (SD 19.6) years against 40.8 (SD 16.9) years, respectively. Men comprised 67.9% (144/212) of the sample. A sizeable 49.5% (105/212) of the sample suffered from a pre-existing condition, which is overrepresented, and 64.6% (137/212) of the sample ultimately died, rendering the final class balance highly skewed.

### Correlation Matrix of Features

Before analyzing the prediction model performance, [Figure 1](#) outlines the main cross-correlation of patient characteristics and their correlation with an outcome of death. We note that the most explanatory features raising mortality risk are age (correlation coefficient 0.51), whether a patient has a pre-existing chronic condition (correlation coefficient 0.59), and the number of pre-existing conditions (correlation coefficient 0.53). This is followed by particularly risk-elevating conditions, such as diabetes and hypertension, and specific symptoms of advanced disease progression, such as pneumonia and acute respiratory distress syndrome.

**Figure 1.** Correlation matrix of patient demographics, symptoms, and pre-existing conditions with each other and with an outcome of death. ARDS: acute respiratory distress syndrome; BPH: benign prostatic hyperplasia.



**Feature Importance Analysis**

As outlined in the methodology, dimensionality reduction techniques were applied to generate two extracted data sets, one with 7 features and one with 1 feature. The extraction was repeated at each cross-validation fold to avoid lookahead bias, making the final feature sets less auditable. In this section, we anticipate subsequent results by providing a brief overview of the 7 most salient features (Table 1) selected solely using mutual

information across the entire 212-patient sample rather than individual training folds.

We note that with the exception of fever, symptoms were not featured in the reduction, in favor of the increased importance of pre-existing conditions and age as a general all-encompassing feature. Among comorbidities, diabetes and hypertension stood ahead of the others in impact, while the overall number of concomitant comorbidities in a single patient was also significant.

**Table 1.** Features included in a reduced 7-variable data set derived using mutual information on the full 212-patient data set.

Feature	Univariate mutual information
Age	0.35
Number of chronic diseases	0.22
Presence of chronic diseases	0.20
Hypertension	0.19
Pneumonia	0.11
Fever	0.09
Diabetes	0.09

## Mutual Information Feature Reduction

This study compares the impact of two dimensionality reduction methods—mutual information and chi-square tests—on model performance. Table 2 outlines the out-of-sample performance of models trained on the full 25-feature data set compared to 7-feature and 1-feature variations extracted through mutual information. All metrics were calculated over multiple repetitions of 3-fold cross validation. Due to differences in class balance across folds and simulated repetitions, accuracy metrics are not necessarily a weighted average of their sensitivity and specificity.

We note that performance across all models and datasets is sound, with no accuracy below 79.2%. The best random forest classifier performed substantially above the best logistic classifier, with respective accuracies of 90.8% and 83.5%.

In assessing the impact of dimensionality reduction, we note that transitioning from 25 features to 7 improved the

performance of the random forest classifier (89.2% to 90.8% accuracy), while a minor (considering the extent of feature shrinkage) reduction in performance was observed in the logistic classifier (83.5% to 79.2%). The latter may be overstated by the model's decision threshold, as the AUC decrease was minor (88.6% to 88.4%).

Finally, extreme reduction to a single most important attribute—in most folds, age—resulted in substantially reduced performance in the random forest classifier (89.2% to 80.1% compared to the full data set baseline) but more muted loss in the logistic classifier (83.5% to 81.5%).

All models were drawn from Python's scikit-learn libraries. For reproducibility, random forest models were run with 100 estimator trees and a 2-sample minimum split criterion, while logistic models were run on default parameters with no regularization.

**Table 2.** Mortality prediction performance of selected classifiers on various reduced data sets extracted via mutual information.

Model and data set granularity	Average values across folds (%)			
	Specificity <sup>a</sup> (95% CI)	Sensitivity <sup>a</sup> (95% CI)	Accuracy <sup>a</sup> (95% CI)	AUC <sup>b</sup> (95% CI)
<b>Random forest</b>				
25-feature data set	83.2 (80.1-86.3)	89.1 (86.8-91.4)	89.2 (88.0-90.4)	96.3 (95.9-96.6)
7-feature data set	88.3 (86.2-90.6)	90.0 (88.3-91.6)	90.8 (89.8-91.7)	95.0 (94.4-95.5)
1-feature data set	84.9 (83.3-86.2)	76.8 (74.9-78.7)	80.1 (79.8-81.7)	88.1 (87.1-89.0)
<b>Logistic regression</b>				
25-feature data set	82.9 (79.9-85.9)	79.6 (76.0-83.2)	83.5 (81.9-85.1)	88.6 (87.5-89.7)
7-feature data set	86.5 (83.9-89.1)	70.3 (65.4-75.2)	79.2 (76.9-81.5)	88.4 (87.4-89.4)
1-feature data set	80.3 (79.4-81.3)	80.7 (79.3-82.0)	81.5 (81.0-82.0)	84.2 (83.4-84.9)

<sup>a</sup>Reported performance metrics represent averages across multiple simulations of 3-fold cross validation and, due to class balance variation between folds, accuracy metrics are not always a weighted average of their sensitivity and specificity.

<sup>b</sup>AUC: area under the curve obtained from the receiver operating characteristic curve.

## Chi-Square Feature Reduction

The impact of mutual information having been assessed, Table 3 outlines the out-of-sample performance of models training on reduced data sets extracted via chi-square significance rather than mutual information.

We note that the trends are generally similar between reduction methods, but some important divergences are present. Random forest performance improvement in transitioning from 25

features to 7 is larger when extracting features through chi-square significance, with accuracy now improving from 89.2% to 92.5%. Performance loss in the logistic classifier is also less severe, falling from 83.5% to only 79.8% while the AUC increases (from 88.6% to 89.5%).

Performance differentials in transitioning to a single feature data set are similar to those summarized using mutual information.

**Table 3.** Mortality prediction performance of selected classifiers on various reduced data sets extracted via chi-square significance.

Model and data set granularity	Average values across folds (%)			
	Specificity <sup>a</sup> (95% CI)	Sensitivity <sup>a</sup> (95% CI)	Accuracy <sup>a</sup> (95% CI)	AUC <sup>b</sup> (95% CI)
<b>Random forest</b>				
25-feature data set	83.2 (80.1-86.3)	89.1 (86.8-91.4)	89.2 (88.0-90.4)	96.3 (95.9-96.6)
7-feature data set	90.7 (89.1-92.3)	92.0 (91.0-92.9)	92.5 (91.9-93.0)	95.5 (95.2-95.8)
1-feature data set	84.8 (83.3-86.2)	77.6 (76.6-78.6)	81.1 (80.7-81.6)	88.5 (88.1-89.0)
<b>Logistic regression</b>				
25-feature data set	82.9 (79.9-85.9)	79.6 (76.0-83.2)	83.5 (81.9-85.1)	88.6 (87.5-89.7)
7-feature data set	90.4 (89.1-91.8)	69.9 (64.9-74.8)	79.8 (77.3-82.1)	89.5 (88.4-90.6)
1-feature data set	80.2 (79.4-81.0)	80.9 (79.8-82.1)	81.6 (81.1-82.1)	84.2 (83.5-84.9)

<sup>a</sup>Reported performance metrics represent averages across multiple simulations of 3-fold cross validation and, due to class balance variation between folds, accuracy metrics are not always a weighted average of their sensitivity and specificity.

<sup>b</sup>AUC: area under the curve obtained from the receiver operating characteristic curve.

## Discussion

### Principal Findings

Models trained on a high-quality 212-patient data set containing 25 symptom, comorbidity, and demographic variables showed strong detection ability, with the highest-performing model achieving specificity of 90.7% (95% CI 89.1%-92.3%) and sensitivity of 92.0% (95% CI 91.0%-92.9%). The impact of dimensionality reduction on performance was explored by extracting features, first via mutual information and second via chi-square significance, to create two reduced data sets, one containing 7 features and one containing a single feature.

