**Title:** The health impact of social exclusion: a systematic review and meta-analysis of morbidity and mortality data from homeless, prison, sex work and substance use disorder populations in high-income countries.

**Authors:** Robert W Aldridge PhD, Alistair Story PhD, Prof Stephen W Hwang MD, Prof Merete Nordentoft DMSc, Serena A Luchenski MFPH, Greg Hartwell MFPH, Emily J Tweed MFPH, Dan Lewer MFPH, Srinivasa Vittal Katikireddi PhD, Prof Andrew C Hayward MD.

1. Centre for Public Health Data Science, Institute of Health Informatics, University College London, 222 Euston Road, London, NW1 2DA, UK.
2. The Farr Institute of Health Informatics Research, University College London, 222 Euston Road, London, NW1 2DA, UK.
4. Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute, St Michael’s Hospital, Toronto, ON, Canada.
5. Mental Health Centre Copenhagen and Faculty of Health and Medical Sciences, University of Copenhagen, Denmark.
6. Department of Social and Environmental Health Research, London School of Hygiene & Tropical Medicine, London WC1H 9SH, UK.
7. MRC/CSO Social & Public Health Sciences Unit, University of Glasgow, Top floor, 200 Renfield Street, G2 3QB, UK.
8. Institute of Epidemiology and Health Care, University College London, 1-19 Torrington Place, London WC1E 6BT, UK.

*Corresponding Author
Robert W Aldridge
The Farr Institute of Health Informatics Research
University College London
222 Euston Road
London NW1 2DA
Email: r.aldridge@ucl.ac.uk
Telephone: +44 20 3549 5541
Abstract

Background:

Inclusion health focuses on people in extremes of poor health due to poverty, marginalisation and multiple morbidity. We aimed to synthesise morbidity and mortality data on overlapping populations experiencing deep social exclusion evident by homelessness, substance use disorders, sex work and imprisonment.

Methods:

We searched Medline, Embase and the Cochrane Library for studies published January 2005-October 2015. We included articles written in English from high-income countries that were conducted in populations with histories of homelessness, imprisonment, sex work and substance use disorder (excluding cannabis and alcohol). Primary outcomes were measures of morbidity (prevalence or incidence) and mortality (standardised mortality rates – SMRs – and mortality rates).

Findings:

Our search identified 7946 articles, with 337 studies included. All-cause SMRs were significantly raised in 98.9% (91/92) of extracted data points and were 11.9 (95% CI 10.4–13.3; I² 94.1%) in females and 7.9 (95% CI 7.0–8.7; I² 99.1%) in males. Heterogeneity was high between studies. Summary SMR estimates for ICD-10 categories with two or more included data points were highest in deaths due to injury and poisoning in males (7.9; 95% CI 6.4–9.4; I² 98.1%) and females (18.7; 95% CI 13.7–23.7; I² 91.5%). Disease prevalence was consistently raised across infections, mental health, neoplasms, cardiovascular, gastroenterological and respiratory conditions.

Interpretation:

Socially excluded populations experience extreme health inequalities, far greater than those observed amongst people living in areas of high social deprivation. These inequalities occur across the full spectrum of health conditions, with the relative impact of exclusion being greater in females than males. Measures of morbidity and mortality were much higher than those observed across area based measures of social deprivation highlighting the need for better data on these populations who are largely invisible in routine health information systems. The extreme health inequity demonstrated demands intensive cross sectoral policy and service action to prevent exclusion and improve health outcomes in those already marginalised.

Funding

Wellcome Trust, NIHR, NHSE, NRS Scottish Senior Clinical Fellowship, Medical Research Council, Chief Scientist’s Office, Central and North West London NHS Trust.
Introduction

Inclusion health is a research, service, and policy agenda that aims to prevent and redress health and social inequities among people in extremes of poor health due to poverty, marginalisation and multiple morbidity (cross reference IH paper 2). It is well established that in high income countries, health outcomes are strongly influenced by socioeconomic status. The association between socioeconomic status and health outcomes is well established. For example, the standardised mortality rates for those aged 15–64 in the most deprived twentieth of areas in England are is 2.8 times the rate in the least deprived areas for men and 2.1 times the rate for women. However, analyses based on geographical location may obscure these commonly observed social gradients in health may not capture the true full extent of health inequities in for those who experiencing deep social exclusion.

