

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Demographic, Clinical Guideline Criteria, Medicaid Expansion and State of Residency: A Multilevel Analysis of PrEP use on a Large US Sample
AUTHORS	Carneiro, Pedro; Mirzayi, Chloe; Jones, Scott; Rendina, Jonathon; Grov, Christian

VERSION 1 – REVIEW

REVIEWER	Schumacher, Christina Johns Hopkins University School of Medicine, Pediatrics
REVIEW RETURNED	08-Oct-2021

GENERAL COMMENTS	<p>This is an interesting question that aims to answer whether a structural factor (Medicaid Expansion, and therefore greater access to U.S. Federal/State health insurance) is associated with HIV Pre-exposure prophylaxis. Though the paper is interesting, I think some revisions could substantially strengthen this manuscript.</p> <p>My main comment is with respect to the outcome definition The outcome chosen is self-report of PrEP use at the time that the participant completed the survey. However, the recall period for behavioral factors that serve as criteria for PrEP use varied between 12m and 3m. There is an increasing body of evidence showing that retention in PrEP care and persistent PrEP use wanes substantially after several months. Did the authors consider examining expanding their outcome definition from current PrEP use to use in the past 12m (if these data were available), and if so, if this changed the results at all.</p> <p>The authors note that they sought to examine whether living in a Medicaid expansion state could explain observed racial disparities in PrEP use. White cisgender men who have sex with men were most likely to report current PrEP use, and that these same men are more likely to be wealthier and have private health insurance. This may render any effect of living in a Medicaid vs. Medicaid expansion state irrelevant (b/c they are less likely to need Medicaid). The authors may consider an analysis stratified by race OR a subanalysis among just Black or just racial minorities to see if there are differences in the association between living in a Medicaid expansion state with PrEP use by race.</p> <p>Other comments: Intro: The intro is long and I think could be streamlined. In particular, I think paragraphs 1 and 2 could be shortened.</p>
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	<p>The beginning of the paragraph that starts on page 7, line 8 that discussed of limits of use of pharmacy data to estimate PrEP uptake and lack of account for HIV-related risk factors may be better placed in the earlier paragraph that begins on page 5, line 29.</p> <p>This is a nit-pick, but the sentence on page 5, line 35 "...users also need to stay engaged and persist." would be more accurate if stated as "users also need to stay engaged and persist for as long as they remain at risk for HIV acquisition." Risk is time-variant and we have a tendency to analyze metrics on PrEP retention in the same way we analyze HIV care retention. Basically, the view is often ceasing PrEP use = bad, when this is not necessarily true. This is also why I think it may be helpful to also examine any PrEP use in the past 12m as an outcome if the data are available.</p> <p>Methods What was the % enrollment in these two studies among app-users who completed the screening survey?</p> <p>The authors noted that age was categorized as < 18, 18-24, 25-29, 30-49 and 50+, but then in the results the <18 were collapsed with the 18-24 group. This should be updated to reflect what was actually done.</p> <p>Results On page 10, line 38, the authors note that PrEP use was greater in older vs. younger adults (68% vs. 51%); however they present 4 age categories. This should be clarified.</p> <p>Table 1 - The title should include more details about the study population, time frame etc. Tables should be able to stand on their own (i.e., I know exactly what the study population is) without having to refer back to the text.</p> <p>Table 1 - Something is wrong with the n's presented in each column under the gender identity column as they don't add up.</p> <p>Discussion Limitations - It would be nice if the authors could acknowledge limitations regarding potential selection biases and generalizability of these results as these are two substantial limitations of these cohorts.</p>
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REVIEWER	Jonas, Kai Maastricht University
REVIEW RETURNED	15-Nov-2021

GENERAL COMMENTS	<p>The authors present a MS on determinants of PrEP use in the US based on a large sample of MSM and TGNB taking clinical and Medicaid expansion determinants into account.</p> <p>The sample size (coming from the Together 5000 and UNITE study) is clearly a strong point of the MS, at first glance. Looking into the demographics a bit more in detail, the percentage of TGNB sampled is very minimal, 1.7% of the total sample (but see my comment below). This really limits the interpretation for this sub-population. Furthermore, the sample is quite dated by now, since it is from 2017/18.</p> <p>In the Introduction, the authors cite research (often based on more novel data) that supports their research questions, both for clinical</p>
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	<p>determinants and health care insurance status. This leaves the question open why this analysis is still necessary or what it can contribute above and beyond the existing literature. The authors should make this more explicit in their write-up.</p> <p>Information on the racial and age distribution by state/medicaid expansion is missing. Currently, it is not possible to determine whether certain age/race configurations are (not) present in certain states/medicaid expansion contexts - it is possible that skewed sample distribution is driving effects found / or is making it impossible to obtain them.</p> <p>I have difficulties to match up the percentages reported on gender: In Table 1 85.2% identify as male, and minimal percentages as female, TG etc. - and the rest? Is there missing data?</p> <p>In sum, I think the MS would benefit from a more detailed analysis of clinical and sociodemographic determinants x state level, and the authors should explain better why this study based on dated data is still contributing to the literature</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Comments to the Author:

This is an interesting question that aims to answer whether a structural factor (Medicaid Expansion, and therefore greater access to U.S. Federal/State health insurance) is associated with HIV Pre-exposure prophylaxis. Though the paper is interesting, I think some revisions could substantially strengthen this manuscript.

