PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	PrEP distribution in pharmacies: a systematic review
AUTHORS	Kennedy, Caitlin; Yeh, Ping; Atkins, Kaitlyn; Ferguson, Laura; Baggaley, R; Narasimhan, Manjulaa

VERSION 1 – REVIEW

REVIEWER	Katrina Ortblad University of Washington , Department of Global Health
REVIEW RETURNED	27-Jul-2021

GENERAL COMMENTS	OVERALL: An important paper on the potential for retail pharmacies to deliver PrEP to increase the reach and access of PrEP services in diverse settings. This paper highlights the lack of evidence on the comparative effectiveness of pharmacy- vs. clinic-delivered PrEP on initiation, retention, adherence, and HIV incidence, while also highlighting the potential feasibility of pharmacy-based PrEP delivery in diverse settings, as demonstrated in numerous case studies, value/preferences studies, and costing studies. To date, most of the evidence has on pharmacy-delivered PrEP services has come from US settings – more evidence on the acceptability, feasibility, and effectiveness of this novel model is needed in high HIV prevalence settings outside the US. Just a few minor comments below. I enjoyed reading this paper. MINOR: • (Intro, paragraph 1): Note that not all forms of PrEP are available in settings globally (i.e., only daily oral PrEP available in most low-income countries). • (Methods): Please clarify the publication dates that were included in the review and/or the date the search was conducted, as there are some newer studies on values/preferences I do not see included in this review (e.g., Roche S et al, 2021), but that is likely because they were published after this search was conducted. • (Discussion, paragraph 2): Might also want to consider commenting on the need for simplified laboratory testing for PrEP delivery (i.e., creatinine testing has been largely waived in some international settings) and the use of self-testing (e.g., HIVST) for PrEP continuation.

REVIEWER	Maria Lopez Mission Wellness Pharmacy
REVIEW RETURNED	02-Aug-2021

GENERAL COMMENTS	This is an interesting paper. Study design question may need to be re defined, however. Overall the summary and work into writing this review is notable with some editing and corrections it could be a

	useful review. Page 7, line 16 Question 1 Initiation Population: Individuals interested in PrEP Intervention: PrEP access through a pharmacy without a prescription by a health care provider. As written, it appears authors are possibly stating that a pharmacist is not a healthcare provider. Disagree with this statement. In the U.S. when a pharmacist initiates PrEP they do indeed write a prescription and it is incorrect to state the access to PrEP in a pharmacy is without a prescription. Recommend change to “PrEP access through a pharmacy” period. Comparator: PrEP access by prescription from a health care provider PICO Question 2, Continuation page 7, line 42 Intervention: PrEP access through a pharmacy without a prescription by a health care provider Same comment as above; As written, it appears authors are possibly stating that a pharmacist is not a healthcare provider- Disagree with this statement. In U.S. when a pharmacist initiates PrEP they do indeed write a prescription and it is incorrect to state the access to PrEP in a pharmacy is without a prescription. Recommend change to “PrEP access through a pharmacy” period. Comparator: PrEP access by prescription from a health care provider Search terms page 8 line 5-13 Comment: While the paper discussed initiation, the search methodology excluded the terms “initiation, pharmacist initiated” This either should be noted in discussion or perhaps consider expanding search as the more common terms in the U.S. are “initiate” and “initiation” to describe pharmacist prescribing. Page 11, lines 19-22 However, we did identify seven “case studies” where PrEP was offered through pharmacies, but where there was no data comparing this to provision by prescription only. These were reported collectively in six articles and three abstracts.[16-24]- Note likely no data as the term prescription only is problematic as previously discussed. Page 11, line 26 Most described operation through a collaborative practice agreement (CPA), where pharmacists operated under physician oversight to conduct activities that might otherwise be considered beyond their scope of practice. Disagree. It is within the scope of practice to work under collaborative practice. Scope is defined by states in the USA and pharmacists can prescribe under CPA—definitely within scope. Page 13-15, chart includes telePrEP program in GA. Note to authors two other telePrEP pharmacy programs in Ohio and Iowa have been described. There may be reasons these were excluded, but wanted to point out in case these were missed by accident. Page 16, line 16-19, 23. Most (women) generally preferred clinics- this study was conducted in Africa, where authors point out USA

	only had pharmacy PrEP models. Recommend authors elaborate the difference in USA vs Africa pharmacy clinic vs health clinic models. Page 21 to 22 lines 55-6. Mention “quality control” more challenging. Please define quality control that could be more challenging when having a pharmacist initiate therapy vs a non pharmacist (i.e. compared to an NP or RN or MD who often do not have nearly as much training in pharmacotherapy and monitoring for efficacy, toxicity and safety, as a pharmacist, for example).