Application of either mutual information or chi-square significance to reduce the data set to 7 features resulted in improvement of the predictive performance when using a random forest classifier and in mixed performance variation when using a logistic classifier. These results strongly suggest that dimensionality reduction can be beneficial to model performance or can provide reduced dependence on large feature sets at minimal cost to performance. We also note that all models tested on either the 25-feature or 7-feature data sets performed roughly in line with or not much worse than existing studies drawing on a plethora of additional blood markers and vitals [12-15].

Further analyzing the effect of dimensionality reduction between reduction methods showed disparity in the final performance impact. Comparing the performance of a random forest classifier trained on 25 features against that trained on 7 features derived through feature extraction, mutual information reduction resulted in an increase in accuracy from 89.2% to 90.8%, compared to 92.5% when employing chi-square methods. In the logistic model, mutual information resulted in a decrease in accuracy from 83.5% to 79.2%, compared to 79.8% using chi-square methods; additionally, it should be noted that although the AUC decreased from 88.6% to 88.4% in the former case, it substantially increased to 89.5% in the latter. This suggests there can be significant variation in performance based on the choice of reduction methods, and it is strongly advised that in future studies—especially those containing hundreds of features

initially sifted by feature extraction methods—a wide array of dimensionality reduction methods should be employed and tested as hyperparameters when cross-validating models as opposed to arbitrarily selecting one ex ante.

Beyond reduction to 7 features, an extreme reduction to a single most salient feature—often age—was tested to highlight the ability of the models to generalize in even the most constraining scenario; this resulted in decreased but still sound predictive performance and demonstrated the high baseline predictive power that age or other salient comorbidity variables have as standalone variables in mortality detection, with remaining variables providing marginal additional explanatory power.

Variable importance using mutual information was explored by reporting the 7 most salient features; symptom data—with the exception of fever—were found to be less impactful than comorbidities (particularly hypertension and diabetes), age, and a proxy for the number of concomitant comorbidities. Studies [22] with a similar focus on feature extraction confirm the importance of these same selected features, with additions such as chronic obstructive pulmonary disease and heart failure, although variations in importance can be noted by age strata.

The classifiers explored in this study have been shown to have very high mortality prediction accuracy, confirming the utility of this class of models for patient prognosis and triage. In hospital settings, patient histories at admission include all relevant attributes necessary to obtain a mortality prediction from our classifiers, resulting in timely assignment to relevant wards based on risk level, allocation of additional monitoring equipment, consideration for additional screenings, escalation to a secondary prediction model with more elaborate features, or allocation of scarce or experimental preventive treatment.

### Limitations

The study's main limitations are the period its data relate to, which spans the first 4 months of the COVID-19 pandemic and does not include information on new variants of concern or current dominant strains, and the relatively even class balance in the sample, with 64.6% of the 212 patients (n=137) dying from disease progression. The latter in particular means that the



performance reported above, while representative, could experience a greater disparity in sensitivity and specificity balance when testing on the more uneven class balance implied by the current COVID-19 mortality rate.

## Conclusion

This study has confirmed the substantial accuracy that machine learning models can bring to the early detection of mortality in

COVID-19. Additionally, we demonstrated that dimensionality reduction can at best further increase said accuracy or at worst materially aid hospitals in reducing the number of diagnostic variables needed before obtaining usable predictions with only marginal costs to performance.

## Conflicts of Interest

None declared.

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## Abbreviations

**AUC:** area under the curve

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Original Paper

# Influence of Mass Media on Italian Web Users During the COVID-19 Pandemic: Infodemiological Analysis

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## Abstract

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**Background:** Concurrently with the COVID-19 pandemic, the world has been facing a growing infodemic, which has caused severe damage to economic and health systems and has often compromised the effectiveness of infection containment regulations. Although this infodemic has spread mainly through social media, there are numerous occasions on which mass media outlets have shared dangerous information, giving resonance to statements without a scientific basis. For these reasons, infoveillance and infodemiology methods are increasingly exploited to monitor information traffic on the web and make epidemiological predictions.

**Objective:** The purpose of this paper is to estimate the impact of Italian mass media on users' web searches to understand the role of press and television channels in both the infodemic and the interest of Italian netizens in COVID-19.

**Methods:** We collected the headlines published from January 2020 to March 2021 containing specific COVID-19-related keywords published on PubMed, Google, the Italian Ministry of Health website, and the most-read newspapers in Italy. We evaluated the percentages of infodemic terms on these platforms. Through Google Trends, we searched for cross-correlations between newspaper headlines and COVID-19-related web searches. Finally, we analyzed the web interest in infodemic content posted on YouTube.

**Results:** During the first wave of COVID-19, the Italian press preferred to draw on infodemic terms (rate of adoption: 1.6%-6.3%) and moderately infodemic terms (rate of adoption: 88%-94%), while scientific sources favored the correct names (rate of adoption: 65%-88%). The correlational analysis showed that the press heavily influenced users in adopting terms to identify the novel coronavirus (cross-correlations of  $\geq 0.74$  to  $\leq 0.89$ ,  $P$  value  $< .001$ ; maximum lag=1 day). The use of scientific denominations by the press reached acceptable values only during the third wave (approximately 80%, except for the television services Rai and Mediaset). Web queries about COVID-19 symptoms also appeared to be influenced by the press (best average correlation=0.92,  $P < .007$ ). Furthermore, web users showed pronounced interest in YouTube videos of an infodemic nature. Finally, the press gave resonance to serious "fake news" on COVID-19, which caused pronounced spikes of interest from web users.

**Conclusions:** Our results suggest that the Italian mass media have played a decisive role in spreading the COVID-19 infodemic and addressing netizens' web interest, thus favoring the adoption of terms that are unsuitable for identifying COVID-19. Therefore, the directors of news channels and newspapers should be more cautious, and government dissemination agencies should exert more control over such news stories.

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## KEYWORDS

COVID-19; Google Trends; infodemiology; infoveillance; infodemic; media coverage; mass media influence; mass media; social media

## Introduction

### Background

The COVID-19 pandemic has placed a strain on economies and health systems worldwide [1,2]. As of March 21, 2020, the death toll had reached approximately 2.71 million, and the trend continued to grow [3]. In addition to the disease, the world faced a growing infodemic that is capable of causing damage of equal severity [4]. The role of social and traditional media in spreading disinformation and misinformation has now been recognized in a substantial number of literature reports [5-10]. Indeed, numerous conspiracy hypotheses have circulated on the web regarding the imposition of lockdowns as tools of social control, the anthropogenic origin of the virus, its remedies and cures, and vaccines. This type of “fake news” can compromise compliance with antipandemic regulations and generate vaccine hesitancy [11-14]. Moreover, less obvious but equally incisive aspects exist within an infodemic. In particular, the assignment of scientific denominations to a new pathology represents a historically known public health issue [15]. For example, names such as “swine flu” and “Middle Eastern respiratory syndrome” have unwittingly contributed to fomenting racism and causing economic damage to specific industries [16]. The adoption of inappropriate nomenclature in the medical field has led to the administration of incorrect drugs; moreover, during the COVID-19 pandemic, the generic name “coronavirus” led the public to consult material relating to previous coronaviruses [17-19]. Some of the consequences are even unpredictable; for example, the name “coronavirus” has also been mistakenly associated with the Mexican firm Corona [16,20]. As shown by Su et al [21], mass media outlets such as newspapers and television news have played a relevant role in the proliferation of the COVID-19 infodemic, contributing to the resonance of stigmatizing names such as “Chinese virus.” In this scenario, Italy—the nation most affected by COVID-19 between the end of February and mid-March 2020 [2]—suffered damage from a severe infodemic. Although a large amount of misinformation has circulated on social networks, numerous television personalities, politicians, media outlets, and even scientists have contributed to spreading infodemic monikers, conspiracy theories (eg, the unproved laboratory origin of SARS-CoV-2), and misleading health-threatening information (eg, COVID-19 is like seasonal influenza) [9,10]. This climate of uncertainty immediately compromised trust in institutions (whose nonpharmacological interventions were often catalogued as exaggerated), fueled racism toward Chinese individuals residing in Italy, and altered the risk perception of the population. Hence, the Italian people have been fractionated between deniers,

conspiracy theorists, reductionists, and people who are aware of the disease's dangers.