Thanks so much for you comments.

My main comment is with respect to the outcome definition The outcome chosen is self-report of PrEP use at the time that the participant completed the survey. However, the recall period for behavioral factors that serve as criteria for PrEP use varied between 12m and 3m. There is an increasing body of evidence showing that retention in PrEP care and persistent PrEP use wanes substantially after several months. Did the authors consider examining expanding their outcome definition from current PrEP use to use in the past 12m (if these data were available), and if so, if this changed the results at all.

We agree with the reviewer, however we did not ask across both baseline surveys if participants had used PrEP in the past 12 months. This question was used to screen out participants on one of the studies, as this was a criteria for enrollment. Future studies from this research, which may include follow up surveys originating from this sample, should explore this question with a broader definition of PrEP use.

The authors note that they sought to examine whether living in a Medicaid expansion state could explain observed racial disparities in PrEP use. White cisgender men who have sex with men were most likely to report current PrEP use, and that these same men are more likely to be wealthier and have private health insurance. This may render any effect of living in a Medicaid vs. Medicaid expansion state irrelevant (b/c they are less likely to need Medicaid). The authors may consider an analysis stratified by race OR a subanalysis among just Black or just racial minorities to see if there are differences in the association between living in a Medicaid expansion state with PrEP use by race.

We appreciate your comment, and indeed a subanalysis of this data focusing on ethnic minorities may best highlight equity issues. There are two reasons why we could not perform this analysis at this point. The first and most objective is for editorial parsimony of the paper, which is already running over the preferred word count. We defer to the editor for guidance on further increasing the number of tables and words on the manuscript. Lastly, we believe this analysis deserves its own manuscript, and the unit of area used for MLA should be further reduced (from state to county, perhaps) to make it more valuable to these communities. In its current state, our main goal was to explore the role of Medicaid expansion on the state level on PrEP uptake on the individual level, something that we discuss anecdotally, with little data to back up.

Other comments:

Intro:

The intro is long and I think could be streamlined. In particular, I think paragraphs 1 and 2 could be shortened.

We have significantly shortened the introduction.

The beginning of the paragraph that starts on page 7, line 8 that discussed of limits of use of pharmacy data to estimate PrEP uptake and lack of account for HIV-related risk factors may be better placed in the earlier paragraph that begins on page 5, line 29.

We moved the paragraphs following this advice.

This is a nit-pick, but the sentence on page 5, line 35 "...users also need to stay engaged and persist." would be more accurate if stated as "users also need to stay engaged and persist for as long as they remain at risk for HIV acquisition." Risk is time-variant and we have a tendency to analyze metrics on PrEP retention in the same way we analyze HIV care retention. Basically, the view is often ceasing PrEP use = bad, when this is not necessarily true. This is also why I think it may be helpful to also examine any PrEP use in the past 12m as an outcome if the data are available.

Thank you for your comment. Not nit-picky at all, we appreciate you bringing this up, and we have adjusted accordingly. Regarding, the last part, as previously mentioned, we were unable to perform the analysis in that manner.

Methods

What was the % enrollment in these two studies among app-users who completed the screening survey?

About 70% of participants who took the eligibility survey, went on to enroll on the studies.

The authors noted that age was categorized as < 18, 18-24, 25-29, 30-49 and 50+, but then in the results the <18 were collapsed with the 18-24 group. This should be updated to reflect what was actually done.

This was completed.

Results

On page 10, line 38, the authors note that PrEP use was greater in older vs. younger adults (68% vs. 51%); however they present 4 age categories. This should be clarified.

This was corrected. "significantly greater in adults older than 29 y.o"

Table 1 - The title should include more details about the study population, time frame etc. Tables should be able to stand on their own (i.e., I know exactly what the study population is) without having to refer back to the text.

The title of the table was changed to “Demographics and Clinical Guideline-related Characteristics of National Sample of Cisgender Men and Transgender People who have Sex with Men”

Table 1 - Something is wrong with the n's presented in each column under the gender identity column as they don't add up.

The numbers have been addressed. We really appreciate the attention to detail, and apologize for the oversight.

Discussion

Limitations - It would be nice if the authors could acknowledge limitations regarding potential selection biases and generalizability of these results as these are two substantial limitations of these cohorts.

We have expanded this section and included additional limitations of our data.

Reviewer: 2

Comments to the Author:

The authors present a MS on determinants of PrEP use in the US based on a large sample of MSM and TGNB taking clinical and Medicaid expansion determinants into account.

The sample size (coming from the Together 5000 and UNITE study) is clearly a strong point of the MS, at first glance. Looking into the demographics a bit more in detail, the percentage of TGNB sampled is very minimal, 1.7% of the total sample (but see my comment below). This really limits the interpretation for this sub-population.

Furthermore, the sample is quite dated by now, since it is from 2017/18.

