PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Respiratory health screening for opiate misusers in a specialist community clinic: a mixed methods pilot study, with integrated staff and service user feedback.
AUTHORS	Mitchell, Caroline; Pitt, Alice; Hulin, Joe; Lawsin, Rod; Ashby, Fleur; Appelqvist, Ivan; Delaney, Brigitte

VERSION 1 - REVIEW

REVIEWER	Tim Millar Centre for Mental Health and Safety Institute of Brain, Behaviour and Mental Health Faculty of Medical & Human Sciences The University of Manchester Manchester UK
REVIEW RETURNED	05-Jul-2016

GENERAL COMMENTS	General comments: This manuscript reports a pilot study of respiratory health screening among opiate users treated in an outpatient clinic in the UK. As a pilot the study is, inevitably, subject to some limitations, but these are properly acknowledged. The manuscript makes relatively little mention of tobacco smoking as a contributory factor to poor respiratory health in this population. This might perhaps be given a little more prominence, given that tobacco smoking is highly prevalent in this population (note that all participants were smokers or ex-smokers of tobacco). The possible synergistic effects of tobacco smoking and heroin inhalation could have been discussed. There are clear clinical implications with respect to addressing continued tobacco use in this population which, although mentioned briefly in the Conclusions section, could be explored more fully in the Discussion. Also, the Discussion & Introduction sections might perhaps mention the particular danger of opioid-induced respiratory depression, thus elevated risk of overdose, among those with already-poor respiratory function. This work is timely, given concerns regarding premature mortality among an ageing cohort of opiate users and recent increases in the number of drug related deaths in this group. Although, as the authors properly acknowledge, the sample is small, nonetheless publication will help to highlight the issue of poor respiratory health in this population to a general medical audience.

	Specific comments: Intro, first para: the reference in support of the assertion re smoking heroin being the norm is rather old (1997) and may not obviously relate to the current situation. I concur that smoking heroin is now the predominant mode of administration and that the reasons cited for the shift to smoking are likely to be valid, and I am not aware of a more recent alternative reference to substitute here. However, the authors might consider rephrasing the opening sentence slightly, to reflect that this finding reflects the situation as it was reported some time ago. Intro, second para: a recent study has highlighted the contribution of circulatory and respiratory disease to premature mortality among opioid users in England (Pierce et al, 2015, Drug & Alcohol Dependence, 146, 17-23). I am an author of that paper, but it or a similar alternative might help to add weight to the importance of the issue. Intro, second para, typo: “Criminal Reduction Initiative services” – should this refer to “Crime Reduction Initiative services”, which was (at the time) the correct title of the treatment agency? Intro, second para: “Inhalation of opiates has been linked to early onset Chronic Obstructive Pulmonary Disease (COPD) (6)” the reference cited here also highlights the difficulty of teasing out the overlapping contribution of tobacco smoking (almost all of the target group are tobacco smokers) which warrants additional emphasis (and see General Comments, above). Intro, final para: “The study also aimed to assess the feasibility of using routinely collected clinical data, with informed consent, in opiate misuse clinics”. There is a large body of published research that uses such data and, given the small sample, it is not immediately clear how the current study adds to knowledge here. Consider removing this aim (and related material), as it detracts a little from the otherwise neat focus of the manuscript. Method, para one, typo: “Voluntary ‘drop–in lung health assessment’ were”; “assessments” or “was”? Method: a little more detail would be helpful here, e.g. on recruitment, eligibility, time period, etc. Suggest that the authors re-visit and consider STROBE checklist. Method: details of research ethics approvals are missing. Please include. Results: EQ5D is mentioned in the Methods section but there are no results reported for this. Results: only 34/36 participants had smoked heroin. Given the focus of the study is on respiratory effects among opiate users and that the Introduction focuses exclusively on heroin inhalation, the authors might consider adding additional justification or explanation regarding the inclusion of two participants who appear not to have smoked heroin. It would also be helpful here to indicate the time period to which the observations re drug inhalation relate; it is not clear whether these refer to lifetime or recent inhalation.