### Countermeasures to the Infodemic

The COVID-19 situation requires an infoveillance system that is effective and efficient. The purpose of this system is not only to monitor information but address the community's concerns [14]. Specifically, the discipline that deals with the determinants and distribution of health information and misinformation is called *infodemiology*, from the union of the terms “information” and “epidemiology.” Because the internet has accelerated and expanded the amount of information circulating globally, the primary purpose of infodemiology is to catalog disinformation (ie, the voluntary sharing of infodemic material) and misinformation (ie, the involuntary sharing of infodemic material) by seeking to identify the sources of and reasons for these phenomena [4,9,10]. During the COVID-19 pandemic, scientists have exploited different infodemiological approaches, ranging from machine learning to questionnaires [22,23]. However, these methods, although innovative and/or precise, need long implementation times before providing usable results. For this reason, a large part of the scientific community has conducted surveys through Google Trends, a tool developed by Google LLC that allows the user to obtain quantitative data on the web search volumes related to specific keywords in specific geographical areas during a preselected time period [24]. Google Trends dramatically simplifies and speeds data collection on netizens' web interests, and it has been used to conduct medical, psychological, sociological, epidemiological, and economic investigations [25]. However, many authors have questioned its reliability because of the mass media's influence on web searches [25-28]. Although this influence may jeopardize the adoption of Google Trends in many research areas, it remains suitable for conducting infodemiological investigations; in fact, if certain conditions are met (ie, high internet penetration, high Google use, and data set stability), the relative search volumes (RSVs) on Google Trends faithfully reflect the interests of a population [25]. Moreover, Sato et al [29] proposed a new method to evaluate, quantify, and eliminate the media disturbance in data sets.

### Research Questions

The internet represents a fast, user-friendly means to seek health-related information [9,10,30-32]. During a pandemic or any major health crisis, the need for quality web information is more pressing than ever; fear, anxiety, stress, and confusion due to the overabundance of often conflicting or dramatic news increases the consultation of web sources to seek remedies or

reassurance [4,9,32-37]. As discussed above, the mass media plays an important role in managing an infodemic and conditioning web users' behavior. Considering the vast infodemic that affected Italy during the COVID-19 crisis, this paper aims to answer the following research questions:

- R1: How much has the Italian media influenced Italian web users in the adoption of terms to identify COVID-19?
- R2: How much has the Italian media influenced the web interest in COVID-19?
- R3: Among the content disseminated by mass media channels, how much interest was aroused by infodemic news?

Alongside these questions, our analysis can provide further evidence on the reliability of Google Trends for studies other than infodemiological ones.

## Methods

### Design

To evaluate the impact of the media on Italian users' web interest, we compared the use of specific keywords by the main Italian media with the RSVs of the same keywords, looking for significant and substantial (cross-)correlations, triggering events, and similarities in keyword adoption rates. Furthermore, we

compared the use of scientific and infodemic names by the most-consulted newspapers and news channels with those of other platforms, such as PubMed, Google, and the website of the Italian Ministry of Health.

### Data Collection

Given the heterogeneity of the data collected, different methods were used for each type of source investigated. Specific keywords were selected in specific periods according to Table 1.

These keywords have been carefully selected through a previous literature analysis to represent the most adopted terms to identify SARS-CoV-2 and the consequent disease, COVID-19 [9,10]. We exploited the *infodemic scale* (I-scale) to assess the infodemicity of the terms examined: each moniker was assigned 1 to 2 points per category (ie, generic, misinformative, discriminatory, deviant, other specificities), ranging from 0 to 10. Based on the sum of the I-scale scores, the infodemic monikers were classified as follows: not infodemic (0), slightly infodemic (1), moderately infodemic (2-4), highly infodemic (5-8), and extremely infodemic (9-10). Further details on the use of the I-scale are given in [10].

Because search algorithms do not work in the same way on all databases, we provide below a summary schema of our collecting procedure.

**Table 1.** List of keywords searched on web-based platforms.

Investigated period	Period number	Searched keywords
Jan 1-Feb 13, 2020	1	<i>2019-ncov, novel coronavirus, coronavirus, chinese virus, chinese coronavirus</i>
Feb 11-May 18, 2020	2	<i>sars-cov-2, covid-related (ie, covid, covid 19, covid19, covid-19), novel coronavirus, coronavirus</i>
May 19, 2020-Mar 17, 2021	3	<i>sars-cov-2, covid-related (ie, covid, covid 19, covid19, covid-19), novel coronavirus, coronavirus</i>

### PubMed

We searched PubMed [38] for each keyword individually and counted the results found. The *coronavirus* query also contained the results of the *novel coronavirus* query; therefore, calling the two set dimensions N and n, respectively, we calculated the number of results for the *novel coronavirus* query by subtracting n from N. We chose this source because it represents the largest medical database in the world.

### Italian Ministry of Health

We searched the website of the Italian Ministry of Health [39] for each keyword individually and counted the results found. Specifically, we counted the number of official press releases per keyword. We chose this source because it is the official government website of the Italian Ministry of Health.

### Google

We searched Google [40] for each keyword individually and counted the results found. In this case, we ensured that each webpage contained the specified keyword by including the latter in quotes (eg, "*coronavirus*"). We chose this source because Google represents the most adopted web engine in Italy [41].

### Google Trends

We searched Google Trends for each keyword individually. We set the search category to "All categories" and downloaded the data as .csv files. We set the geographical region to "Italy" and analyzed the national web searches.

### La Repubblica

We searched *La Repubblica* [42] for each keyword individually and counted the results found. Specifically, we retrieved the number of headlines starting on January 11, 2020, day by day (ie, from January 11 to 12, January 11 to 13, and so on). After that, we calculated the daily increment by subtracting the values of 2 consecutive days. We used the "advanced search" and "exact search" filters. We chose this source because it represents the second most read newspaper in Italy [43].

### Il Corriere della Sera

We searched for each keyword on *Il Corriere della Sera* [44] individually and counted the results found. Specifically, we retrieved the number of headlines starting on January 11, 2020, day by day (ie, from January 11 to 12, January 11 to 13, and so on). After that, we calculated the daily increment by subtracting the values of 2 consecutive days. Because the *coronavirus* query

also contained the results of the *novel coronavirus* query, calling the two set dimensions  $N$  and  $n$ , respectively, we calculated the number of results for the *novel coronavirus* query by subtracting  $n$  from  $N$ . We chose this source since it represents the most read newspaper in Italy [43].

### **TitoliGiornali (Other Newspapers)**

We searched the website TitoliGiornali [45] for each keyword individually and counted the results found. Specifically, we counted the number of headlines per keyword. We chose this source because it includes the headlines of a wide variety of Italian newspapers.

### **Rai (Google News)**

We searched Google [40] for each keyword individually, adding the term *rai* to each query, selected the item “Google News,” and counted the results found. We chose this source because Rai is the main Italian public television channel.

### **Mediaset (Google News)**

We searched Google [40] for each keyword individually, adding the term *mediaset* to each query, selected the item “Google News,” and counted the results found. We chose this source because Mediaset is the main Italian private television channel.

### **YouTube**

We searched YouTube [46] for each keyword individually and counted the results found. We added specific YouTube channel names to each query. We used the “sort by number of views” filter. We chose this source because it represents the largest video-sharing platform in the world.

## **Statistical Analysis**

### **Linear Regression**

When data were normally distributed, the angular coefficient  $m$  of the interpolating line was calculated to evaluate the importance of a trend. Moreover, Pearson  $R$  and adjusted Pearson  $*R$  coefficients were calculated.

### **Mann-Kendall Test**

To detect trends, after an initial graphical analysis, the Mann-Kendall test was used. Furthermore, the trend relevance was evaluated with the Sen slope ( $SS$ ).

