PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A systematic literature review of adopting eHealth in pharmaceutical care during COVID-19 pandemic: recommendations for strengthening pharmacy services
AUTHORS	CEN, Zhi Feng; TANG, Pou Kuan; Hu, Hao; Cavaco, Afonso; ZENG, Luoxin; LEI, Sut Leng; Ung, Carolina Oi Lam

VERSION 1 – REVIEW

REVIEWER	Saha, Manika Monash University, Action Lab, Department of Human-Centred Computing
REVIEW RETURNED	09-Aug-2022

GENERAL COMMENTS	This is an important piece of systematic review work. I believe this study has the potential to make a significant contribution to knowledge. However, I am listing the following issues to improve the work to make it more sound in terms of methodological clarification and overall presentation as a systematic review work.
	- More clarification needs on research aims and queries. It is mentioned that ".....to perform certain interventions or achieve predefined outcomes amid the challenges of the COVID 19 pandemic". But what were the predefined outcomes? These are not clearly explained.
	- The study methodology was not very clear. For instance, what were the inclusion and exclusion criteria? Need more description on the search strategy. For example, this study needs a brief explanation of how the researchers checked the reference lists of retrieved articles and how that screening was done. Need more description on the screening process. How were Chinese papers translated for other authors' discussion? It is mentioned in the "Search strategy" that a research question was developed, but what was the research question?
	- The method section of the abstract need to improve after working on the paper's methods section.
	- A summary of search terms used in the electronic database is helpful, but it could be presented more smartly in a table. Please see other systematic review papers to have more ideas.
	- Outcomes and discussion of the research are well presented. However, some of the findings could be presented in a table to take the key messages easily. For instance, key results from the sections include "Tool(s) involved in the PC-eHealth service models", "output of PC-eHealth interventions", and "Input relevant

	to establishing PC-eHealth service model" could also be presented in tables.

REVIEWER	Stanimirovic, Dalibor Univ Ljubljana, Department of Organization and Informatics
REVIEW RETURNED	13-Sep-2022

GENERAL COMMENTS	- Have you considered including the following constructs as outputs or even outcomes in Figure 2. The logic model of adopting eHealth in pharmaceutical care during the COVID-19 pandemic: - What about standardized and faster procedures for dispensing medication? - What about simplified and streamlined organization of business processes? - What about greater efficiency in drug dispensing procedures? - Greater safety of the use of dispensed medicines for patients - Reduction in the rate of hospitalization due to the elimination of errors in dispensing the wrong medications based on previous (paper-based) procedures? - Improved medication adherence - Provision of structured data on medication dispensing for analytics, decision-making and policymaking needs - All eHealth undertakings are massive and may be seen as across-the-board socio-technical projects, therefore, besides technological aspects, social architecture and its evolution in PC deserve particular consideration. I think it would be useful to shed more light on this aspect, even though you have already mentioned some very important parameters in "Contextual factors". This should be further expounded in the "Discussion". - In this sense, it would be necessary to at least indicate and reference the Technology Acceptance Model (TAM) and its upgrades or successors, which largely touch on related issues, as outlined in your article. This should be further expounded in the "Discussion". Formal recommendations - In some places in the text you use the acronym PC, in others you use the term "pharmaceutical care". This needs to be unified. - The article contains some spelling and syntactic errors that need to be corrected (an systemic, a growing research interests, this reviews, implmentation, "enables instead of enablers" in Figure 2, etc.).

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Manika Saha, Monash University

Comments to the Author:
1. This is an important piece of systematic review work. I believe this study has the potential to make a significant contribution to knowledge. However, I am listing the following issues to improve the work to make it more sound in terms of methodological clarification and overall presentation as a systematic review work.

Response:
Thank you for the encouraging feedback. We are also very appreciative for all the comments and will try out best to improve our manuscript accordingly.

2. - More clarification needs on research aims and queries. It is mentioned that ".….to perform certain interventions or achieve predefined outcomes amid the challenges of the COVID 19 pandemic". But what were the predefined outcomes? These are not clearly explained.