Previous research has described the high levels of substance use disorders (SUD) in homeless populations, prisoners, and sex workers, and the increased prevalence of homelessness in prisoners and sex workers. These marginalised populations have common intersecting characteristics and adverse life experiences that lead to deep social exclusion, making them some of the most common powerful determinants of marginalisation in high-income settings.

Marginalised populations when considered separately have been shown to have high levels of all-cause mortality. However, despite the highly overlapping nature of the risk factors and substantially increased mortality, no previous review has attempted to examine their outcomes together.

No universally agreed theoretical framework describes inclusion health. However, we build on existing social exclusion theory and consider the linked and cumulative factors and processes that confound individual and group capacity for hope, opportunity, reciprocity and participation. Our analysis is also informed by an intersectionality perspective, which focuses on how social characteristics combine to impact on health.

Our systematic review examines the health outcomes mortality and morbidity in four overlapping populations together as exemplar determinants of deep exclusion. We aimed to systematically review and meta-analyse mortality and morbidity in homeless, prison, sex work, and SUD populations jointly for the first time.

Methods

We searched the Cochrane Library, Medline and Embase from 1 January 2005 and to 1 October 2015 on 27 October 2015. Full search terms are provided in the supplementary appendix. We searched for papers about the populations of interest (homeless, prison, sex workers and SUD) from systematic reviews, meta-analyses, interventional and observational studies with morbidity and mortality outcomes. We included studies identified from references of included articles.

We recognise that social exclusion has a major impact on health in other groups, such as Gypsies and Travellers and vulnerable migrants, ethnic minorities, indigenous
communities and sexual and gender minorities, most notably transgender populations. Whilst these groups experience social exclusion in many high-income settings, they were considered beyond the scope of this review.

RWA screened titles, abstracts and full texts using Covidence systematic review software (https://www.covidence.org/). All authors contributed to data extraction (conducted using a Google Docs https://docs.google.com/) and were double-checked by a second researcher (RWA, ET, GH or SVK). Extracted items included study design, year(s) of study, country, number of participants, primary outcome(s), and summary description of the study population. We attempted to contact authors if we were unable to locate papers, or required additional information about the data or study.

We attempted to identify and exclude duplicate data from research studies presented in separate publications. Where we identified multiple studies with duplicated or overlapping data (by population, time, place and outcome) we chose the study with the largest or most representative sample size, and when these were also similar, we present the most recent study. We followed the PRISMA reporting guidelines in the presentation of our manuscript. A review protocol was not published prior to conducting the review.

Outcomes

Outcomes included were measures of morbidity and mortality for ICD-10 defined conditions. Papers use a variety of measures to report outcomes. In order to ensure maximum comparability across studies for mortality outcomes, we extracted, in order of preference the first of: SMRs, relative hazard ratio; mortality rate ratio; or crude mortality rate. For consistency with the majority of studies included in the review, we have not multiplied SMRs by 100. In our results a value of 1 equates to no difference between the expected and observed mortality rate. For morbidity outcomes, we extracted, in order of preference the first of: prevalence; incidence; prevalence risk ratio (PRR); incidence rate ratio (IRR); prevalence odds ratio (POR); or incidence odds ratio (IOR). Where available, we used data where the comparison group was selected as a socially deprived population or measures adjusted for area-based or income-based deprivation.

Statistical analysis

We include all extracted data in an online supplementary appendix. For the quantitative findings analysed in the paper we focus on the primary outcome of SMRs. SMRs for all-cause mortality and by ICD-10 chapter were summarised in forest plots. We anticipated high levels of heterogeneity a-priori, and therefore created summary estimates using random effects models using Stata v.13 (Statacorp LP, College Station, TX, USA). We used the I^2 transformation to describe the proportion of total variation in study estimates due to heterogeneity. We explored potential sources of heterogeneity by stratifying the analyses by country and by inclusion health population group. We describe the results of studies of disease prevalence individually. We report summary estimates of morbidity and mortality of recently published meta-analyses found by our search within our results and did not attempt to update each of these within our review. In addition to our
Role of the funding source

The study sponsors had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication. All authors had access to all the data, and were responsible for the decision to submit the manuscript.