### **Mean Values**

All average values are presented in the form of mean (standard error of the mean [SEM]). The variability of a data set was evaluated through the percentage standard deviation ( $SD\%$ ), calculated as the ratio between the standard deviation and the mean value multiplied by 100.

### **Normality Test**

To verify the distributive normality of a data set, we used the Shapiro-Wilk test plus a graphical check of histograms and quantile-quantile diagrams.

### **Percentage Increases**

We have indicated the percentage increases with the symbol  $\Delta\%$ .

### **Percentage Differences**

We have indicated the percentage differences with the symbol  $\delta\%$ .

### **Pearson and Spearman Cross-Correlations**

When the data sets were normally distributed, the Pearson correlation  $R$  was used; otherwise, the Spearman correlation  $r$  was used. The correlation strength was assessed independently of the  $P$  values. The lag range was set at a maximum of 50% of the data set size. The Olkin-Pratt method was used to calculate the weighted mean of a list of correlations ( $\rho$ ).

### **P Values**

$P$  values were used as a continuous measure of the strength of evidence against the null hypothesis.

### **Seasonalities**

To evaluate time-series seasonalities, we used a graphical check and the Time Series Analysis tool of the XLSTAT package (Addinsoft). In particular, we divided each signal into trend, seasonal, and random components. Finally, we calculated the autocorrelogram plot.

### **Welch t Test**

When the data sets were found to be normally distributed, the Welch  $t$  test was used. Furthermore, when the size of the analyzed sets exceeded 30 elements, the central limit theorem was exploited to use the Welch  $t$  test even with data that were not normally distributed [47,48].

### **Software**

Excel 2020 (Microsoft Corporation) was used for data analysis. In addition, the Real Statistics and XLSTAT packages were used.

## **Results**

### **Media Influence on Italian Web Users**

At the beginning of the COVID-19 pandemic, we found a substantial difference in the adoption of the scientific names “2019-nCoV” and “novel coronavirus” against the more infodemic term “coronavirus” between the most read Italian newspapers and sources such as Google and PubMed (Table 2).

Moreover, although the streaming video portals RaiPlay and MediasetPlay by Rai and Mediaset (the main Italian television broadcasters) did not show any results for the item *2019-ncov*, they produced several results for the queries *Chinese virus* and *Chinese coronavirus*. These websites also have special sections entitled “Coronavirus.” According to Google results from January 1 to February 13, 2020, the same websites used the term *coronavirus* in 93.8% of article titles, compared to 6.3% for *2019-ncov* and 0% for *novel coronavirus*. In this context, the Italian web users immediately preferred the term *coronavirus* (mean  $RSV=14$ ) over all the others ( $\forall RSV<1$ ), showing values comparable to those of the most relevant newspapers and television broadcasters in Italy. Moreover, *Chinese virus* and *Chinese coronavirus* were the second most commonly used keywords during this phase (mean  $RSV=22$  vs mean  $\forall RSV\leq 1$ ,

excluding the query *coronavirus*), showing further similarities with the Italian media.

Considering the keyword *coronavirus*, the weekly-cumulative RSV showed a pronounced correlation with its weekly

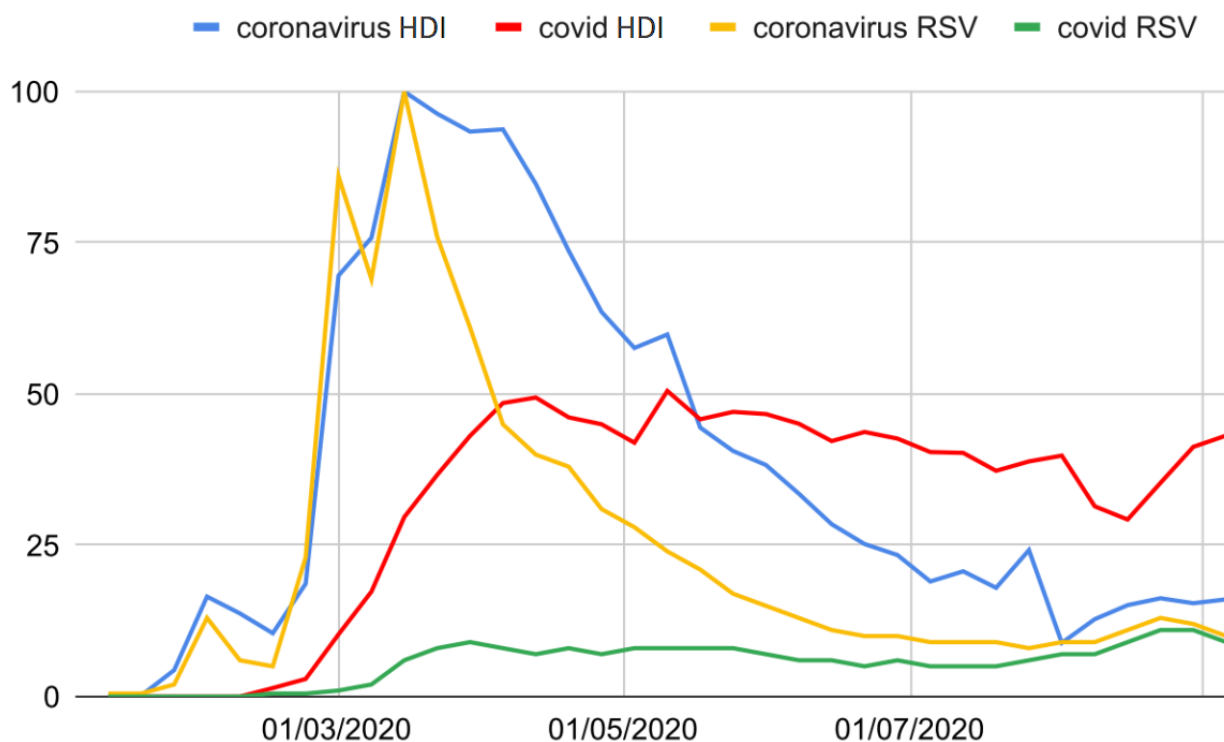
cumulative use by the newspaper *La Repubblica* (Figure 1). The best overall cross-correlation was  $r=0.89$  (95% CI 0.80-0.95),  $P<.001$ ; lag=0 weeks.

**Table 2.** Rates of adoption of COVID-19–related terms at the start of the pandemic (January 1 to February 13, 2020).

Source	Rate of adoption (%)			
	2019-ncov (infodemic scale: 0)	Novel coronavirus (infodemic scale: 1)	Coronavirus (infodemic scale: 4)	Chinese (corona)virus (infodemic scale: 9)
PubMed	42.7	45.2	12.1	<0.1
Italian Ministry of Health	11.8	52.9	35.3	0.0
Google	29.3	25.9	27.6	17.2
<i>La Repubblica</i>	0.2	5.3	92.9	1.6
<i>Il Corriere della Sera</i>	1.3	4.7	87.7	6.3
Other newspapers <sup>a</sup>	0.5	0.1	93.9	5.4
Rai (Google News)	1.6	0	96.8	1.6
Mediaset (Google News)	0	0	97.8	2.2

<sup>a</sup>This item includes *Il Sole 24 Ore*, *Il Fatto Quotidiano*, *Il Giornale*, and *La Stampa*.

**Figure 1.** Comparison of the weekly RSVs of the keywords *coronavirus* (yellow) and *covid* (green) with the number of times the terms were adopted by the newspaper *La Repubblica* (blue and red, respectively) from January 1 to September 6, 2020. All values were normalized to 100. HDI: headlines daily increase; RSV: relative search volume.



In the period from the week of January 13 to 19 to that of the peak during March 9 to 15, the average percentage discrepancy between all data pairs was significantly smaller than in the following months up to August ( $\delta\%=51.4$ ,  $t=3.8$ ). By restricting the analysis to the period from January 19 to March 12, 2020 (initial phase), to observe daily cumulative values (Figure 2), 5 trends with significant correlates were observed (Multimedia

Appendix 1). The unlagged initial phase correlation was  $r=0.93$  (95% CI 0.88-0.96),  $P<.001$ , while the optimum cross-correlation was  $r=0.94$  (95% CI 0.91-0.97),  $P<.001$ , lag=1 day. From March 13 onward, a decreasing trend was observed for both variables until the week of August 2 to 8, 2020.

