ARTICLE DETAILS

TITLE (PROVISIONAL) Is the promise of methadone Kenya's solution to managing HIV and addiction? A mixed-methods mathematical modelling and qualitative study

AUTHORS Rhodes, Tim; Guise, Andy; Ndimbii, James; Strathdee, Steffanie; Ngugi, Elizabeth; Platt, Lucy; Kurth, Ann; Cleland, Charles; Vickerman, Peter

GENERAL COMMENTS

This is a nice piece of research. The attached comments are more in the nature of discussion stimulated by the manuscript than suggestions for the article. In addition I note a few very minor errors that need to be corrected:
p3, line 42: "investigating" should be "investigate"
p7, line 21: "upon depth" should be "upon in-depth"
p8, line 43-44: "salience of narratives of addiction recovery desire despite..." is very awkward wording - perhaps "salience of narratives of desire for addiction recovery despite..."

Rhodes et al. have combined mathematical modelling with qualitative research to provide a powerful analysis of expectations of opioid substitution treatment in Kenya. The mathematical modelling provides a realistic estimate of what can be expected from the introduction of opioid substitution treatment in terms of reduction of HIV incidence and prevalence amongst people who inject drugs within the constraints of the health care system in Kenya. The qualitative component of the research provides insight into the expectations of people who inject drugs and key stakeholders for opioid substitution treatment. These dimensions can be weighed against what is known about the outcomes of opioid substitution treatment.

As identified by Rhodes et al., much of the evidence regarding the effectiveness of opioid substitution treatment in reducing the transmission of HIV comes from developed, Western countries, although there is evidence that opioid substitution treatment does transfer effectively to other contexts, including countries with low socioeconomic status [1]. There is considerable ambivalence towards opioid substitution treatment and, given that HIV prevention is a major factor driving the introduction of opioid substitution...
treatment in many countries, it is important that expectations are kept realistic, and consider the particular circumstances of the country.

The actual findings of this work are of course specific to the circumstances in Kenya, but the approach taken by the authors is transferable to other countries, and the modelling has the potential to be able to be adjusted as the circumstances in Kenya change, or as increased knowledge is gained about the variables incorporated into the model. It would also be of interest to consider a modification of the model to incorporate amphetamine use as a variable. Amphetamines are used by injection, and may be associated with high risk sexual behaviours. In a context of higher incidence of sexual transmission of HIV, injecting use of amphetamines could significantly impact on the capacity of opioid substitution treatment to reduce injecting behaviour and the transmission of HIV. This may not be a consideration in Kenya, but would be relevant were this approach to be transferred to countries in parts of Asia.

The qualitative component of the research draws out an important consideration that contributes to ambivalence towards opioid substitution treatment, which is the desire for recovery, and the extent to which abstinence is perceived as an important indicator of recovery [2]. The combination of qualitative and modelling approaches provides a broad picture of expectations at baseline, at the time of introduction of opioid substitution treatment in Kenya. Comparisons with the actual outcomes achieved and changes in expectations and attitudes provide the potential for interesting research in the next few years.


recommend the primary subject heading to be HIV/AIDS rather than addiction.

2) The proportion of PWID defined as high-risk for the mathematical model is based on a community-based sample from Tanzania. However, previous research in Tanzania has shown that enrollees into the methadone program - especially in the earlier, high threshold stages - tended to people with a lower risk profile than what is observed in the PWID community (See 'Identifying Programmatic Gaps: Inequities in Harm Reduction Service Utilization among Male and Female Drug Users in Dar es Salaam, Tanzania' in PLoS ONE). Does the model account for the fact this will likely be the case among what appears to be the establishment of a high threshold program in Kenya? If not, can you mention this limitation and place the findings in the context of this likely dynamic (high threshold program enrolling clients with a lower risk profile) in Kenya?

3) Does the model factor in the higher likelihood of access to ART among PWID as a function of the OST program facilitating access and adherence to ART and the subsequent HIV prevention benefits? Based on my read, I don't think that it does. If it does, I would make this more clear in the methods, and if it doesn't I would consider including this parameter.

4) Survival time while on ART - is this based on PWID who are on OST or PWID who are not on OST? I think the former would be preferred.

5) At the end of the manuscript, the authors discuss the development of a new form of implementation science called, Implementation Social Science. While I completely agree with the authors of the importance to understand how new interventions sit within the social context, be it perceptions, attitudes, beliefs or 'what is said' about the intervention, it is unclear to me how this pursuit differs from what has been already put forth in implementation science/research frameworks, such as the Consolidated Framework for Implementation Research (CFIR). Rather than develop a 'new form' of implementation science and propose a new term, I would encourage the authors to place their work in the context of the CFIR, which to my understanding includes domains similar to the issues that the authors discuss.

VERSION 1 – AUTHOR RESPONSE

REVIEWER 1
p3, line 42: "investigating" should be "investigate"
p7, line 21: "upon depth" should be "upon in-depth"
p8, line 43-44: "salience of narratives of addiction recovery desire despite..." is very awkward wording - perhaps "salience of narratives of desire for addiction recovery despite..."

RESPONSE: All of the above corrections have been made.

... Amphetamines are used by injection, and may be associated with high risk sexual behaviours. In a context of higher incidence of sexual transmission of HIV, injecting use of amphetamines could significantly impact on the capacity of opioid substitution treatment to reduce injecting behaviour and the transmission of HIV. This may not be a consideration in Kenya, but would be relevant were this approach to be transferred to countries in parts of Asia.