Response:
Thank you for the comment. We have added examples of predefined outcomes after "At present, there is little systematic research about the "know-how" of integrating eHealth services and tools in PC to perform certain interventions or achieve predefined outcomes amid the challenges of the COVID-19 pandemic." to improve clarity as shown in the following:

"Considering the potential benefits of applying eHealth in maintaining pharmaceutical services, empowering patients to improve compliance and adherence, reducing the risks of drug related problems (e.g adverse drug reactions or drug interactions) and supporting pharmacovigilance amid the challenges of the COVID-19 pandemic17-19, this reviews aims to determine how eHealth was adopted…."

3. The study methodology was not very clear. For instance, what were the inclusion and exclusion criteria? Need more description on the search strategy. For example, this study needs a brief explanation of how the researchers checked the reference lists of retrieved articles and how that screening was done. Need more description on the screening process. How were Chinese papers translated for other authors' discussion? It is mentioned in the "Search strategy" that a research question was developed, but what was the research question?

Response:
Thank you for the questions. We have revised the manuscript to provide more description about the inclusion and exclusion criteria, the search strategy, and the screening process. The team members responsible for literature screening included two Master students (ZC and PT) and two senior researchers (HH and COLU) who were fluent in both Chinese and English. All the papers included in the review were written in English so no translation from Chinese to English is needed for discussion among all the team members during data extraction, analysis and synthesis. The research question is now clearly indicated in the manuscript. The revised section is shown in the following:

Search strategy
The research question "How did pharmacists employ eHealth during the COVID-19 pandemic for the provision of care to their patients?" was developed using the population, intervention, comparison, outcome and time frame (PICOT) framework. 18 In the PICOT framework, the population referred to pharmacists, either practiced alone or as a member of an inter-professional team and regardless of their work setting; the intervention referred to adopting eHealth for the purpose of tele-education, tele-consultation, tele-monitoring, tele-case-management, tele-mentoring); the comparison is not applicable; the outcome referred to the impact of the care on people cared by pharmacists via eHealth; and the time frame was the period of COVID-19 pandemic.

Considering the three major concepts "pharmaceutical care", "eHealth", and "COVID-19 pandemic" that constituted the research question of this review, their Medical Subject Headings (MeSH) terms as well as the corresponding keywords and phrases identified in related literature were used to formulate a comprehensive search strategy. Terms within 'pharmaceutical care', 'eHealth', and 'COVID-19 pandemic' were combined with OR, and this results from each concept were combined with AND (Table 1). A detailed description of the search strategies for each chosen database is provided in

Appendix. Additionally, the reference lists and citations of included articles were examined to identify further papers for inclusion.

Eligibility criteria

Studies which reported the use of eHealth in any aspects of PC during the COVID-19 pandemic, published between December 2019 (when cases of COVID-19 infection were first reported) and March 2022, written in English or Chinese, and published in peer-reviewed journals were included. The study types were limited to descriptive studies, prospective observational studies, retrospective cohort studies, retrospective chart reviews, cross-sectional surveys, and qualitative studies. Studies which reported about the use of eHealth to support the use of medicines during the COVID-19 pandemic by healthcare professionals other than pharmacists were not considered. In addition, opinion articles, conference abstracts, correspondence, letters, and editorials were excluded.

Study selection, data extraction and presentation

All members in the research team responsible for literature screening which included two Master students (ZC and PT) and two senior researchers (HH and COLU) were fluent in both English and Chinese. Two of the authors (ZC and PT) independently conducted the literature search and applied the inclusion and exclusion criteria. After the removal of duplication, citations were screened for inclusion by title first, and the remaining papers were then screened by abstracts (ZC and PT). After initial screening, the full text of studies were screened (ZC and PT) with guidance from one of the senior researchers (COLU) who randomly selected and checked a percentage of the included and excluded articles to ensure the eligibility of the included papers and the appropriateness of the excluded papers. Any differences were discussed and resolved among ZC, PT, HH and COLU by consensus.