For *Il Corriere della Sera*, the results were slightly different: first, the percentage discrepancies between the RSV and daily

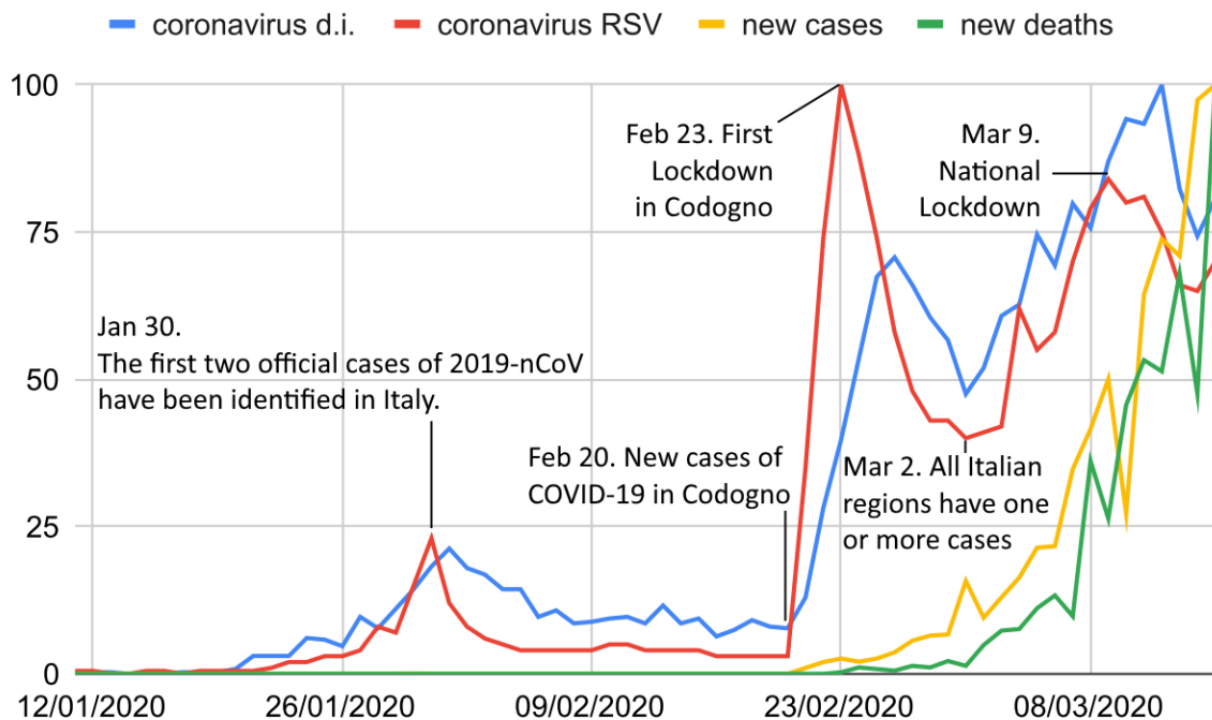
increase in headlines for *coronavirus* were statistically confident ( $\delta\% = 7.6$ ,  $t = 0.5$ ); second, among the 6 investigated correlations, some were weak (Multimedia Appendix 1). However, the optimum initial phase correlation was  $r = 0.84$  (95% CI 0.71-0.92),  $P < .001$ , lag = 0 days, and the best overall cross-correlation was  $r = 0.85$  (95% CI 0.73-0.92),  $P < .001$ , lag = 0 weeks.

After the introduction of the scientific names SARS-CoV-2 and COVID-19, the use of the moderately infodemic and noninfodemic or slightly infodemic names partially changed compared to the previous period (Table 3). However, even in this case, all the media are characterized by greater use of the generic name “coronavirus.”

In the period from February 11 to May 18, 2020, the terms SARS-CoV-2 and COVID-related were used differently by Italian users ( $\nabla\text{RSV} < 1$  vs mean RSV = 64, respectively). The term

COVID-related was used less frequently than coronavirus until the second week of September ( $\Delta\% = 404$ ,  $t = 5.0$ ). Before the second week of May, the weekly adoption of the term COVID-related by *La Repubblica* was significantly lower than that of the term coronavirus ( $\nabla\Delta\% \in [18; 642]$ ). Furthermore, the percentage discrepancies between the RSV and daily increase in headlines for COVID-related were substantial (mean  $\Delta\% = 509$ , SEM 32, in the whole investigated period). Nonetheless, correlations were found from the week of February 10 to 16 to that of July 20 to 26 (optimum overall cross-correlation:  $r = 0.74$ , 95% CI 0.49-0.88;  $P < .001$ ; lag = 0 weeks). Finally, among all the COVID-19-related terms, covid was the one most exploited by users despite the more appropriate and specific covid-19 (mean RSV = 47 vs mean RSV = 2). The results for *Il Corriere della Sera* were similar (mean RSV  $\Delta\% = 773$ , SEM 69; optimum overall cross-correlation:  $r = 0.73$ , 95% CI 0.48-0.88;  $P < .001$ ; lag = 0 weeks).

**Figure 2.** Comparison between the daily RSVs (red) of the keyword *coronavirus*, new COVID-19 cases, and COVID-19 deaths, and the number of times they were adopted by the newspaper *La Repubblica* (blue) from January 11 to March 15, 2020. All values are normalized to 100. The black lines represent the beginning or the end of a trend. d.i.: daily increase; RSV: relative search volume.





**Table 3.** Rates of adoption of COVID-19-related terms during the lockdown (February 11 to May 18, 2020).

Source	Rate of adoption (%)			
	SARS-CoV-2 (infodemic scale: 0)	COVID (and related) (infodemic scale: 1)	Novel coronavirus (infodemic scale: 1)	Coronavirus (infodemic scale: 4)
PubMed	27.5	38.6	28.8	5.1
Italian Ministry of Health	1.3	78.2	9.0	11.5
Google	24.3	28.4	25.7	21.6
<i>La Repubblica</i>	0.6	33.2	1.3	64.8
<i>Il Corriere della Sera</i>	1.2	44.0	1.0	53.8
Other newspapers <sup>a</sup>	1.6	39.9	1.4	57.1
Rai (Google News)	0.0	15.4	0.6	84.0
Mediaset (Google News)	0.0	7.0	0.7	92.3

<sup>a</sup>This item includes *Il Sole 24 Ore*, *Il Fatto Quotidiano*, *Il Giornale*, and *La Stampa*.

### Evidence Supporting Causation

Noncausal correlations could be due to stochastic phenomena (hypothesis a) or other triggering phenomena (spurious correlations, hypothesis b). We found up to 6 significant consecutive trends (Mann-Kendall mean  $P=0.007$ , SEM .006;  $\sqrt{P}<.03$ ) and as many strong correlations between RSVs and newspaper headlines (Multimedia Appendix 1). Let us consider hypothesis a, thus supposing that the correlations found are due to chance. A realistic estimate was obtained by generating random values using the random number generator provided by Haahr [49]: in particular, by generating 50 data series composed of 6 numbers and looking for 1225 Pearson and Spearman correlations between them, significant correlations (ie, close to the threshold  $\alpha=0.05$ ) were obtained in approximately 6.5% of cases; consequently, the probability of obtaining 6 consecutive significant correlations was  $(6.5/100)^6 < 10^{-6}$ . Furthermore, the hypothesis investigated was targeted, avoiding the problem of the look-elsewhere effect. Indeed, this targeting was based on data from this paper (eg, the rate of adoption of COVID-19-related terms) and previous works. Hence, these correlations can be considered to be not due to chance.