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Katrina Ortblad, University of Washington

Comments to the Author:
OVERALL: An important paper on the potential for retail pharmacies to deliver PrEP to increase the reach and access of PrEP services in diverse settings. This paper highlights the lack of evidence on the comparative effectiveness of pharmacy- vs. clinic-delivered PrEP on initiation, retention, adherence, and HIV incidence, while also highlighting the potential feasibility of pharmacy-based PrEP delivery in diverse settings, as demonstrated in numerous case studies, value/preferences studies, and costing studies. To date, most of the evidence has on pharmacy-delivered PrEP services has come from US settings - more evidence on the acceptability, feasibility, and effectiveness of this novel model is needed in high HIV prevalence settings outside the US. Just a few minor comments below. I enjoyed reading this paper.

Thank you for your very positive comments.

MINOR:
* (Intro, paragraph 1): Note that not all forms of PrEP are available in settings globally (i.e., only daily oral PrEP available in most low-income countries).

Thank you for this note. We have added a comment to our introduction's first paragraph, which now reads:

HIV pre-exposure prophylaxis (PrEP) is the use of antiretroviral drugs by HIV-uninfected individuals to prevent HIV infection. PrEP may either be taken orally in a daily pill (generally containing tenofovir plus emtricitabine), event-driven (at the time of sex), or in the form of a dapivirine vaginal ring; recent data suggest that long-acting injectable PrEP may soon be an additional option. However, not all forms of PrEP are available in all settings globally; in most low-income countries, only daily oral PrEP is available. The World Health Organization (WHO) recommends that people at substantial risk of HIV infection should be offered PrEP as an additional prevention choice as part of a combination prevention approach [1] which includes integration of sexual and reproductive health (SRH), HIV, and sexually transmitted infections (STI) services.[2]

* (Methods): Please clarify the publication dates that were included in the review and/or the date the search was conducted, as there are some newer studies on values/preferences I do not see included in this review (e.g., Roche S et al, 2021), but that is likely because they were published after this search was conducted.

The date that the database search was conducted was December 2, 2020, and is noted in the "search strategy" section of the Methods section (and has also now been added to the abstract). We have added the search date to our limitations in the discussion section and have also added a mention of this particular additional article to the discussion. It now reads as follows:

"We also acknowledge that this is a new and rapidly growing field; we may have excluded articles which would have met our inclusion criteria but were published after our search date, including at least one acceptability and feasibility study conducted among clients and providers in Kenya which reinforced our findings of support for expanding PrEP to retail pharmacies, though participants wanted to ensure that such services would be “private, respectful, safe, and affordable” [48]."

* (Discussion, paragraph 2): Might also want to consider commenting on the need for simplified laboratory testing for PrEP delivery (i.e., creatinine testing has been largely waived in some international settings) and the use of self-testing (e.g., HIVST) for PrEP continuation.

Thank you for this suggestion. We have added the following sentence to the second paragraph of the discussion section:

“In some settings, health systems have developed simplified laboratory testing for PrEP delivery for example by waiving creatinine testing or have allowed HIV self-testing for PrEP continuation.”

Reviewer: 2
Dr. Maria Lopez, Mission Wellness Pharmacy

Comments to the Author:
This is an interesting paper. Study design question may need to be re defined, however. Overall the summary and work into writing this review is notable with some editing and corrections it could be a useful review.

Thank you for your positive comments.

Page 7, line 16
Question 1 Initiation
Population: Individuals interested in PrEP
Intervention: PrEP access through a pharmacy without a prescription by a health care provider. As written, it appears authors are possibly stating that a pharmacist is not a healthcare provider. Disagree with this statement. In the U.S. when a pharmacist initiates PrEP they do indeed write a prescription and it is incorrect to state the access to PrEP in a pharmacy is without a prescription. Recommend change to "PrEP access through a pharmacy" period.
Comparator: PrEP access by prescription from a health care provider

PICO Question 2, Continuation
page 7, line 42
Intervention: PrEP access through a pharmacy without a prescription by a health care provider Same comment as above; As written, it appears authors are possibly stating that a pharmacist is not a healthcare provider- Disagree with this statement. In U.S. when a pharmacist initiates PrEP they do indeed write a prescription and it is incorrect to state the access to PrEP in a pharmacy is without a prescription. Recommend change to "PrEP access through a pharmacy"
period.
Comparator: PrEP access by prescription from a health care provider

Thank you for this suggestion. We agree that pharmacists are healthcare providers and apologize for this oversight. Since this PICO question was developed for the WHO guidelines, we wanted to retain the original wording so that it matches with the WHO guidelines. However, we have now added the clarification “(defined as a non-pharmacist health worker)” to the phrase “health provider” in the PICO definition section.