Upon confirmation of the included studies, the reference lists were first examined to identify any further papers for inclusion (ZC and PT). This was followed by data extraction in which the required data from each included study was extracted and input into a pre-designed Excel table (ZC and PT). The design of the Excel table was informed by the logic model featuring the key components of goals, input, activities, output and contextual factors.19 Any divergences during the data extraction process were resolved through discussion among ZC and PT, and subject to agreement by HH and COLU and final confirmation by all authors. Narrative synthesis was undertaken to summarize and report the findings.

4. The method section of the abstract need to improve after working on the paper's methods section.

Response:
Thank you for the comment. The method section of the abstract has been revised accordingly to improve the clarity.

5. A summary of search terms used in the electronic database is helpful, but it could be presented more smartly in a table. Please see other systematic review papers to have more ideas.

Response:

Thank you for the comment. We agree that search terms presented in a table would benefit clarity and we had included the search terms used in each of the databases in the Appendix during the original submission. Considering the author guideline that "recommends the article does not exceed 4000 words, with up to five figures and tables" and we already have 5 figures and tables in the original manuscript, we have now included another table (Table 1) in the appendix to clearly indicate the search terms under the 3 concepts.

6. Outcomes and discussion of the research are well presented. However, some of the findings could be presented in a table to take the key messages easily. For instance, key results from the sections include "Tool(s) involved in the PC-eHealth service models", "output of PC-eHealth interventions", and "Input relevant to establishing PC-eHealth service model" could also be presented in tables.

Response:
Thank you for the comment. In Figure 2 of the original manuscript, we have already listed out the items under "input" (which included eHealth tools and the supported needed from the government, pharmacist professional organizations, hospital/pharmacy, and pharmacists), "activities" , "output" and "outcome" identified from this review. Considering the author guideline that "recommends the article does not exceed 4000 words, with up to five figures and tables" and we already have 5 figures and tables in the original manuscript, we suggest that we do not add an extra table. Instead, we have added a sentence to the first paragraph of the Results section "The overall logic model detailing the items under "input", "activities", "output", "outcome" and "contextual factors" is depicts in Figure 2." to draw readers' closer attention to the information provided in Figure 2.

Reviewer: 2
Dr. Dalibor Stanimirovic, Univ Ljubljana

Comments to the Author:

1. The article addresses a very important and interesting topic, and as such has considerable potential. A lot of effort and time was evidently invested in the research and preparation of the article, for which the authors deserve a lot of credit. On the other hand, some parts of the text are rather trivial and lacking in detail and need significant enhancement. Below are presented some recommendations for improvement:

Response:
Thank you for the encouraging feedback. We are also very appreciative for all the comments and will try out best to improve our manuscript accordingly.

Material recommendations
2. The research questions/objectives are not precisely defined in the "Introduction". The current formulation is too broad and allows for different interpretations of research questions and/or research objectives.

Response:
To improve clarity, we have added further information about the context whereby eHealth may be applied in PC and the potential benefits before stating the study objective in the Introdction:

"while most of the current research focused on how eHealth might benefit the continuous access to essential pharmacy services in the absence of in-person interactions between pharmacists and their patients, there is little systematic research about the "know-how…"

"Considering the potential benefits of applying eHealth in maintaining pharmaceutical services, empowering patients to improve compliance and adherence, reducing the risks of drug-related problems (e.g. adverse drug reactions or drug interactions) and supporting pharmacovigilance amid the challenges of the COVID-19 pandemic17-19, this review aims to…. "

3. The "Methods" section is rather modest and inconsistent. Some essential segments of the methodological approach are not mentioned at all. Why was a particular methodology chosen? When were the research activities carried out? Why these six databases? Which browser was used, etc.?

Response:
Thank you for the comment. We have revised the Methods section to improve transparency and clarity, and added the following:

"The use of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 statement for guidance was to transparently report why the review was done, what the authors did, and what had been found during the course of identifying, selecting, appraising, and synthesizing studies. 17"

We have also clearly indicated that the search of literature in six databases was completed on 15 April 2022. A combination of 6 databases were used to optimize the retrieval of all relevant research and the databases (including PubMed, Scopus, Medline, Web of Science, Science Direct and China National Knowledge Infrastructure (CNKI)) were selected because they specialized in scholarly literature related to health and medical topics. Microsoft Edge was used when conducting the literature search. We have supplemented the Methods section with additional information accordingly.