Results

We searched the bibliographic databases was conducted on 27th October 2015 and identified 7,946 articles with 1,274 duplicate articles then excluded (Figure 1). Of the 711 full text articles retrieved, 418 met the inclusion criteria, but a further 81 were excluded due to overlapping data. A total of 337 studies were included in the review, with including 3,219 ‘data points’ (meaning an unique estimate for a unique population) extracted and 2,835 included after removal of duplicates.

The included studies presented data from 38 out of 80 high-income countries (Figure 2) studies were from 38 countries (See Figure S1 in supplementary appendix). USA (698 data points), Australia (460), Sweden (309), Canada (257), and United Kingdom (234) were the five countries with[the highest number of data points (number in brackets for each) included in the review after de-duplication. SUD populations were the most studied sub-group groups, accounting for contributing to 42.1% (1,192/2,835) of all data points (after de-duplication), followed by prisoners (27.1%; 769/2,835), homeless (26.6%; 754/2,835) and sex workers (4.2%; 119/2,835).

Infectious diseases and mental and behavioural disorders were the two most studied ICD-10 chapters with a total of 897 (31.6%; 897/2,835) and 715 (25.2%; 715/2,835) included data points respectively (Figure 3). Injury and poisoning only contributed 3.4% (98/2,835) of all extracted data points.

Our meta-analyses focused on SMRs (Tables 1 and Figures 3, 4, and 5). The most studied causes of death were ‘all-causes’ (XX% of data points) and ‘injury, poisoning and external causes’ (XX% of data points). Most studies in the meta-analysis were of SUD groups, including (XX% of all studies) studies of all-cause mortality. Cause-specific studies in males and females were split between prisoners and SUD groups, while cause-specific studies for both sexes combined were in SUD groups only. There were only (three) studies of homeless people included in the meta-analysis and none of FSW.

Our all-cause meta-analyses focused on SMRs, with 31 studies contributing 92 data points (Table 1 & Figures 3, 4 & 5). 98.9% (91/92) of all included all-cause SMRs were increased and overall we estimated that summary all-cause SMRs were higher in females 11.9 (95% CI 10.4–13.3; I^2 94.1%) than males 7.9 (95% CI 7.0–8.7; I^2 99.1%). We provide summary estimates of SMRs, however, data were heterogeneous as measured by the I^2 statistic in many of our analyses (which we have explored further and therefore these summary measures must be interpreted with appropriate caution. Heterogeneity was not substantially reduced when...
analyses by population subgroup were undertaken. Insufficient data were available to conduct subgroup analyses by country.

Summary SMRs were higher in females than in males for all-cause mortality and mortality in each of the ICD-10 chapters. In some ICD-10 chapters, the summary SMR for both sexes combined did not fall between the male and female estimates. This is because the meta-analyses draw on different studies (rather than the estimate for both sexes combined being drawn from the same male and female populations).

Infectious and parasitic diseases were the most studied disease conditions in the largest populations in North America (668,500). A meta-analysis of the prevalence data extracted (Table 2). Summary estimates of SMRs for infectious diseases were raised for males (2.8; 95% CI 1.6-4.1; I² 65.4%) and females (5.6; 95% CI 1.5-9.7; I² 60.0%). Disease prevalence was high but heterogeneous. HIV ranged from 0.0% (0/146) to 61.5% (44/69). Hepatitis C from 0.1% (1/734) to 92.8% (64/69). Hepatitis B from 1.7% (2/119) to 65.0% (67/103), and latent tuberculosis infection from 1.2% (1/82) to 50.6% (133/263).

It was estimated that 2.2 million prisoners globally were hepatitis C positive with the largest populations in North America (668,500). A meta-analysis of the prevalence of sexually transmitted infections (STIs) in prisoners found marked wide variation and reported a pooled prevalence for Chlamydia of 5.8% (95% CI 5.0-6.5%) in men and 12.3% (95% CI 10.6-14.0%) in women; gonorrhoea, 1.4% (95% CI 1.1-1.7%) in men and 5.7% (95% CI 4.8-6.7%) in women; and syphilis, 2.5% (95% CI 2.1-2.8%) in men and 6.1% (95% CI 4.8-7.5%) in women.