Search terms page 8 line 5-13
Comment: While the paper discussed initiation, the search methodology excluded the terms "initiation, pharmacist initiated" This either should be noted in discussion or perhaps consider expanding search as the more common terms in the U.S. are "initiate" and "initiation" to describe pharmacist prescribing.

Thank you for this suggestion. Because the review has already been conducted and used for WHO guidelines (published summer 2021), we opted not to expand the search terms at this point. However, we have added to our discussion section to note in the limitations that this term was missing. Thankfully, we would have caught articles had used the term "pharmacist initiated" because we used the term "pharmacist" and "pharmacy" very broadly – it would only have been if the article talked about PrEP initiation in a pharmacy without using the word "pharmacy" or "pharmacist" that we would have missed it. We have added the following to our limitations:

"We missed the words "initiation", "initiate", and "initiated" in our search terms, but believe that most articles describing pharmacist initiation of PrEP would have used either "pharmacy" or "pharmacist" so would have been captured by our search."

Page 11, lines 19-22
However, we did identify seven "case studies" where PrEP was offered through pharmacies, but where there was no data comparing this to provision by prescription only. These were reported collectively in six articles and three abstracts.[16-24]- Note likely no data as the term prescription only is problematic as previously discussed.

Thank you for this comment. We agree that the terms used were not as precise as they could have been. As noted above, we have retained the wording of the original PICO questions to match the WHO guidelines and have added the limitation that our search terms may not have been complete and may have caused us to miss articles that may have met our inclusion criteria. However, we did not restrict our search terms to “prescription only” and would have included any intervention that broadly met our criteria even if they did not use this particular term to describe their comparison group.

Page 11, line 26
Most described operation through a collaborative practice agreement (CPA), where pharmacists operated under physician oversight to conduct activities that might otherwise be considered beyond their scope of practice. Disagree. It is within the scope of practice to work under collaborative practice. Scope is defined by states in the USA and pharmacists can prescribe under CPA-definitely within scope.

Thank you for the insight on interpretations of "scope of practice". We have removed the latter half of this sentence to say more simply: "Most described operation through a collaborative practice agreement (CPA), where pharmacists operated under physician oversight."

Page 13-15, chart includes telePrEP program in GA. Note to authors two other telePrEP pharmacy programs in Ohio and Iowa have been described. There may be reasons these were excluded, but wanted to point out in case these were missed by accident.

Thank you for noting this. We conducted this review concurrently with another WHO review on telemedicine options for PrEP. We therefore were focused on in-person pharmacies rather than telemedicine approaches to PrEP. However, we realize this distinction was not clear in our final write-up. We have now added the following sentence to the methods: “We focused on in-person pharmacy initation and continuation, and excluded telemedicine-based approaches.” We also realized that one included case study was a telemedicine program (reported in only a conference abstract, so we had not focused on this aspect of the intervention). We have now removed this study from the review and updated all references and information in the review accordingly.

Page 16, line 16-19, 23. Most (women) generally preferred clinics-this study was conducted in Africa, where authors point out USA only had pharmacy PrEP models. Recommend authors elaborate the difference in USA vs Africa pharmacy clinic vs health clinic models.

Thank you for this comment. The sentence the reviewer is referring to describes results from a specific study in Africa. We have left this as is for now, and later in the discussion come back to comparisons across settings (e.g. US, Africa) in terms of the evidence base available in different parts

of the world, different health systems (including types of health workers, scope of practice for pharmacists, etc.), and possible differences in quality control and training.

Page 21 to 22 lines 55-6. Mention "quality control" more challenging. Please define quality control that could be more challenging when having a pharmacist initiate therapy vs a non pharmacist (i.e. compared to an NP or RN or MD who often do not have nearly as much training in pharmacotherapy and monitoring for efficacy, toxicity and safety, as a pharmacist, for example).

In this sentence, we discuss how quality control varies based on regulatory and training standards in different settings around the world. We are not saying at all that pharmacists have less training than nurses or physicians. To clarify, we have added the following sentence: "Training may also vary significantly by type of health worker, as pharmacists (compared with nurses or physicians) typically receive more robust training in pharmacotherapy as well as monitoring for efficacy, toxicity and safety; the team-based approach to pharmacy distribution of PrEP may synergize the strengths of each type of health worker."

VERSION 2 – REVIEW

REVIEWER	Maria Lopez Mission Wellness Pharmacy
REVIEW RETURNED	17-Nov-2021

GENERAL COMMENTS	The reviewer completed the checklist but made no further comments.