4. Sections "Study characteristics", "Purposes of adopting eHealth in PC during the COVID-19 pandemic" and "Tool(s) involved in the PC-eHealth service models" should be at least partially included in the Methods section, possibly in the new subtitle "Research sample and eHealth/digital tools involved".

Response:
Thank you for the comment. We have added the following to the Methods section:

"In addition to the characteristics of the included studies (such as first author, year of publication, study type, study location, study aim, targets of eHealth pharmacy service, and types of pharmacists involved), the design of the Excel table was also informed by the types of eHealth involved and the logic model featuring the key components of goals, input, activities, output and contextual factors.19 For the purpose of this study within the context of the logic model, "input" referred to the eHealth tools involved and the support from different stakeholders such as the government, pharmacist professional organizations, hospital, pharmacy and pharmacist; "activities" referred to services provided by pharmacists with eHealth; "output" and "outcome" referred to the impact of the services pharmacists provided with eHealth on the people they cared for."

5. "Results" should start with "Interventions provided by pharmacists with eHealth"

Response:
Thank you for the comment. We agree that "Interventions provided by pharmacists with eHealth" deserves a higher priority and have therefore moved the section up after "Purposes of adopting eHealth in PC during the COVID-19 pandemic". We have also restructured the Results section so that the findings are now reported in the following order:

- Study characteristics
- Purposes of adopting eHealth in PC during the COVID-19 pandemic
- Interventions provided by pharmacists with eHealth
- Tool(s) involved in the PC-eHealth service models
- Other input relevant to establishing PC-eHealth service model
- Output of PC-eHealth interventions
- Contextual factors affecting the adoption of eHealth in PC during the pandemic

6. The use of eHealth solutions in only one segment, such as PC, actually tells us little about the proliferation of eHealth solutions and their use in healthcare during the pandemic.

Response:
We agree that this study only revealed how eHealth has been integrated in a small sector of healthcare services (ie PC). However, considering the study objective, it is difficult to extrapolate the result findings towards the overall healthcare service landscape.

7. Is it possible, for example, that the use of eHealth solutions has increased in the PC segment and decreased in other segments, such as primary care, hospital care, social care, laboratory activity, etc.? We don't know that, but would that mean a distorted picture of the findings in this research? Given that the ultimate goal of all eHealth initiatives is probably focused on increasing the use of eHealth solutions in all areas of the healthcare system?

Response:
For the purpose of this study, the primary focus is on how eHealth was adopted during the COVID-19 pandemic to ensure the continuity of care from pharmacists which could have been compromised by various public health measures (social distancing, lockdown, etc). The scope was mostly confined to PC but not the shifting of non-PC services from other segments of healthcare towards the pharmacy practice. We have added the following in the section of "Moving forward" to highlight the relationship between eHealth in PC and the overall Healthcare landscape:

"Indeed, any eHealth interventions in PC should be viewed a catalyst for change in the overall healthcare sector"

8. Is reduced need for physical contact always a benefit? This article states it categorically, leaving no room for doubt. What are the potential side effects and consequences of this approach?

Response:
As explained in the Introduction, "Since the onset of the COVID-19 pandemic, the delivery of PC has been inevitably disrupted by major public health measures compromising the provision of medicines and care" and the primary purpose of adopting eHealth was to overcome the challenges. we agree that the downside of eHealth when applied in PC is also worth exploring . As such, we have added "However, due to the lack of face-to-face interactions, pharmacists may not be able to accurately evaluate the complete situation of patients especially to those who were not very proficient in using information technology. As such, the effectiveness of the pharmacy service provided via eHealth might be affected." to the first paragraph of the Discussion. We have also added the following to the section of Moving forward - "A more balanced research approach to investigate the pros and cons

when adopting eHealth in PC is also warranted to better inform actions that support wider use of eHealth in PU as well as other areas of healthcare services."