	Results, para two: “L-TOPs data was collected”, first occurrence of the acronym L-TOPs (vs. TOP); requires explanation. Results, para three: “the majority were unemployed and lived with parents (Table 1)” Just a minor point, but rephrase slightly: because living arrangements and employment status are not cross-tabulated to support this assertion and because, actually, a minority (25%) lived with parents. Additionally, employment, work and living arrangement status may be superfluous detail, especially given the small n, and are not mentioned elsewhere. Perhaps consider omitting? Results, Tables 1 & 2, titles: Please indicate the sample size (preferably in title). Results, Table 2: noteworthy that 93% inhaled cocaine (although should that perhaps be specified as crack cocaine?) and 86% cannabis. This warrants more prominent mention in the Discussion section than is provided at present. Moreover, all were tobacco smokers or ex-smokers, which receives scant mention (& see general comments). Results, section “Participants with prior diagnosis of asthma”: The details regarding the test threshold scores might better sit in the Methods than the discussion. Although in juxtaposition with the results they serve to highlight the very significantly poor scores of this group, that commentary might better sit in the Discussion. Similarly “NICE guidance was used to categorize airways obstruction as measured without bronchodilation (14,15).” sits better in the Methods section. Results, section “Spirometry” and “The Treatment Outcome Profile (TOP)”: these sections sit within the heading “Participants with prior diagnosis of asthma” but appear to relate to the full sample? Results, section “The Treatment Outcome Profile (TOP)” (and corresponding section in Methods): entirely appreciate the difficulty in obtaining complete TOP data. Given the poor coverage and inconsistent data the authors might consider dropping this from the manuscript, or relegating it to only brief mentions in the Methods and Discussion sections. Results, section “Patient and practitioner feedback”, first para: this para describes the method whereby feedback was obtained, thus would sit better in the Methods section. Results, section “Recognition of respiratory co-morbidity”: I was surprised not to see mention of tobacco smoking here. Did the PPI groups cover this area? Discussion, para 1, typos: “Service users willing” ... “...were willing”? “...undertake respiratory screening routine settings” ... “... in routine settings”? Discussion, first para: first appearance of acronym CRI, should appear in Introduction (re Crime Reduction Initiatives). Discussion, para 2: Perhaps over-states the case for /against use of TOP data in research, given the small sample. It is already used

	reasonably widely in research so it is not convincing that the current study adds very much here (apologies if I have misunderstood the intention of this para). Discussion, final para: “participants in this study may have differed from the general clinic population.” It is good to see that the authors have noted this limitation in the manuscript. Perhaps add that service users may have self-selected on the basis that they experienced respiratory problems, to add emphasis here? Discussion could perhaps draw out a little more clearly, and make more of, what this study adds to the previous literature, especially in respect of the prior study that is cited (Lewis-Burk et al, reference 9). References 1, 9 22, 23, 24, 25, & 26 – journal title is missing, please add. Figure 2: key required (missing at present) to explain the different colours here. Please expand title to reflect the composition and size of the sample.

REVIEWER	Dr Caitlin Notley Norwich Medical School University of East Anglia UK
REVIEW RETURNED	15-Jul-2016

GENERAL COMMENTS	This pilot study of respiratory screening for opiate misusers takes a mixed methods iterative approach, adhering to the early phases of the MRC complex intervention guidance. I recommend that the paper is accepted for publication, subject to some revisions, as outlined below. Although conclusions are tentative due to the small sample size, this well designed study demonstrates that it is feasible and acceptable to patients to offer respiratory screening to a population of treatment seeking opiate misusers. There is clearly a need for this screening, as respiratory problems are highly prevalent in this group, who may be less likely than general population samples to access healthcare. The authors background literature review also points out that two thirds of those affected by COPD are undiagnosed, so there is potentially a clear rationale for screening of high risk populations, who would benefit from earlier identification of respiratory problems. There would also clearly be a benefit and cost saving to healthcare systems of early identification. It would be advantageous if the authors were able to draw on any existing estimates of likely cost effectiveness of screening to further strengthen this rationale, if such estimates exist? If not, then a rationale for a larger study could develop this point, that feasible cost effectiveness measures need to be integrated into a subsequent trial. Findings of the study will be of interest and use to the future design of screening interventions. Some more nuanced findings, such as in relation to incentives and the feasibility of recruitment from the perspectives of healthcare workers, will be of particular interest to those designing a fully powered trial to ensure that recruitment barriers are addressed at the design stage. Methods: Pilot study outcomes are clearly defined and appropriately identified drawing on high quality evidence and involvement of a