RESPONSE: We agree with the reviewer on this point and will definitely amend the model when we
consider a setting where this type of drug use is important. We have added into the discussion to indicate that care should be taken to adjust such a model to reflect local patterns of drug use and their potential linkage with sexual and other risk practices, also adding a reference to amphetamines (Colfax et al., Lancet). However, it should also be noted that great care was taken in trying to incorporate the degree of sexual HIV transmission occurring in this Kenyan setting to prevent us from over estimating the likely impact of OST by attributing too much of the HIV transmission to injecting risks.

We now comment in the discussion:
Model adjustments might also be required in light of local patterns of injecting drug use and how these potentially link to risk practices, such as sexual risk in light of amphetamine injection.[54]

… The combination of qualitative and modelling approaches provides a broad picture of expectations at baseline, at the time of introduction of opioid substitution treatment in Kenya. Comparisons with the actual outcomes achieved and changes in expectations and attitudes provide the potential for interesting research in the next few years.
RESPONSE: We agree it is now important to evaluate the potential impact of OST in Kenya as it is scaled up and that this analysis should be considered as a first step in the process. We also note the need for prospective analyses in the contribution of the study statement.

REVIEWER 2
Given the focus on HIV/AIDS of the overall manuscript, I would recommend the primary subject heading to be HIV/AIDS rather than addiction.
RESPONSE: We maintain the mention of ‘HIV’ first in the title and throughout in terms of emphasis, but propose maintaining mention of ‘addiction’ too given the strong narrative of expectation emerging in relation to methadone being cast as a treatment for addiction recovery.

… Previous research in Tanzania has shown that enrollees into the methadone program - especially in the earlier, high threshold stages - tended to people with a lower risk profile than what is observed in the PWID community… Does the model account for the fact this will likely be the case among what appears to be the establishment of a high threshold program in Kenya? If not, can you mention this limitation and place the findings in the context of this likely dynamic (high threshold program enrolling clients with a lower risk profile) in Kenya?
RESPONSE: We thank the reviewer for pointing us towards the study by Bowring et al and Lambdin et al studies, which we now cite. We have now included a sentence in the model methods to emphasise that we do not assume differing uptake of OST amongst high risk PWID, and mention this as a limitation in the discussion.

In the methods, we note:
‘The projections assume that low and high risk PWID are equally likely to go on OST, and to be conservative they do not assume that PWID on OST have better ART outcomes as suggested by other studies [16-21].’

In the discussion, we write:
“It is also important that the nature of sexual HIV transmission is included with greater realism in future models, incorporating gender heterogeneities in the degree to which they drive sexual HIV transmission [40], as emphasised in a recent PWID study from Tanzania[52], and differences in the degree to which they are recruited onto OST.”

We have added the following citations:


Does the model factor in the higher likelihood of access to ART among PWID as a function of the OST program facilitating access and adherence to ART and the subsequent HIV prevention benefits? Based on my read, I don’t think that it does. If it does, I would make this more clear in the methods, and if it doesn’t I would consider including this parameter.

RESPONSE: We have made this clearer in the methods and mentioned it as a possible factor that if included could have increased our OST impact projections in the discussion. In the discussion, we now say:

“However, it is also possible that OST may have greater impact than we projected because of improvements in the uptake and outcomes of ART amongst PWID on OST. [16-21]”

Survival time while on ART - is this based on PWID who are on OST or PWID who are not on OST? I think the former would be preferred.

RESPONSE: We have assumed general survival times for PWID on ART and have not incorporated the effect of OST on this because of a lack of a systematic review on this interaction. However, because of the short duration of injecting it is unlikely that incorporating increased survival duration of ART for those on OST will have much effect to our modelling projections.

At the end of the manuscript, the authors discuss the development of a new form of implementation science called, Implementation Social Science. While I completely agree with the authors of the importance to understand how new interventions sit within the social context, be it perceptions, attitudes, beliefs or ‘what is said’ about the intervention, it is unclear to me how this pursuit differs from what has been already put forth in implementation science/research frameworks, such as the Consolidated Framework for Implementation Research (CFIR). Rather than develop a ‘new form’ of implementation science and propose a new term, I would encourage the authors to place their work in the context of the CFIR, which to my understanding includes domains similar to the issues that the authors discuss.

RESPONSE: We agree, that rather than envisaging the type of social science investigation proposed as creating a “new form of implementation science”, it implies expanding the type of social science incorporated within implementation science as popularly understood. Accordingly, we have changed the sub-title of this concluding section, which no longer refers to “Implementation social science” but to “Developing implementation science”. We therefore have de-emphasised any sense of us promoting a parallel movement in implementation science in favour of making it clear we are talking about implementation science incorporating a range of social sciences, including those more ‘critical’ in their study about how ‘evidence’ is made.

VERSION 2 – REVIEW

<table>
<thead>
<tr>
<th>REVIEWER</th>
<th>Linda Gowing</th>
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<tr>
<td>University of Adelaide, Australia</td>
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| REVIEW RETURNED   | 12-Jan-2015 |

| GENERAL COMMENTS  | No further comments - the authors have appropriately addressed comments on the first version of the manuscript. |

| REVIEWER          | Barrot Lambdin |

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| **Pangaea, United States of America** |  |
| **REVIEW RETURNED** | 13-Jan-2015 |

**GENERAL COMMENTS**

All of my comments from the first round of review have been sufficiently addressed.
Is the promise of methadone Kenya's solution to managing HIV and addiction? A mixed-method mathematical modelling and qualitative study

Tim Rhodes, Andy Guise, James Ndimbii, Steffanie Strathdee, Elizabeth Ngugi, Lucy Platt, Ann Kurth, Charles Cleland and Peter Vickerman

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