SMRs for males and females were exclusively from prison populations. SMR data for both sexes combined were from SUD populations only, with all subgroups by sex having fewer than three studies included.

Other non-communicable diseases

Summary estimates of SMRs due to neoplasms were raised in males (1.6; 95% CI 1.3-1.9; I² 88.7%), females (1.9; 95% CI 1.3-2.5; I² 62.8%) and both sexes combined (2.2; 95% CI 1.6-2.8; I² 90.6%). In homeless adults in Toronto, 59% had moderate, severe or very severe symptoms of dyspepsia (around twice as many as in the general population). In prisoners in the USA, 4.9% of male and 9.6% of females had a history of hepatitis and 1.2% of men and 2.1% of women had a history of cirrhosis. A dental survey of inmates in a juvenile detention facility in Texas showed higher Decayed, Missing or Filled scores than age and ethnicity matched population controls. Dental health problems were also common in homeless people.

The available body of evidence is largest for infectious diseases, with considerable existing research on morbidity associated with mental and behavioural disorders. In
contrast, there is a relative paucity of evidence on non-communicable diseases and injury, poisoning and external causes despite these causes having the highest SMRs across ICD-10 categories. SMRs across disease categories were consistently higher in females than males. Of the four inclusion health populations considered, sex workers were the least well investigated, which should be addressed as a matter of priority.

Our study comprehensively describes for the first time the relative mortality and morbidity burden in selected inclusion health populations. We have synthesised the significant existing literature in this area using a comprehensive search strategy to identify the current balance of evidence available to inform policymaking around inclusion health. Data were extracted and reviewed by a second author reducing the likelihood of errors. Our approach has allowed us to identify relative gaps in terms of both categories of disease and inclusion health categories. Our analysis was informed by an intersectionality perspective, which focuses on how social characteristics in combination impact on health. We have therefore specifically investigated how the health consequences of exclusion may vary by other socially influenced characteristics, with differences by gender particularly noteworthy.

A number of limitations should be considered. Caution must be taken when interpreting the summary estimates of SMRs due to the high level of heterogeneity found in studies. A lack of internationally agreed definitions for the populations considered in this review means of inclusion health groups, there is variation in the levels of risk for included studies which is likely to explain some of this variation. Similarly, comparison groups varied, with some studies comparing to general population estimates and others to those from socially deprived areas using the general population and others using groups living in socially deprived areas. Studies also varied according to the extent that analyses adjusted for social deprivation and other risk factors. However, we have utilised a random-effects method to model the data appropriately and note existing recommendations that meta-analysis should be pursued whenever possible, with appropriate acknowledgement of its limitations when acknowledging heterogeneity is high. We limited our search to 2005 onwards and therefore longer term time trends are not possible to examine with this analysis. We have not examined longer-term trends. Furthermore, there is a need for future investigation of how contextual factors, such as a country’s social policies, influence health outcomes for excluded groups. Lastly, for pragmatic reasons, we were unable to investigate many other dimensions of social exclusion. We therefore other health inclusion groups and believe that further work is required to investigate the health experiences of other socially excluded groups describe their health experiences.

We found consistently higher SMRs for females than males. Since general population mortality rates are lower in women than men for most conditions this does not necessarily indicate worse outcomes in women in inclusion health groups compared with men. It may, however, reflect an increased vulnerability of women in inclusion health populations or different risk distributions among women and men in inclusion health groups. SMR is a relative measure and the lower SMRs for common conditions such as cardiovascular disease and cancer may underplay the number of excess cases. Conversely, high SMRs may not indicate a large number of excess
cases if the condition is rare. Further work should report absolute as well as relative measures of mortality. SMR is a relative measure, consequently less extreme SMRs seen for common conditions such as cardiovascular disease and cancer may underplay the importance of these outcomes at a population level. Conversely high SMRs for rare conditions may inflate their apparent relevance. Further work should report absolute as well as relative measures of mortality for different conditions to enable a better assessment of the contribution of different causes of mortality. These extreme inequalities demand an intensive cross-sectoral policy and service response to prevent exclusion and improve health outcomes. An accompanying review (cross reference IH paper 2) outlines interventions that respond to these increases in morbidity and mortality. Here we focus on research recommendations in relation to disease burden measurement to address issues identified by our review and we briefly discuss the health system response.