We agree with the reviewer, this is a very small number, however in thinking of quasi-national sample the number of TGNB people may resemble the general population. One of the studies is actually conducting a sub-study to oversample trans people for that very reason. Regarding the timing, we understand your concern and have addressed in the limitation section. Though our sample is dated, the uptake of PrEP numbers have not changed ever since. In fact, this month in the FDA released its approval of injectable PrEP, it mentioned the 200,000 PrEP users in the US, which is a number that have remained unchanged since 2017. For that reason, we find our study relevant for exploring the role of Medicaid expansion on an individual's PrEP uptake, which is an anecdotal variable widely used, but with little data to back it.

In the Introduction, the authors cite research (often based on more novel data) that supports their research questions, both for clinical determinants and health care insurance status. This leaves the question open why this analysis is still necessary or what it can contribute above and beyond the existing literature. The authors should make this more explicit in their write-up.

We have made significant changes to our introduction that we hope have made clear our purpose and relevance of our study.

Information on the racial and age distribution by state/Medicaid expansion is missing.

Currently, it is not possible to determine whether certain age/race configurations are (not) present in certain states/medicaid expansion contexts - it is possible that skewed sample distribution is driving effects found / or is making it impossible to obtain them.

For MLA, we build the models with both individual levels and state-level variables. These models are powered to account for the differences on variance of the different types of distributions. Therefore, we would not account for individual-level variable distribution on the state-level. We welcome the reviewer to refer to the following papers for more details on MLA

Austin PC, Merlo J. Intermediate and advanced topics in multilevel logistic regression analysis. *Statistics in medicine*. 2017;36(20):3257-3277.

Merlo J, Chaix B, Ohlsson H, et al. A brief conceptual tutorial of multilevel analysis in social epidemiology: using measures of clustering in multilevel logistic regression to investigate contextual phenomena. *Journal of Epidemiology & Community Health*. 2006;60(4):290-297.

I have difficulties to match up the percentages reported on gender: In Table 1 85.2% identify as male, and minimal percentages as female, TG etc. - and the rest? Is there missing data?

Thanks so much for your attention. These numbers have been corrected.

In sum, I think the MS would benefit from a more detailed analysis of clinical and sociodemographic determinants x state level, and the authors should explain better why this study based on dated data is still contributing to the literature

We have added additional information on our limitations section to address the data timeframe.

VERSION 2 – REVIEW

REVIEWER	Jonas, Kai Maastricht University
REVIEW RETURNED	04-Jan-2022

GENERAL COMMENTS	<p>I have seen a previous version of the MS and I am happy to see that the authors tried to address the issues mentioned in the reviews as much as possible. I agree that the MS has gained in clarity and that previous issues have been clarified. From my perspective one aspect still remains to be clarified, and maybe I was not clear enough in my first review. I had mentioned in my first review that the absence of/low numbers of certain race/age configuration by state/medicaid expansion could bias the MLA results.</p> <p>Information on the racial and age distribution by state/medicaid expansion is missing.</p> <p>The authors argue that their models are powered to account for the differences in variance of the different types of distributions. I agree that the models account for differences in variance, but they cannot account for distributions if certain expressions of characteristics are not present at all in certain states. I would ask the authors to provide descriptive statistics of the sample per state, so that the reader can inform about the general distributions/expressions of characteristics. Maybe my concern is not warranted, and there are sufficient - as the authors put it - "similar individuals" from different states</p>
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	(Medicaid expansion states, compared to those not living in Medicaid expansion states). But, in case that there are relevant gaps of similar individuals, I would welcome that the authors reconsider their interpretation of their MLA results, or their robustness.
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VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Dr. Kai Jonas, Maastricht University

Comments to the Author:

I have seen a previous version of the MS and I am happy to see that the authors tried to address the issues mentioned in the reviews as much as possible. I agree that the MS has gained in clarity and that previous issues have been clarified. From my perspective one aspect still remains to be clarified, and maybe I was not clear enough in my first review. I had mentioned in my first review that the absence of/low numbers of certain race/age configuration by state/medicaid expansion could bias the MLA results.

Information on the racial and age distribution by state/medicaid expansion is missing.

The authors argue that their models are powered to account for the differences in variance of the different types of distributions. I agree that the models account for differences in variance, but they cannot account for distributions if certain expressions of characteristics are not present at all in certain states. I would ask the authors to provide descriptive statistics of the sample per state, so that the reader can inform about the general distributions/expressions of characteristics. Maybe my concern is not warranted, and there are sufficient - as the authors put it - "similar individuals" from different states

(Medicaid expansion states, compared to those not living in

Medicaid expansion states). But, in case that there are relevant gaps of similar individuals, I would welcome that the authors reconsider their interpretation of their MLA results, or their robustness.

We thank the reviewer for the clarification. We have added the information by state to the supplemental material and mentioned it in the text.

VERSION 3 – REVIEW

REVIEWER	Jonas, Kai Maastricht University
REVIEW RETURNED	16-Jan-2022
GENERAL COMMENTS	Thank you for the revisions made. I have no further comments.