Now, suppose that both RSVs and newspaper headlines were causally influenced by a third quantity  $x$ . This quantity must have been linked to the COVID-19 epidemic. For this reason, we started searching for correlations between RSV and COVID-19 cases and deaths (C19). As shown in Figure 2, the trend of C19 shows a monotonic increase, while that of the web searches is not monotonic; this precludes the occurrence of global correlations. Thus, we start assuming the existence of local cross-correlations of type *COVID-19 symptoms*  $\rightarrow$  *RSV*  $\rightarrow$  *C19* (ie, such that web searches are predictive of C19). Based on the incubation and swab analysis periods, the average lag between web searches and symptom identification should be around 6 to 9 days [50-52]; nevertheless, Figure 2 shows that the first RSV trend precedes the growth of COVID-19 cases by 1 month. In contrast, suppose now a causal cross-correlation of type *C19*  $\rightarrow$  *RSV*. Considering the time-lapse from February 20 to March 13, 2020, we found 3 distinct groups of correlations (2 positives and 1 negative, with  $0.83 \leq |r| \leq 0.98$ ,  $\forall P \leq .02$ ) (Figure

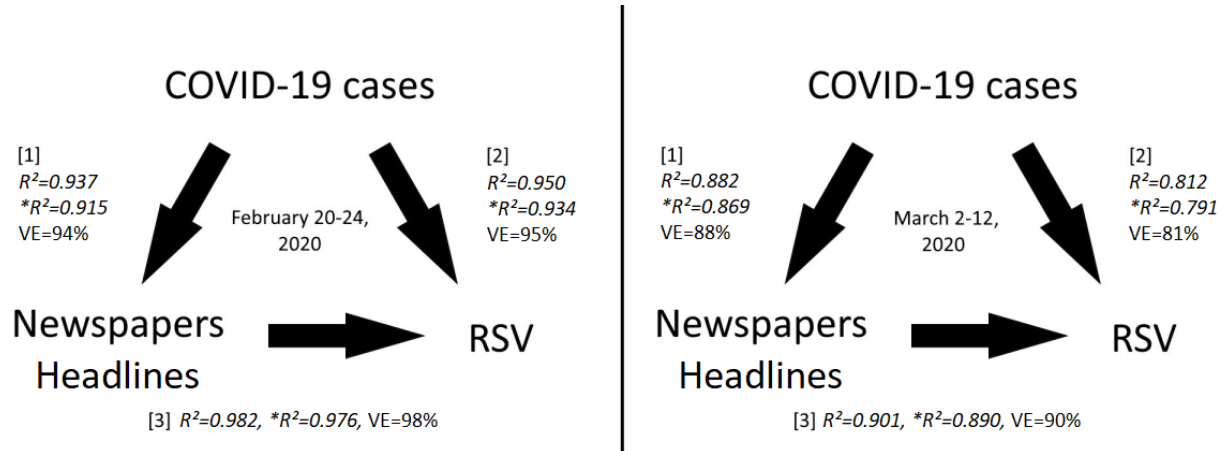
2). After that, although COVID-19 cases continued to rise until April, both the RSV and “coronavirus” newspaper headlines started to decline. Alongside this, we performed multiple regression analyses between the quantities *COVID-19 cases*, *newspaper headlines*, and *RSV* following the scheme shown in Figure 3. These results also suggest a greater influence of newspapers on RSV, although there is a marked dependence among all the variables. By restricting the data sets to the periods where a positive correlation was found and improperly assuming independence between the normalized variables *COVID-19 cases* ( $X_1$ ) and *newspaper headlines* ( $X_2$ ), we calculated the least squares multiple regression plan for the *RSV* ( $y$ ), obtaining  $y = 16X_1 + 1.7X_2 - 17$  and  $y = 0.05X_1 + X_2 - 15$ .

Although it is clear that in some cases, both COVID-19 cases and newspapers contributed to conditioning Italian web users, COVID-19 cases had a more temporary and discontinuous effect than newspaper headlines. At any rate, it must be considered that even this type of news is disseminated by disclosure sources, which can be official government sources (ie, the Italian Ministry of Health, hypothesis I), private websites, blogs, and social networks (hypothesis II), or media (hypothesis III). Hypothesis I assumes that all citizens, once the COVID-19 issue became known, consulted official sources. Considering that the official Italian Government Printing Offices used, in the vast majority of cases, fewer infodemic names (83.5%), and the amount of news they reported was limited and not correlated with RSV (eg, from January 1 to March 12, the Ministry of Health produced 91 articles, compared to tens of thousands by media outlets), we can exclude this hypothesis. Hypothesis II assumes that the RSV was influenced by unofficial sources not directly related to press and newscasts. Because press and newscasts have their own independent sources and we already excluded every random correlation as well as any global correlations with COVID-19 cases, we can only suppose a causal global process of the type *media*  $\rightarrow$  *private websites, blogs, social networks*  $\rightarrow$  *RSV*, which confirms the fundamental role of media. Therefore, the only hypothesis with empirical evidence is that media, such as press and newscasts, have predominantly determined the web search trends and the terms used to conduct these searches (ie, Hypothesis III). Further support for this conclusion is provided by the fact that RSV peaks are always

associated with highly impacting media events, such as lockdowns and outbreaks (Figure 2). Finally, web searches

related to COVID-19 symptoms followed a very similar trend (Multimedia Appendix 1).

**Figure 3.** Causal implications scheme and linear regression results. RSV: relative search volume; VE: variability explained.



**COVID-19 Web Interest During the Second Wave**

The *coronavirus + covid* query had a near-stationary RSV between early June and early August (Mann-Kendall  $P=.14$ ,  $SS=-0.09$ ,  $SD\%=8.3$ ). This was much less pronounced than during the first wave ( $\Delta\%=-71.4$ ,  $t=-14.2$ ) due to the sharp decrease in COVID-19 cases and the easing of containment measures. From August 2020 to March 17, 2021, web interest in COVID-19 remained significantly lower than that during the first lockdown ( $\Delta\%=-57.8$ ,  $t=-4.2$ ), thus showing spikes of RSV at the start of the second wave ( $RSV_{max}=23$ , SEM 0.4, August 2020), a steep rise of cases from October 1, 2020, until around mid-November ( $RSV_{max}=35$ , SEM 0.7) and mid-February, anticipating the increase in infections at the end

of February by approximately 10 days ( $RSV_{max}=23$ , SEM 0.5). The use of the term *covid* surpassed that of the more generic and infodemic term *coronavirus* (59% vs 41% from September 2020 to March 2021, respectively). In contrast, the more technical term *SARS-CoV-2* was not adopted by web users ( $\forall RSV < 1$ ). On this occasion, as far as the adoption of COVID-19-related terms was concerned, strong differences were noticed between newspapers and other sources, including Rai and Mediaset (Table 4).

Although the use of COVID-19-related terms by newspapers exceeded that of the generic term *coronavirus* in May 2020, web users showed a delay of 4 months before doing the same. Finally, web users' interest in COVID-19 decreased by approximately 20% compared to that during the first wave.

**Table 4.** Rates of adoption of COVID-19-related terms during the lockdown (May 19, 2020, to March 17, 2021).

Source	Rate of adoption (%)			
	SARS-CoV-2 (infodemic scale: 0)	COVID (and related) (infodemic scale: 1)	Novel coronavirus (infodemic scale: 1)	Coronavirus (infodemic scale: 4)
PubMed	26.6	42.9	27.6	2.8
Italian Ministry of Health	0.9	90.9	1.8	6.4
Google	25.7	28.6	22.9	22.9
<i>La Repubblica</i>	0.9	76.5	0.3	22.3
<i>Il Corriere della Sera</i>	1.5	75.1	0.6	22.7
Other newspapers <sup>a</sup>	1.1	74.0	0.1	24.8
Rai (Google News)	0.5	49.3	0.0	50.2
Mediaset (Google News)	0.0	38.6	1.3	60.1

<sup>a</sup>This item includes *Il Sole 24 Ore*, *Il Fatto Quotidiano*, *Il Giornale*, and *La Stampa*.