	multi-disciplinary consensus group of clinicians. The study involved appropriate PPI feedback. Ethical approval confirmation and details need to be included Results: the gender distribution of participants matches that for larger samples. The age mean seems relatively low however, and the range does not capture the oldest age group that might be in treatment nationally. A comment on this in the discussion is needed, perhaps by comparing to national TOPs data. Current smoking status is especially high in this pilot sample. Possibly higher than other samples of in treatment opiate misusers (marginally, as I think nationally the figure is around 90%). This needs to be checked against national data (obtained via available NDTMS figures) and a comment on the comparisons with this sample would be desirable in the discussion. The qualitative findings on barriers to accessing healthcare services are interesting. The discussion could relate these findings to the wider literature on barriers to healthcare for those either in or out of treatment for opiate misuse, such as 1. Notley, C Blyth, A, Maskrey, V, Craig, J V & Holland R (2013) The Experience of Long-Term Opiate Maintenance Treatment and Reported Barriers to Recovery: A Qualitative Systematic Review Eur Addict Res 2013;19:287-298 (DOI: 10.1159/000346674) http://www.karger.com/DOI/10.1159/000346674 2. Notley, C, Maskrey, VL and Holland, RC (2012) The needs of problematic drug misusers not in structured treatment - a qualitative study of perceived treatment barriers and recommendations for services. Drugs: Education, Prevention & Policy, 19 (1). pp. 40-48. Other points for discussion: The discussion demonstrates that it is feasible and acceptable to patients to offer respiratory screening in the substance misuse treatment service arena. There are some caveats that researchers designing a trial should address, such as the feasibility in collecting reliable and valid TOP outcome data. The authors make valuable suggestions for how this might be achieved. It would be advantageous to include a comment on the very high smoking prevalence amongst this population and how this also interacts with respiratory disease (as the authors do in relation to other inhaled substance misuse). See comment in methods section above. This links to one of the limitations discussed that the small sample size may not be reflective of the larger clinical population The discussion makes the point that this mixed methods study suggests it is feasible to conduct screening for respiratory conditions amongst opiate misusers. There is also the suggestion that this would be cost effective in identifying conditions earlier. Could the authors make any tentative estimates of likely cost savings to the NHS here? Although I recognise estimates may be tentative based on this pilot data, it would further strengthen the rationale for the importance of screening amongst this population. The statement 'it has been noted that cost-effective evidence is available for the opportunistic case finding of respiratory health issues in patients with at higher risk of disease development, such as smokers and individuals aged over 35 years' requires a reference. Conclusions: The final conclusion: ' the development of a pharmacy based intervention to improve the safety profile of asthma inhaler usage and overall medicines adherence with a personalised asthma plan and the offer of pharmacy based smoking cessation support and flu jabs for opiate misusers was seen as a potentially useful

	setting for care.' Come rather out of the blue. The authors should reconsider this as a final conclusion of their study, or if retaining it, should provide data in the results section to suggest that service users or staff have indicated community pharmacy as a potentially useful setting.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

Intro, first para: the reference in support of the assertion re smoking heroin being the norm is rather old (1997) and may not obviously relate to the current situation. I concur that smoking heroin is now the predominant mode of administration and that the reasons cited for the shift to smoking are likely to be valid, and I am not aware of a more recent alternative reference to substitute here. However, the authors might consider rephrasing the opening sentence slightly, to reflect that this finding reflects the situation as it was reported some time ago.

To address this issue the authors once again reviewed the literature for more current data on heroin inhalation rates. However, as the reviewer has noted there is no conclusive data available. The authors have therefore edited the first two sentences of the opening paragraph of the introduction to clearly state that although inhalation of opiates was the most frequent form of inhalation by the 1990s, there is a lack of current evidence to suggest this still the case.