Determining the burden of disease remains challenging in inclusion health populations as membership of an inclusion health population is not recorded in most vital registration and health information systems. Deaths and health service usage in excluded populations are therefore a largely invisible and neglected problem as far as routine statistics are concerned. By contrast, the availability of area-based measures of social deprivation across high income countries has allowed measurement of the major population level impact of less extreme social inequalities. This has supported extensive cross sectoral policy initiatives to address these inequalities. Better routine data is also needed to drive the policy response to the inclusion health agenda.

There are two broad potential approaches to tackling the lack of routine mortality and health service data for inclusion health groups this problem. Routinely recording membership of inclusion health groups in health and mortality records is a possibility. Firstly, health services could routinely record membership of health inclusion groups. This would require clear agreed definitions of excluded populations each group to be agreed along with standard outcome measures. Those responsible for recording data would need clear guidance to help them ascertain membership of inclusion health groups and sensitivity would be needed to ensure this does not reinforce existing stigma for socially excluded groups. The feasibility of routinely recording membership of these inclusion health groups this approach outside the context of specialist services remains unclear. Alternatively, and more feasibly in the short term, data linkage methodologies could be used to match data from services that work with excluded populations inclusion health groups, with vital registration data, electronic health records, and existing infectious and non-communicable disease surveillance systems. These linked datasets would then facilitate systematic estimates of mortality and morbidity over time. This has been the primary method used to estimate SMRs in the studies reported in this paper. These linked datasets would facilitate systematic estimates of mortality and morbidity over time and help to measure the impact of interventions. Routine linkage of such datasets could facilitate systematic estimates of mortality and morbidity over time and help to measure the impact of policies and interventions.
As part of this wider Lancet Series we held an engagement workshop with people with lived experience of homelessness and social exclusion (described in more detail in paper 2). We asked this group about their views on collecting operational data with ethical and appropriate research governance approvals, but without specific individual level consent. Although this was only a small sample (and we acknowledge that people who face exclusion and are willing to come in to a workshop may differ from those who do not) acceptability of collection of this sort of data was extremely high. 100% of users were happy for homeless hostel records to be collected, 73% agreeing to the collection of criminal records, 62% to health records, and 85% agreeing to these records being linked together.

A vertical approach to tackling inclusion health (i.e. one that focusses on specific diseases or specific risk groups) can ignore and neglect multiple morbidity and the social issues faced by excluded populations. This can result in inefficiencies and missed opportunities for prevention, early diagnosis and management as well as missed opportunities for mitigation of social risk factors. The emerging field of inclusion health should advocate for and deliver joined up health and social services for overlapping marginalised groups. These services should address not only diseases with extreme disparities, but also prevention and management of more common conditions with a lower relative risk but high disease burden, such as cardiovascular disease. The ability of health and social policy to address the needs of the most marginalised populations should be a key indicator of quality. Such initiatives need to be supported by robust information systems that can provide data for continuing advocacy, guide service development and monitor the health of marginalised populations over time.

Research in context

Evidence before this study
There is a comprehensive body of research on the health impact of inequality, much of which focusses on disparities in morbidity and mortality, and is based on area based measures of social deprivation/common measures of socioeconomic status such as neighbourhood deprivation and occupational class. The evidence of a consistent relation between ill health and increasing levels of social deprivation has underpinned a broad range of social policies and public health initiatives. Such geographical based analyses cannot adequately assess the extent of health inequalities experienced by those experiencing deep social exclusion. In preparation for the inclusion health series we searched the Cochrane Library, Medline and Embase from 2000 to 30th September 2013. We searched for systematic reviews, meta-analyses, cohort and cross-sectional studies containing morbidity and mortality outcomes for the four inclusion health populations of interest (substance use disorders, homeless populations, prisoners, and sex workers). The studies identified described the highly overlapping nature of inclusion health populations, the increased risk factors for disease, and poor mortality outcomes compared with the general population.

