PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Opioid substitution therapy as a strategy to reduce deaths in prison: Retrospective cohort study
AUTHORS	Larney, Sarah; Gisev, Natasa; Farrell, Michael; Dobbins, Timothy; Burns, Lucinda; Gibson, Amy; Kimber, Jo; Degenhardt, Louisa

VERSION 1 - REVIEW

REVIEWER	Josiah D. Rich, MD, MPH Brown University The Center for Prisoner Health and Human Rights The Miriam Hospital Providence, RI, USA I have worked closely with the lead author on several manuscripts and am hosting her as a visiting scholar. I have not worked with her on this manuscript or topic.
REVIEW RETURNED	13-Feb-2014

GENERAL COMMENTS	This is a well written description of an elegant study looking at in prison mortality in Australian prisoners with a history of opiate addiction. There is a high prevalence of OST for prisoners in Australia, which is certainly very different than most of the US and many other nations where OST is very limited for prisoners. The key question I have is why were some prisoners not given OST, while most were? Any information about this would help the readers to understand better the implications of the results. For specific comments: p-8, line 6, change "used" to "using" p-10, line 46, mention is made of 35%. What proportion of all prisoners were in this cohort of prisoners with opiate addction? p-11, CMR- What is the CMR of this cohort when they are not incarcerated? How about on, or off OST? It seems to me that overall, the mortality rate is relatively low. If so, does that imply that prisons are protective (at least in the short run) against death? "gender" is a less confusing term than "sex" Although I may be a "biased" reviewer due to my association with the lead author, I believe this is a very important article that has implications for many other countries. It deserves an accompanying editorial. I would be happy to suggest many possible authors of such an editorial, or to write it myself. Thank you for the opportunity to review this manuscript.

REVIEWER	MEROUEH FADI Unité Sanitaire

	France I am invited to meetings/conventions by pharmaceutical companies
REVIEW RETURNED	27-Feb-2014

GENERAL COMMENTS	An important prospective study describing the relation between OST, deaths and re-incarceration was conducted in 2005/2006 and was not cited at all in this article, nor in the bibliography. (See: http://onlinelibrary.wiley.com/doi/10.1111/j.1360-0443.2009.02558.x/abstract)

REVIEWER	Barbara Broers Unit for Dependence in Primary Care Department of Community Health and Primary Care Geneva University Hospital
REVIEW RETURNED	02-Mar-2014

GENERAL COMMENTS	I prefer not to judge the statistics part and leave that to a specialist This is a very well-written, straightforward and relevant study and paper. The criteria to be selected in the cohort was being opioid-dependent=having at least once an OST. This means that part of the opiod users who never received OST were not in the cohort, they were probably at least half of opiod dependent inmates (citation in setting). Is it possible to discuss this potential selection bias more? I suggest in the setting description be adressed more when and how the OST was provided in prison (diagnosis of dependence? urine check? daily delivery under supervision?), what were the safety measures taken to avoid misuse (injection, different dosage) of OST or sale of the medication to others? In correlation with that: are there data on opiod overdose deaths in the study period among inmates who were not in the cohort? If this as zero or very low this could be considered an indicator of relative safety of OST in prison. Hope the authors will analyse also the impact of OST on mortality post-release...

VERSION 1 – AUTHOR RESPONSE

Reviewer Name Josiah D. Rich, MD, MPH
Institution and Country Brown University
The Center for Prisoner Health and Human Rights The Miriam Hospital Providence, RI, USA
Please state any competing interests or state ‘None declared’: I have worked closely with the lead author on several manuscripts and am hosting her as a visiting scholar. I have not worked with her on this manuscript or topic.

Although I may be a "biased" reviewer due to my association with the lead author, I believe this is a very important article that has implications for many other countries.
It deserves an accompanying editorial.

I would be happy to suggest many possible authors of such an editorial, or to write it myself.
Thank you for the opportunity to review this manuscript.
This is a well written description of an elegant study looking at in prison mortality in Australian prisoners with a history of opiate addiction.

Response: Thank you to the reviewer for these positive comments.

Comment: There is a high prevalence of OST for prisoners in Australia, which is certainly very different than most of the US and many other nations where OST is very limited for prisoners. The key question I have is why were some prisoners not given OST, while most were? Any information about this would help the readers to understand better the implications of the results.

Response: OST is provided in NSW prisons under the same clinical guidelines as in the community. We have revised and added to the text under the 'setting' subheading of the Methods section as follows:

"Health services in NSW prisons are provided by the Ministry of Health, not correctional authorities. There is a well-established OST program in NSW prisons that operates as part of the state-wide opioid treatment program.12 13 People who enter prison while in OST continue treatment while incarcerated, and OST can be commenced during incarceration if clinically indicated.12 Clinical indications for OST are the same as in community settings.13"

For specific comments:
p-8, line 6, change "used" to "using"

Response: This change has been made.

p-10, line 46, mention is made of 35%. What proportion of all prisoners were in this cohort of prisoners with opiate addiction?