Intro, second para: a recent study has highlighted the contribution of circulatory and respiratory disease to premature mortality among opioid users in England (Pierce et al, 2015, Drug & Alcohol Dependence, 146, 17-23). I am an author of that paper, but it or a similar alternative might help to add weight to the importance of the issue.

The authors agree that the inclusion of the above reference further highlights the importance of the issue and have therefore added this reference alongside a sentence explaining the findings of the study to the second paragraph of the introduction.

Intro, second para, typo: "Criminal Reduction Initiative services" –should this refer to "Crime Reduction Initiative services", which was (at the time) the correct title of the treatment agency?

The term has been amended to state "Crime Reduction Initiative Services".

Intro, second para: "Inhalation of opiates has been linked to early onset Chronic Obstructive Pulmonary Disease (COPD) (6)" the reference cited here also highlights the difficulty of teasing out the overlapping contribution of tobacco smoking (almost all of the target group are tobacco smokers) which warrants additional emphasis (and see General Comments, above).

An additional sentence has been added to this paragraph to describe how a failure to control for tobacco smoking in the previous literature makes it difficult to determine the independent effects of opiate misuse on lung health.

Intro, final para: "The study also aimed to assess the feasibility of using routinely collected clinical data, with informed consent, in opiate misuse clinics". There is a large body of published research that uses such data and, given the small sample, it is not immediately clear how the current study adds to knowledge here. Consider removing this aim (and related material), as it detracts a little from the otherwise neat focus of the manuscript.

This aim has now been deleted from the introduction. Related material on the routine collection of data in other sections of the manuscript has also been minimised. This material has not been removed completely due to positive comments from the 2nd reviewer, which state that valuable suggestions have been made regarding the collection of TOP data.

Method, para one, typo: “Voluntary ‘drop–in lung health assessment’ were”; “assessments” or “was”?

Due to the addition of further information in the methods section regarding details of the recruitment process, this sentence has now been re-worded and the typo has been removed from the manuscript.

Method: a little more detail would be helpful here, e.g. on recruitment, eligibility, time period, etc. Suggest that the authors re-visit and consider STROBE checklist.

Further detail has been added to the opening sentences of the method section in accordance with the STROBE checklist. This includes additional information on the recruitment time period, the sampling methods used and the eligibility criteria for participants.

Method: details of research ethics approvals are missing. Please include.

Details of the ethical approvals have been added to the opening sentence of the methods section.

Results: EQ5D is mentioned in the Methods section but there are no results reported for this.

The results from the EQ-5D have now been added to the results section in text and in Table 3.

Results: only 34/36 participants had smoked heroin. Given the focus of the study is on respiratory effects among opiate users and that the Introduction focuses exclusively on heroin inhalation, the authors might consider adding additional justification or explanation regarding the inclusion of two participants who appear not to have smoked heroin. It would also be helpful here to indicate the time period to which the observations re drug inhalation relate; it is not clear whether these refer to lifetime or recent inhalation.

A sentence has been added to the opening paragraph of the method section to explain the inclusion of two participants who were non-heroin smokers. In this instance all participants who had history of opiate misuse were included in the study in order to gain an indication of the rates of heroin inhalation in this population. A sentence has also been added to explain that the inhalation rates related to all lifetime inhalation, both present and past.

Results, para two: “L-TOPs data was collected”, first occurrence of the acronym L-TOPs (vs. TOP); requires explanation.

This has been amended to TOP.

Results, para three: “the majority were unemployed and lived with parents (Table 1)” Just a minor point, but rephrase slightly: because living arrangements and employment status are not cross-tabulated to support this assertion and because, actually, a minority (25%) lived with parents. Additionally, employment, work and living arrangement status may be superfluous detail, especially given the small n, and are not mentioned elsewhere. Perhaps consider omitting?

The authors agree with the above comments and have subsequently removed the sentence regarding living arrangements and employment status. However, the authors feel that the inclusion of the data on living arrangements and employment status still warrant inclusion in the table, as they provide

some indication of the environmental factors that could impact upon the respiratory health of this population, which are later discussed in the manuscript.

Results, Tables 1 & 2, titles: Please indicate the sample size (preferably in title).

Sample sizes have been added to the titles of all tables.