9. You emphasize the need for supporting actions at the levels of government, hospital/pharmacy, pharmacists and patients. You have also written about these aspects and highlighted some challenges and potential solutions. I think it would be useful to write a little more about business challenges, process and organizational, education and training, and technological aspects.

Response:
Thank you for the suggestions. We have added further discussion about business challenges, process and organizational, education and training, and technological aspects under the section of "Adopting eHealth in PC in the context of the health system in the Discussion section as shown in the following:

Adopting eHealth in PC in the context of the health system
In order to better develop and promote the measures to provide pharmacy services through eHealth during the epidemic, the government can try to take the lead in incorporating eHealth to support the role of pharmacists in public health measures. One of the essential criteria was for pharmacists and patients to acquire the necessary skills and to come to term the benefits of adopting eHealth. According to the technology acceptance model (TAM), an information systems theory that describes the acceptance and usage of a new technology from the users' perspective, there are 2 major factors affecting users' decision about when and how to use it: perceived usefulness (PU) and perceived ease-of-use (PEOU).85 In other words, if a person believes that using a particular new technology would enhance the performance of some sort, and the new technology is easy to use, he/she will have the positive attitude and intention to use the new technology. As such, training and evidence-based use of eHealth in improving PC for pharmacists and public education about basic skills of information technology and benefits of eHealth are important for achieving high proficiency and wide acceptance of eHealth in PC.

In addition, resources are needed to "upgrade" the healthcare system infrastructure to integrate eHealth into day-to-day practice. Equipment, internet access, information technology systems and process, sustainable engagement and initiative, competent staff and a well-designed, close-loop evaluation mechanism should be in place to form the basic infrastructure for eHealth in PC.86 A lack of an appropriate infrastructure might affect the quality of PC leading to more harm than benefits.87 In the context of a business operation such as community pharmacies, cost is one other key factors when adopting eHealth. The investment to achieve the readiness of the infrastructure can be expensive considering the costs of both hardware and software. While the focus on leveraging the advantage of any existing information and communication technology infrastructure should be prioritized, it is also necessary to monitor and manage the costs over time.88

10. Have you considered including the following constructs as outputs or even outcomes in Figure 2. The logic model of adopting eHealth in pharmaceutical care during the COVID-19 pandemic:
- What about standardized and faster procedures for dispensing medication?
- What about simplified and streamlined organization of business processes?
- What about greater efficiency in drug dispensing procedures?
- Greater safety of the use of dispensed medicines for patients
- Reduction in the rate of hospitalization due to the elimination of errors in dispensing the wrong medications based on previous (paper-based) procedures?
- Improved medication adherence

- Provision of structured data on medication dispensing for analytics, decision-making and policymaking needs

Response:
Thank you for pointing this out. We have revised the items under the "Output" section in Figure 2 accordingly:
- standardized and faster procedures for dispensing medication – newly added
- simplified and streamlined organization of PC – newly added
- Greater efficiency in drug dispensing procedures? – already in the logic model
- Improved drug safety – newly added
- Reduced errors – newly added
- Enhanced medication adherence – newly added
- Address analytics, decision-making and policymaking needs with structured data – newly added

More discussion about the effectiveness of adopting eHealth in PC has also been added to the Discussion section as shown in the following:

The effectiveness of adopting eHealth in PC
Numerous studies have demonstrated the value of eHealth in healthcare services including PC. The effectiveness of eHealth adoption can be reflected in two aspects. On the one hand, the increase in the number of users receiving PC via eHealth. For example, Reardon et al. showed that 1.5% of 2036 initial patient appointments were conducted virtually via eHealth prior to the pandemic. This increased to 64% for follow-up appointments in 2019, indicating that an increasing number of patients rely on the PC delivered via eHealth.34 Ibrahim et al. also reported that the proportions of COVID-19 cases (either probable and confirmed) who received pharmaceutical services were 31.90% versus 11.74% and 6.07% versus 0.36%, respectively, in pharmacies with remote services (test group) versus pharmacies without remote services (control group).58