**Web Users' Interest in Mass Media Infodemic Videos**

The YouTube channels of the following news broadcasts were investigated: Rai (4.08 million subscribers), LA7 Attualità (730,000 subscribers), MediasetPlay (605,000 subscribers), *La Repubblica* (576,000 subscribers), *Corriere della Sera* (145,000 subscribers), and Tgcom24 (52,700 subscribers). Only videos

with over 100,000 views were considered for analysis. The views of videos containing the keyword *coronavirus* were substantially higher than those of videos containing the keywords *COVID-related* and *sars-cov-2* (50.07 million views vs 8.51 million views,  $\delta\%=141.9$ ). Moreover, some of the videos with the most views had extremely infodemic titles, such as the following Italian headlines, here provided as their English

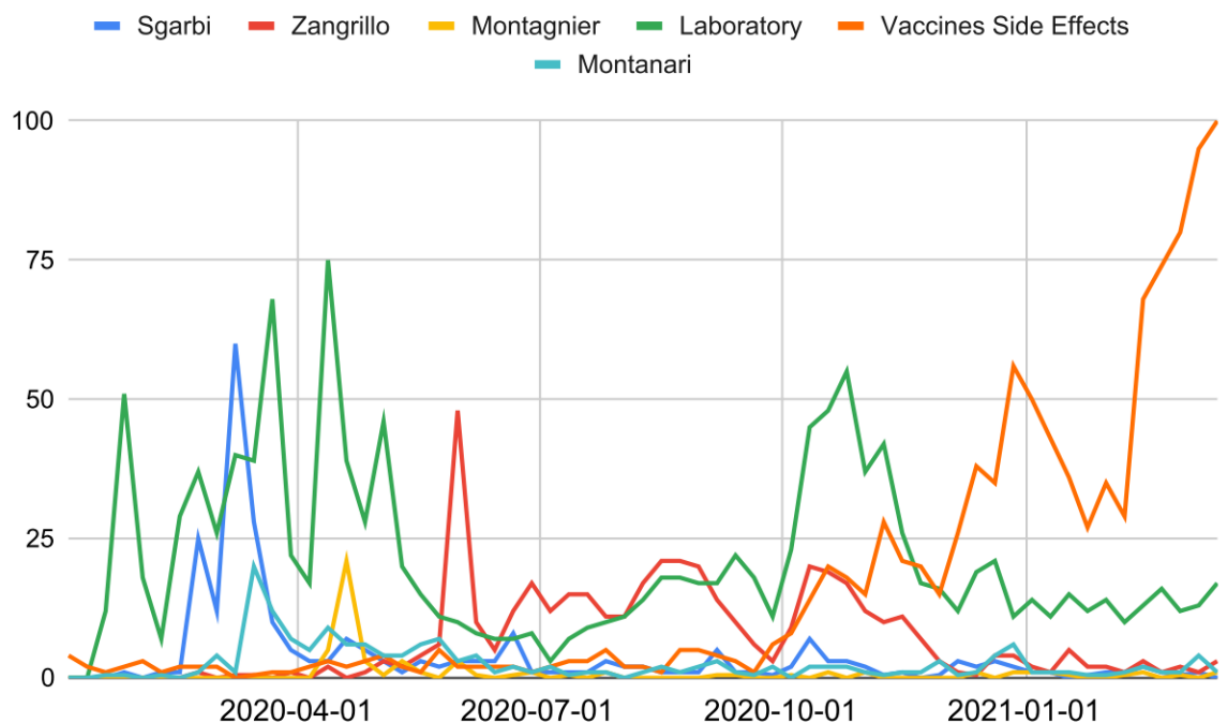
translations: “Covid does not exist” (621,945, first on La7 Attualità), “The 2015 Rai-Leonardo video on the virus created in China in the laboratory. The scientific community...” (401,648, fourth on *Il Corriere della Sera*, “Coronavirus, Vittorio Sgarbi: ‘It is not an epidemic because there is no risk of death’” (440,296, second on La7 Attualità), “Coronavirus, Sgarbi: The confinement of asymptomatic people is fascism” (396,144, sixth on *Il Corriere della Sera*), “Coronavirus, the Senate conference of ‘deniers’: In Italy, the virus no longer exists” (189,655, 47th on *La Repubblica*), “Covid, Prof. Roberto Bernabei: It’s a normal disease...” (141,233, 21st on La7 Attualità), “Coronavirus, the reassurance of the infectious disease specialist Matteo Bassetti: It’s not an infection...” (the video discusses the similarities between COVID-19 and common seasonal influenza; 203,347, 14th on La7 Attualità). Finally,

the presence of growing interest in information channels that disclose serious fake news must be taken into account. In particular, the YouTube channel ByoBlu (524,000 subscribers) often shares scientifically unjustified opinions of people who have become famous for their conspiratorial positions on COVID-19. However, an exact estimate of the extent of this phenomenon is difficult to make, as many videos have been blacked out by YouTube due to their misinformative nature [53].

### Web Users’ Interest in Mass Media Infodemic Statements

Some statements from prominent personalities, including scientists, have directed the web interest of users toward disinformation and misinformation (Figure 4).

**Figure 4.** Relative search volumes (RSVs) of infodemic queries since the start of the COVID-19 pandemic. The *astrazeneca* query is not shown to enable visualization of the other RSV trends.



Among these statements, on February 23, 2020, Dr Maria Rita Gismondo compared COVID-19 to seasonal influenza [54]. On the same day, the RSV of the *coronavirus flu + covid flu* query increased from 0 to 100, maintaining high values until March 22 (mean RSV=40.2, SEM 3.2). On February 24, 2020, politician Vittorio Sgarbi minimized the risk of death from COVID-19 without any supporting scientific evidence [55]. On the same day, the proper RSV of the *coronavirus sgarbi + covid sgarbi* query increased from 2 to 75. Moreover, Sgarbi became the protagonist of a long series of infodemic statements, including incitement to violate the anti-COVID-19 regulations [56]. Over the same period, the RSV from the previous query remained high, achieving two new maxima on March 10 and 14 (RSV=100 and 93, respectively). Other major fake news stories that circulated through the media involved the creation of COVID-19 in a Chinese laboratory. This phenomenon was

supported by a 2015 report of a local news program, repurposed by the media; the words of the politician Matteo Salvini; and the statements of the Nobel Prize winner Luc Montagnier [10,57]. Another promoter of conspiracy theories was Dr Stefano Montanari [58]. Soon after his statements, there was a spike in the RSV of the query *montanari coronavirus + montanari covid*. On May 31, 2020, Dr Alberto Zangrillo declared the disappearance of COVID-19 [59]. The same day, there was a heavy rise in the query *coronavirus zangrillo + covid zangrillo*. However, the major infodemic impact of the media has been on vaccines, especially for the AstraZeneca vaccine. Figure 4 shows a clear trend in the weekly RSV of the query *vaccines side effects* from the second week of February 2021 onward (SS=10, Mann-Kendall  $P=.009$ ). By narrowing the range to obtain daily RSVs, a clear level shift can be observed from February 12 to 14, 2021. In particular, comparing the period of

January 20 to February 13 with that of February 17 to March 9, a dramatic percentage increase in web interest ( $\Delta\%=205.7$ ,  $t=17.4$ ) was observed. However, the peak was reached on March 11 (RSV=100), with a sharp rise starting on March 9. In the same period, a long series of misleading headlines were published by the main Italian newspapers, thus fomenting the distrust of vaccines [60,61]. Finally, in the same period, the RSV of the query *astrazeneca side effects* showed an extreme increase ( $\Delta\%=2991.4$ ,  $t=16.9$ ).