Results, Table 2: noteworthy that 93% inhaled cocaine (although should that perhaps be specified as crack cocaine?) and 86% cannabis. This warrants more prominent mention in the Discussion section than is provided at present. Moreover, all were tobacco smokers or ex-smokers, which receives scant mention (& see general comments).

Additional detail has been added to the 4th paragraph of the discussion section which highlights the above issue and also the implications of controlling for such factors in future research into the respiratory health of opiate misusers.

Results, section “Participants with prior diagnosis of asthma”: The details regarding the test threshold scores might better sit in the Methods than the discussion. Although in juxtaposition with the results they serve to highlight the very significantly poor scores of this group, that commentary might better sit in the Discussion. Similarly “NICE guidance was used to categorize airways obstruction as measured without bronchodilation (14,15).” sits better in the Methods section.
These details have now been moved to the methods section.

Results, section “Spirometry” and “The Treatment Outcome Profile (TOP)”: these sections sit within the heading “Participants with prior diagnosis of asthma” but appear to relate to the full sample?

These sections have now been moved from under the “Participants with prior diagnosis of asthma” heading to an earlier section of the results which reports data on the entire sample.

Results, section “The Treatment Outcome Profile (TOP)” (and corresponding section in Methods): entirely appreciate the difficulty in obtaining complete TOP data. Given the poor coverage and inconsistent data the authors might consider dropping this from the manuscript, or relegating it to only brief mentions in the Methods and Discussion sections.

Details regarding the TOP data have been reduced in both the results and methods section. These sections have not been removed completely due to positive comments from the 2nd reviewer on the inclusion of this data.

Results, section “Patient and practitioner feedback”, first para: this para describes the method whereby feedback was obtained, thus would sit better in the Methods section.

This has now been moved to the method section.

Results, section “Recognition of respiratory co-morbidity”: I was surprised not to see mention of tobacco smoking here. Did the PPI groups cover this area?

There was some limited discussion of this in the PPI groups and in accordance tobacco has been added alongside the mention of other inhaled drugs in this section.

Discussion, para 1, typos: “Service users willing” ... “...were willing”? “...undertake respiratory screening routine settings” ... “... in routine settings”?

This sentence has been amended to include the phrase “in routine settings”.

Discussion, first para: first appearance of acronym CRI, should appear in Introduction (re Crime Reduction Initiatives).

This acronym has been added to the introduction section.

Discussion, para 2: Perhaps over-states the case for /against use of TOP data in research, given the small sample. It is already used reasonably widely in research so it is not convincing that the current study adds very much here (apologies if I have misunderstood the intention of this para).

This section has been reduced and moved to the third paragraph of the discussion section. The authors believe that a short discussion of the inclusion of this data is warranted as although this is used widely in substance misuse research, the feasibility of including such routine data in research relating to co-morbid respiratory health in substance misusers, and related factors, has not been widely discussed. Positive comments from the 2nd reviewer regarding the discussion of this data have also supported its inclusion.

Discussion, final para: “participants in this study may have differed from the general clinic population.” It is good to see that the authors have noted this limitation in the manuscript. Perhaps add that service users may have self-selected on the basis that they experienced respiratory problems, to add emphasis here?

An additional sentence has been added to the limitations section to discuss the potential self-selecting nature of the sample.

Discussion could perhaps draw out a little more clearly, and make more of, what this study adds to the previous literature, especially in respect of the prior study that is cited (Lewis-Burk et al, reference 9).

Additional detail has been added to the third paragraph of the discussion section to highlight what this study adds to the previous literature, particularly in relation to the Lewis-Burke study. The authors have noted how the inclusion of additional measures relating to quality of life and asthma control and the integration of PPI feedback provide a more in-depth insight towards the burden of respiratory health in this population, the contributing factors and how this impacts upon the overall wellbeing of this high risk, hard to reach population. In addition the fact that this is the first study assessing the feasibility of interventions aimed specifically at community substance misuse clinics is also stated.

References 1, 9 22, 23, 24, 25, & 26 – journal title is missing, please add.

Journal titles have been added to the above references. The addition of new references means that the original corresponding numbers listed above may now have changed

Figure 2: key required (missing at present) to explain the different colours here. Please expand title to reflect the composition and size of the sample.