On the other hand, the effectiveness of eHealth adoption may also be assessed by comparing pharmacy services in hospitals and community pharmacies with and without eHealth. When providing pharmacy services through eHealth during the epidemic, patients can use relevant eHealth tools to book pharmacist services in advance, and can receive online pharmacy services at any location. Standard and faster dispensing procedures can be realized with the help of advanced technology, which may largely simplify the entire process of PC provision for patients to achieve higher efficiency of the entire pharmacy service process.16,39

With eHealth, electronic transaction and storage of patient information could help pharmacists to prevent mistakes in dispensing which would have happened with paper-based procedures, to help improve medication adherence, and to support analysis and decision making about medication availability with easily-accessible and structured data. Using community pharmacies as an example, the rate of potential OTC abuse across pharmacies with and without eHealth services was 5.8% versus 7.7% and potential OTC misuse across pharmacies with and without eHealth services was 13.7% versus 16.6%.39

11. All eHealth undertakings are massive and may be seen as across-the-board socio-technical projects, therefore, besides technological aspects, social architecture and its evolution in PC deserve particular consideration. I think it would be useful to shed more light on this aspect, even though you have already mentioned some very important parameters in "Contextual factors". This should be further expounded in the "Discussion".

Response:

Thank you for the suggestions. We have added further discussion about

The significance of eHealth to PC in the healthcare system
The accessibility to pharmacies and the perceived affordability positions pharmacists at the first line of contact within the healthcare system especially during a pandemic.74 The emphasis placed on patient-center service has further driven the new paradigm of pharmacy practice and accelerated the adoption of eHealth for the expansion of pharmacists' professional role in pharmaceutical services. This implies a shift of focus towards the delivery of longitudinal value-added services for the patients as well as the closer collaboration with other healthcare professionals with higher level of data sharing. Besides, the use of "smart" technological solutions in the medicine dispensing process could relieve pharmacists' workload, leaving more free time for pharmacists to assume other components of pharmacy practice, allowing the accomplishment of more professional and advanced PC services.75 Such transition, when properly executed, is considered extremely valuable for the patients, other healthcare professionals, and even the health systems in terms of not only improvement in health services quality and in patient health related outcomes, but also greater efficiency and economic savings.76-78

12. In this sense, it would be necessary to at least indicate and reference the Technology Acceptance Model (TAM) and its upgrades or successors, which largely touch on related issues, as outlined in your article. This should be further expounded in the "Discussion".

Response:
Thank you for the suggestion. We have added the Technology Acceptance Model (TAM) when discussing about the acceptance of eHealth in PC from the consumers/patients' perspective.

"According to the technology acceptance model (TAM), an information systems theory that describes the acceptance and usage of a new technology from the users' perspective, there are 2 major factors affecting users' decision about when and how to use it: perceived usefulness (PU) and perceived ease-of-use (PEOU).85 In other words, if a person believes that using a particular new technology would enhance the performance of some sort, and the new technology is easy to use, he/she will have the positive attitude and intention to use the new technology. As such, training and evidence-based use of eHealth in improving PC for pharmacists and public education about basic skills of information technology and benefits of eHealth are important for achieving high proficiency and wide acceptance of eHealth in PC."

Formal recommendations
13. In some places in the text you use the acronym PC, in others you use the term "pharmaceutical care". This needs to be unified.

Response:
Thank you for pointing this out. The manuscript has been checked thorough and revisions have been made accordingly.

14. The article contains some spelling and syntactic errors that need to be corrected (an systemic, a growing research interests, this reviews, implmentation, "enables instead of enablers" in Figure 2, etc.).

Response:
Thank you for pointing this out. The manuscript has been checked thoroughly for any typos and grammatical errors and revisions have been made accordingly.

VERSION 2 – REVIEW

REVIEWER	Stanimirovic, Dalibor Univ Ljubljana, Department of Organization and Informatics
REVIEW RETURNED	11-Oct-2022

GENERAL COMMENTS	Given the scope and structure of the corrections and changes, it is obvious that the authors carefully approached the revision of the article. Even in terms of content, I think that the amendments are mostly adequate and that they satisfactorily address the shortcomings that were identified in the 1st round of reviews. I think that due to the corrections, the text is now much more consistent in terms of structure and compelling in terms of content. Good work!