Response: Unfortunately, it is not possible to determine the proportion of all prisoners that were in our cohort, as we do not know the number of unique prisoners entering and exiting NSW prisons during the observation period. We provide the 35% figure only to give an indication of the extent to which opioid-dependent prisoners contribute to unnatural deaths in NSW prisons.

p-11, CMR- What is the CMR of this cohort when they are not incarcerated? How about on, or off OST? It seems to me that overall, the mortality rate is relatively low. If so, does that imply that prisons are protective (at least in the short run) against death?

Response: We have documented the CMR of this cohort outside of custody in a separate paper in press at Addiction (citation 31 in this paper). In terms of the potential protective nature of prison against mortality, we have added the following text to the third paragraph of the discussion:

"Compared to opioid-dependent populations at liberty, mortality rates were low in opioid-dependent prisoners.10 This is likely a result of limited access to illicit opioids and low exposure to other common causes of death in this population, such as motor vehicle accidents.22"

"gender" is a less confusing term than "sex"

Response: We have replaced "sex" with "gender".

Reviewer Name MEROUEH FADI

Institution and Country Unité Sanitaire
France
Please state any competing interests or state ‘None declared’: I am invited to meetings/conventions by pharmaceutical companies

An important prospective study describing the relation between OST, deaths and re-incarceration was conducted in 2005/2006 and was not cited at all in this article, nor in the bibliography. (See: http://onlinelibrary.wiley.com/doi/10.1111/j.1360-0443.2009.02558.x/abstract)

Response: We have read the paper cited by this reviewer and note that there were no deaths in prison in this study. We have added the following text to the discussion section of the paper:

“Prior studies of OST in correctional settings, including a clinical trial21 and prospective cohort studies,22 23 have not reported any deaths during OST, but these were not powered to detect differences in mortality rates during periods in and out of treatment.”

Reviewer Name Barbara Broers
Institution and Country Unit for Dependence in Primary Care
Department of Community Health and Primary Care Geneva University Hospital
Please state any competing interests or state ‘None declared’: none declared

I prefer not to judge the statistics part and leave that to a specialist

This is a very well-written, straightforward and relevant study and paper.

Response: Thank you to the reviewer for these positive comments.

The criteria to be selected in the cohort was being opioid-dependent=having at least once an OST. This means that part of the opiod users who never received OST were not in the cohort, they were probably at least half of opiod dependent inmates (citation in setting). Is it possible to discuss this potential selection bias more?

Response: It is true that there is a point estimate of OST coverage in NSW prisons of 43%. However, this does not mean that half of prisoners with opioid dependence were not in the cohort, as people were entered into the cohort on the basis of any OST in either prison or the community. We have noted in previous papers that the opioid treatment cohort is highly representative of the opioid-dependent population, including perhaps 80% of the state-wide opioid-dependent population. We have added the following text to this effect in the discussion:
“Although precise data are not available on the representativeness of this population, in sentinel surveillance studies of people who inject drugs in NSW (98% of whom have a history of illicit opioid use) almost 60% of participants are currently in OST, and more than 80% have a history of OST,20 suggesting that the cohort is highly representative of the NSW opioid dependent population. The subset of this population that had been incarcerated was included in this study.”

I suggest in the setting description be adressed more when and how the OST was provided in prison (diagnosis of dependence? urine check? daily delivery under supervision?), what were the safety measures taken to avoid misuse (injection, different dosage) of OST or sale of the medication to others?

Response: In the interests of brevity, we have not reported these details, but have provided references for the interested reader, such as clinical guidelines for the OST program.

In correlation with that: are there data on opiod overdose deaths in the study period among inmates who were not in the cohort? If this as zero or very low this could be considered an indicator of relative safety of OST in prison.

Response: If we are interpreting this comment correctly, the reviewer is suggesting that opioid overdose deaths among people not in the cohort would be evidence of diversion of opioids prescribed for OST in the prison setting. We disagree for several reasons. Although it is possible that opioid overdoses in prison are a result of illicit use of diverted OST medicines, they also occur as a result of heroin use. Furthermore, OST medications may also be smuggled into prison, meaning that even if there was a death due to methadone or buprenorphine among people not currently in OST, it would be difficult, if not impossible, to determine the source of the opioid medication.

Additionally, opioid overdose deaths within the cohort could also be associated with diverted opioid medications, both because cohort members were not in treatment at all times during imprisonment, and also because there may be use of diverted OST medications among those also in treatment.

In any event, we are unable to identify the substances involved in overdose deaths in prison among non-cohort prisoners as these data are not publicly available.

Hope the authors will analyse also the impact of OST on mortality post-release...

Response: A paper on this topic is currently in press at Addiction (Degenhardt et al., The impact of opioid substitution therapy on mortality post-release from prison: Retrospective data linkage study) and is cited in this paper (citation 31).