## Discussion

### Principal Findings

The results of this paper suggest that the main Italian mass media outlets have not only heavily influenced the trend of web interest in COVID-19 but also had a strong impact on the terms adopted by users to identify the novel coronavirus. In particular, although official sources such as the Ministry of Health and PubMed mainly adopted the scientific denominations (eg, 2019-nCoV, COVID-19, novel coronavirus), the principal Italian newspapers and national information channels, such as *La Repubblica*, *Il Corriere della Sera*, Rai, and Mediaset, have given resonance to more infodemic names. However, the use of these terms was neither constant nor homogeneous during the pandemic: indeed, from January to March 2020, the use by the media of monikers such as “coronavirus” and “Chinese coronavirus” reached worrying values (over 90% and 6%, respectively). From April to May 2020, the use of terms such as “COVID” and “COVID-19” became common, although the generic “coronavirus” remained the most popular. From May 2020 to date, COVID-19-related names have become more common (except for Rai and Mediaset, where “coronavirus” is still widely adopted). In this scenario, web searches faithfully followed the news published on COVID-19. Especially during the beginning of 2020, all RSV peaks were associated with outbreaks or lockdown announcements. Moreover, marked and significant correlations were found between newspaper headlines and RSVs. Because similar correlations have not been highlighted with other potentially associable quantities, such as COVID-19 statistics (eg, new cases, new deaths), the terms most adopted by users mirror those used by the press, and numerous publications have previously shown mass media influences on web searches, we conclude that the press played a substantial role in creating a mass culture on COVID-19. Furthermore, our findings show that the terms used by mass media to identify the virus in the very early stages definitely affected users’ vocabulary and were difficult to replace. For example, although the scientific name “COVID-19” was introduced on February 11, 2020, by the World Health Organization and became predominant in major national newspapers in May 2020 [62], Italian netizens equalized it with the use of the name “coronavirus” only in September 2020. Alongside this, web users have shown a strong interest in videos, articles, and services shared by mass media supporting conspiracy theories, fake news, and unjustified claims. Specifically, the authors of this paper express concern that this material has reached millions of views and is very dangerous for public health and safety.

### Comparison With Recent Literature

To the best of the authors’ knowledge, this is the first study to propose a longitudinal analysis on the relationship between web RSVs and the headlines of stories in the main Italian media during the COVID-19 pandemic. Nonetheless, our results are supported by other recent literature. Regarding R1, Su et al [21] criticized the media for having done little to limit the spread of the infodemic during the current global health crisis, stressing the need to improve the communication system. In particular, they harshly criticized the multitude of journalists who, despite the required ethical and professional standards, adopted stigmatizing monikers linked to ethnicities or geographic locations, such as “Chinese virus,” “Wuhan virus,” and “China virus.” Wen et al [63] also denounced the use of headlines such as “Chinese virus pandemonium.” Indeed, the mass media have strict responsibilities for spreading these inappropriate names, which have fueled xenophobia toward the Chinese population and conspiracy theories globally [9,10,63-66]. These considerations acquire greater relevance considering R2: specifically, other studies have highlighted a strong influence of the media on web searches and interests. For example, Szmuda et al [67] showed that Google Trends is better at analyzing COVID-19-related media clamor than actual disease incidence. Tejedor et al [68] examined the front pages of Italian and Spanish newspapers during COVID-19 (including *Corriere della Sera* and *La Repubblica*), emphasizing that “they still play a crucial role in molding public opinion by offering more interpretative content.” The same authors stressed the need to increase information literacy in the population and media professionals “to achieve rigorous and responsible health information.” Huynh Dagher et al [27] showed that even the web interest in cutaneous COVID-19 symptoms was strongly influenced by media coverage and government policies in France, Spain, Italy, and the United States, calling for caution in adopting Google Trends as an epidemiological monitoring tool. In contrast, only weak correlations were found in Germany and the United Kingdom. Ergo, the media impact may be dependent on the country. Likewise, Fernández-Torres et al [69] pointed out that although Spanish citizens are interested in news about the novel coronavirus, the mass media often provide low-quality information. Finally, concerning R3, newspapers, television stations, and news channels have given too much resonance to conspiratorial opinions and uninformed or incompetent people [9,10]. The most striking case is that of the former president of the United States, Donald Trump, who gave extremely dangerous advice on how to fight SARS-CoV-2, such as consuming unapproved drugs or injecting disinfectant [10]. Furthermore, Trump repeatedly accused China of deliberately creating the virus and adopted a wide variety of racist monikers [70]. A second equally notable case is that of Luc Montagnier, winner of a Nobel Prize in Medicine, who claimed, without any supporting scientific evidence, that SARS-CoV-2 was the result of laboratory manipulation of HIV [10]. In this regard, Moscadelli et al [71] reported an increase in web searches for coronavirus laboratory-related keywords in conjunction with Montagnier’s statement and pushed for greater control of information shared by the media. Ferreira et al [72] established a strong dependence of Portuguese citizens on conventional mass media during the COVID-19 pandemic,

underlining that most users have shown greater trust in these media outlets than in social media. Similar findings were found by Fernández-Torres et al [69] for Spain. However, the authors of both papers agree that citizens believe that news and newspapers are not free from false information. This evidence cannot be judged in positive or negative terms because it is not known which types of information are cataloged as such; for example, some Italian conspiracists believe that journalists are purposely exaggerating the number of COVID-19 deaths to instill fear and acquiescence. Nonetheless, this phenomenon testifies to the climate of distrust that afflicts the population and the need to create sources that are perceived as reliable.

### Practical Implications

This study provides evidence that in Italy, the mass media have strongly influenced web users in the adoption of names to identify COVID-19 and favored the diffusion of infodemic monikers (R1); the mass media have determined the trend of web searches on COVID-19 (R2); and the web interest in infodemic news shared by mass media has been high (R3). The use of too-generic terms by the mass media is plausibly an attempt to simplify information for the public. This would justify the easy success of names such as “coronavirus” instead of “novel coronavirus 2019” or “covid” instead of “COVID-19”. Because Italy is one of the nations in the world with the highest percentage of functionally illiterate people [73], using simple and immediately understandable words is a fundamental aspect of health disclosure [74]. In this regard, the first name, 2019-nCoV, may have been too technical to be adopted by citizens. Because the initial denomination of a disease affects the behavior of users over a long period, we suggest that more attention should be paid when making a definitive choice. Alongside this, the use of racist monikers was due both to the naive attempt to contextualize the virus in the geographical scenario and the politicization of COVID-19 [75]. These monikers were often contained in headlines, which can bias the entire reading of an article [76]. For these reasons, we suggest

that government authorities impose more controls and restrictions on newspaper headlines and expect greater discretion and sensitivity from the editors of news organizations.

### Limitations

This analysis was subject to some limitations. First, there are no guarantees that the interest of Italian web users can represent a true-to-life picture of the entire Italian population’s interests; thus, the conclusions of this paper are limited to Italian internet users. Second, causal correlations were only searched between Google Trends RSVs and the headlines used by the two most-read Italian newspapers. Future research could investigate the correlations between the Italian population and the mass media, also involving non-internet users and all Italian media. Thirdly, RSVs provide information about the relative number of web searches on COVID-19 but not their exact number. However, as previous literature has shown that the numbers of COVID-19-related web searches and discussions have always been high [22], related trends also provide valuable information. Finally, the paper cannot represent the totality of the interests of web users that arose during the COVID-19 pandemic.

### Conclusions

Because the leading Italian mass media have strongly influenced both the risk perception and interest of Italian web users toward the novel coronavirus (SARS-CoV-2, which causes COVID-19), we suggest that the Italian authorities place strict and effective controls on the information circulating in Italy. Furthermore, the authors of this paper recommend that the directors of news channels and newspapers adhere to the official name of COVID-19 (as well as any other virus or disease), favoring a less sensationalistic disclosure policy. Finally, the authors of this paper recommend carefully weighing the influence of mass media on users’ web searches before adopting any epidemiological predictive models based on Google Trends or similar infoveillance tools.

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### Authors' Contributions

AR designed the study, collected the data, performed the data analysis, and wrote the manuscript. LC contributed to the collection and analysis of data.

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### Conflicts of Interest

None declared.

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### Multimedia Appendix 1

Trend of COVID-19 symptoms-related web queries from 2017 to 2021 (Google Trends). The relative search volumes shown are cumulative monthly.

[[DOCX File , 163 KB - xmed\\_v2i4e32233\\_app1.docx](#) ]

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## Abbreviations

**C19:** COVID-19 cases and deaths

**I-scale:** infodemic scale

**RSV:** relative search volume

**SEM:** standard error of the mean

**SS:** Sen slope

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