Added value of this study
Our systematic review and meta-analysis provides the most comprehensive examination to date of morbidity and mortality outcomes across a range of inclusion health populations. We find that the extent of the health inequalities seen in
inclusion health populations greatly exceed that observed when comparing the richest and poorest neighborhoods high and low socioeconomic groups. Extremely high mortality rates are seen across ICD-10 disease categories, with relative risks consistently higher in females than males. The relative mortality excess is greatest for injury, poisoning and external causes. However there is also high, although less extreme, relative mortality inequality across more common disease categories such as cardiovascular disease and cancer. Non-communicable diseases and injury, poisoning and external causes were lacking in data despite the high summary Standardised Mortality Ratio estimates. Sex workers were a particularly under-researched group.

Implications of all the available evidence
The extreme burden of disease experienced by inclusion health populations demands a cross-sectoral response to prevent deep social exclusion and an improvement in services working with these populations. This study provides the most comprehensive assessment to date of the scale and distribution of mortality in inclusion health populations in high-income countries. Our research focused on relative measures of mortality and therefore future work should examine absolute measures in greater detail. Inclusion health populations are often invisible within routine health data. This limitation can be tackled by either modifying the instruments used to collect such data or through data linkage studies. Services providing for inclusion health populations should aim to deliver health and social services for overlapping marginalised groups, in order to tackle the poor health outcomes found in this study. These services should also have a greater focus on prevention and management of more common conditions in addition to those traditionally considered high risk for inclusion health groups.

Contributors
RWA, ACH and AS proposed the hypothesis and idea for the systematic review with all authors contributing to its development and the analysis plan. RWA did the literature search. RWA reviewed studies for inclusion. RWA, SL, ET, SVK, GH performed the data extraction and checking. RWA performed all meta-analyses and wrote the first draft of the manuscript. All authors reviewed and interpreted the results and edited the manuscript.

Declaration of interests
ACH is a trustee of the Pathway: Healthcare for homeless people charity. AS is Clinical Lead and Manager for Find&Treat.

Acknowledgments
RWA is supported by an academic clinical lectureship from the UK National Institute for Health Research (NIHR). ACH’s salary is provided by Central and North West London NHS Community Trust. ET and SVK are funded by the Medical Research Council (MC_UU_12017/13 and MC_UU_12017/15) and Chief Scientist’s Office (SPHSU13 and SPHSU15). AS is funded by UCLH Foundation Trust. SVK is also funded by a NRS Scottish Senior Clinical Fellowship (SCAF/15/02). The views expressed are those of the authors and not necessarily those of the Wellcome Trust.
NIHR, NHS, NHS Research Scotland, Medical Research Council, Chief Scientist's Office.
References


87: 486–503.

31 Kapilashrami A, Hill S, Meer N. What can health inequalities researchers learn from an
intersectionality perspective? Understanding social dynamics with an inter-categorical approach?

32 Ioannidis JPA, Patsopoulo NA, Rothstein HR. Reasons or excuses for avoiding meta-analysis in

33 The Marmot Review. Fair Society, Healthy Lives. 2010; published online Feb.

34 Katikireddi SV, Valles SA. Coupled Ethical-Epistemic Analysis of Public Health Research and
Practice: Categorizing Variables to Improve Population Health and Equity. Am J Public Health
2015; 105: e36–42.

35 Aldridge RW, Shaji K, Hayward AC, Abubakar I. Accuracy of Probabilistic Linkage Using the
e0136179.

and implications for health care, research, and medical education: a cross-sectional study. Lancet


38 Vila-Rodriguez F, Panenka WJ, Lang DJ, et al. The hotel study: multimorbidity in a community


40 Pratt D, Piper M, Appleby L, Webb R, Shaw J. Suicide in recently released prisoners: a population-

41 Arendt M., Munk-Jorgensen P., Sher L., Jensen S.O.W. Mortality among individuals with cannabis,
cocaine, amphetamine, MDMA, and opioid use disorders: A nationwide follow-up study of Danish


43 Barrio G, Molist G, de la Fuente L, et al. Mortality in a cohort of young primary cocaine users:


45 Darke S, Mills KL, Ross J, Teesson M. Rates and correlates of mortality amongst heroin users:
findings from the Australian Treatment Outcome Study (ATOS), 2001-2009. Drug Alcohol Depend