The title for Figure 2 has been amended and a note has been added to highlight that the red bars indicate those at a higher risk of developing COPD.

Reviewer 2

Ethical approval confirmation and details need to be included.

Details of ethical approval have been added to the opening of the methods section.

Results: the gender distribution of participants matches that for larger samples. The age mean seems relatively low however, and the range does not capture the oldest age group that might be in treatment nationally. A comment on this in the discussion is needed, perhaps by comparing to national TOPs data.

A discussion of the age range of the sample has been added to the limitations section of the discussion, to highlight the lack of data on older age groups in the current study in comparison to national data obtained from the NDTMS.

Current smoking status is especially high in this pilot sample. Possibly higher than other samples of in treatment opiate misusers (marginally, as I think nationally the figure is around 90%). This needs to be checked against national data (obtained via available NDTMS figures) and a comment on the comparisons with this sample would be desirable in the discussion.

Although the authors could not find directly comparable NDTMS figures, data regarding smoking prevalence from an international systematic review has now been added to the 4th paragraph of the discussion section and contrasted with the pilot study findings.

The qualitative findings on barriers to accessing healthcare services are interesting. The discussion could relate these findings to the wider literature on barriers to healthcare for those either in or out of treatment for opiate misuse, such as
1. Notley, C Blyth, A, Maskrey, V, Craig, J V & Holland R (2013) The Experience of Long-Term Opiate Maintenance Treatment and Reported Barriers to Recovery: A Qualitative Systematic Review Eur Addict Res 2013;19:287-298 (DOI: 10.1159/000346674)
http://www.karger.com/DOI/10.1159/000346674
2. Notley, C, Maskrey, VL and Holland, RC (2012) The needs of problematic drug misusers not in structured treatment - a qualitative study of perceived treatment barriers and recommendations for services. Drugs: Education, Prevention & Policy, 19 (1). pp. 40-48.

The above references have been added to the discussion section alongside a more detailed discussion of the barriers to accessing care for this population and potential strategies for overcoming these barriers.

It would be advantageous to include a comment on the very high smoking prevalence amongst this population and how this also interacts with respiratory disease (as the authors do in relation to other inhaled substance misuse). See comment in methods section above. This links to one of the limitations discussed that the small sample size may not be reflective of the larger clinical population

Additional detail has been added to paragraph 4 of the discussion highlighting the difficulties in determining the independent effects of inhaled poly-drug use and tobacco and the need for future research to control for such factors.

The discussion makes the point that this mixed methods study suggests it is feasible to conduct screening for respiratory conditions amongst opiate misusers. There is also the suggestion that this would be cost effective in identifying conditions earlier. Could the authors make any tentative estimates of likely cost savings to the NHS here? Although I recognise estimates may be tentative based on this pilot data, it would further strengthen the rationale for the importance of screening amongst this population.

Figures taken from a previous study on the potential cost savings have been added to this section of the discussion.

The statement ‘it has been noted that cost-effective evidence is available for the opportunistic case finding of respiratory health issues in patients with at higher risk of disease development, such as smokers and individuals aged over 35 years’ requires a reference.

This reference has now been added.

Conclusions: The final conclusion: ‘ the development of a pharmacy based intervention to improve the safety profile of asthma inhaler usage and overall medicines adherence with a personalised asthma plan and the offer of pharmacy based smoking cessation support and flu jabs for opiate misusers was seen as a potentially useful setting for care.’ Come rather out of the blue. The authors should reconsider this as a final conclusion of their study, or if retaining it, should provide data in the results section to suggest that service users or staff have indicated community pharmacy as a potentially useful setting.

This section has now been removed from the conclusion.

All revisions have been developed in consultation with all co-authors, and each author has given approval to the revised manuscript submitted. Please can it also be noted that the name of the author Rod Lawson has been spelt incorrectly as “Lawsin” via the author centre. We have been unable to edit this. The correct spelling is included in the main document. Thank you for your consideration.

VERSION 2 – REVIEW

REVIEWER	Dr Caitlin Notley University of East Anglia UK
REVIEW RETURNED	10-Sep-2016

GENERAL COMMENTS	I am satisfied that the authors have addressed all my comments and have no further comments to add.