<table>
<thead>
<tr>
<th>Author</th>
<th>Population</th>
<th>Population Description</th>
<th>Number of Participants</th>
<th>Country</th>
<th>Study Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nielsen</td>
<td>Homeless</td>
<td>Females aged 16yr or more with at least one contact with a homeless shelter</td>
<td>32711</td>
<td>Denmark</td>
<td>1999-2009</td>
</tr>
<tr>
<td>Roy</td>
<td>Homeless</td>
<td>Young people aged 14-25 who were &quot;street active&quot;</td>
<td>829</td>
<td>Canada</td>
<td>1995-2001</td>
</tr>
<tr>
<td>Vila-Rodriguez</td>
<td>Homeless</td>
<td>A prospective community sample of adults living in single-room occupancy hotel</td>
<td>293</td>
<td>Canada</td>
<td>2008-2011</td>
</tr>
<tr>
<td>Graham</td>
<td>Prisoners</td>
<td>Males imprisoned for the first time between 1996 and 2007</td>
<td>76627</td>
<td>Kingdom</td>
<td>2007</td>
</tr>
<tr>
<td>Karimnia</td>
<td>Prisoners</td>
<td>All adults who had experienced full-time custody</td>
<td>85203</td>
<td>Australia</td>
<td>1988-2002</td>
</tr>
<tr>
<td>Pratt</td>
<td>Prisoners</td>
<td>All sentenced and remanded prisoners released from prison People receiving treatment in 'specialist institutions' for substance use disorder, reporting cocaine as their primary substance</td>
<td>244988</td>
<td>Kingdom</td>
<td>2002</td>
</tr>
<tr>
<td>Arendt</td>
<td>SUD</td>
<td>Male opiate users aged 15-69 entering treatment Regular cocaine users recruited from drug scenes and non-treatment settings Individuals with opioid addiction hospitalised due to self-poisoning</td>
<td>20581</td>
<td>Denmark</td>
<td>1996-2006</td>
</tr>
<tr>
<td>Bargagli</td>
<td>SUD</td>
<td>Opioid users Opioid-dependent people treated with opioid substitution therapy</td>
<td>2575</td>
<td>Netherlands</td>
<td>2002</td>
</tr>
<tr>
<td>Barrio</td>
<td>SUD</td>
<td>Young (&lt;30yrs) injecting drug users</td>
<td>714</td>
<td>Spain</td>
<td>2004-2006</td>
</tr>
<tr>
<td>Bjrornaas</td>
<td>SUD</td>
<td>Opioid users</td>
<td>185</td>
<td>Norway</td>
<td>1980-2000</td>
</tr>
<tr>
<td>Darke</td>
<td>I</td>
<td>Opioid users</td>
<td>615</td>
<td>Australia</td>
<td>1985-2009</td>
</tr>
<tr>
<td>Degenhardt</td>
<td>SUD</td>
<td>Opioid users Women who were admitted to drug-treatment programs</td>
<td>43789</td>
<td>Australia</td>
<td>2005-2006</td>
</tr>
<tr>
<td>Evans</td>
<td>SUD</td>
<td>Opioid users</td>
<td>644</td>
<td>United States</td>
<td>2005-2006</td>
</tr>
<tr>
<td>Gibson</td>
<td>SUD</td>
<td>Opioid users</td>
<td>2489</td>
<td>Australia</td>
<td>2006-2006</td>
</tr>
<tr>
<td>Hser</td>
<td>SUD</td>
<td>Heroin users attending for opioid substitution therapy</td>
<td>4447</td>
<td>United States</td>
<td>2006-2002</td>
</tr>
<tr>
<td>Lee</td>
<td>SUD</td>
<td>Opioid users</td>
<td>10842</td>
<td>Taiwan</td>
<td>1988-2002</td>
</tr>
<tr>
<td>Mathers</td>
<td>SUD</td>
<td>People who injected opioids and other drugs</td>
<td>101</td>
<td>Denmark</td>
<td>1999</td>
</tr>
<tr>
<td>Merrall</td>
<td>SUD</td>
<td>People in contact with drug treatment services</td>
<td>69456</td>
<td>United Kingdom</td>
<td>2006</td>
</tr>
<tr>
<td>Nyhlen</td>
<td>SUD</td>
<td>Substance abusers admitted for inpatient detoxification Individuals who had visited a public treatment center for problems due to the use/abuse of cocaine</td>
<td>561</td>
<td>Sweden</td>
<td>1970-2006</td>
</tr>
<tr>
<td>Pavarin</td>
<td>SUD</td>
<td></td>
<td>471</td>
<td>Italy</td>
<td>1988-2012</td>
</tr>
<tr>
<td>Author</td>
<td>Year</td>
<td>Location</td>
<td>Sample Size</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>----------</td>
<td>------</td>
<td>--------------</td>
<td>-------------</td>
<td>----------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Rehm54</td>
<td>1994-2000</td>
<td>Switzerland</td>
<td>6281</td>
<td>Participants in heroin-assisted treatment. Patients who had ever been treated or were currently in treatment in methadone.</td>
<td></td>
</tr>
<tr>
<td>Singleton56</td>
<td>1997-2002</td>
<td>Czech Republic</td>
<td>3039</td>
<td>Drug users admitted to hospital for drug related problems. Injection drug users recruited through the social networks of ‘privileged access’ interviewers. Individuals from local methadone outposts, a sexually transmitted diseases clinic, and word of mouth.</td>
<td></td>
</tr>
<tr>
<td>Spittal57</td>
<td>2002</td>
<td>Canada</td>
<td>520</td>
<td>Injection drug users recruited through the social networks of ‘privileged access’ interviewers. Individuals from local methadone outposts, a sexually transmitted diseases clinic, and word of mouth.</td>
<td></td>
</tr>
<tr>
<td>Stove58</td>
<td>2006</td>
<td>Australia</td>
<td>220</td>
<td>Injection drug users recruited through the social networks of ‘privileged access’ interviewers. Individuals from local methadone outposts, a sexually transmitted diseases clinic, and word of mouth.</td>
<td></td>
</tr>
<tr>
<td>van Santen59</td>
<td>2012</td>
<td>Netherlands</td>
<td>1254</td>
<td>All persons who came into contact with the New South Wales Opioid Substitution therapy program.</td>
<td></td>
</tr>
<tr>
<td>Zabransky60</td>
<td>2008</td>
<td>Czech Republic</td>
<td>151</td>
<td>All persons who came into contact with the New South Wales Opioid Substitution therapy program.</td>
<td></td>
</tr>
<tr>
<td>Randall61</td>
<td>2005</td>
<td>Australia</td>
<td>43789</td>
<td>Canadian cohort of daily cocaine injectors.</td>
<td></td>
</tr>
<tr>
<td>Degenhardt62</td>
<td>2004</td>
<td>Canada</td>
<td>717</td>
<td>Canadian cohort of daily cocaine injectors.</td>
<td></td>
</tr>
<tr>
<td>Degenhardt63</td>
<td>2006</td>
<td>Australia</td>
<td>42676</td>
<td>Canadian cohort of daily cocaine injectors.</td>
<td></td>
</tr>
<tr>
<td>ICD 10 chapter</td>
<td>Number of studies</td>
<td>Total number of data points (% of all data points)</td>
<td>Number of mortality data points (% of all mortality data points)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------------</td>
<td>-------------------</td>
<td>--------------------------------------------------</td>
<td>---------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>337</td>
<td>2835 (100)</td>
<td>336 (100)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause</td>
<td>32</td>
<td>140 (5)</td>
<td>92 (27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infectious and parasitic diseases</td>
<td>160</td>
<td>899 (32)</td>
<td>21 (6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neoplasms</td>
<td>4</td>
<td>145 (5)</td>
<td>41 (12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood</td>
<td>18 (1)</td>
<td>--</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocrine</td>
<td>66 (2)</td>
<td>66 (2)</td>
<td>6 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental and behavioural disorders</td>
<td>90</td>
<td>715 (25)</td>
<td>6 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous system</td>
<td>4</td>
<td>43 (2)</td>
<td>6 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye and adnexa</td>
<td>14 (0)</td>
<td>--</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ear</td>
<td>4</td>
<td>--</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diseases of the circulatory system</td>
<td>44</td>
<td>149 (5)</td>
<td>17 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory system</td>
<td>79 (3)</td>
<td>8 (2)</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digestive system</td>
<td>82 (3)</td>
<td>34 (10)</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>44 (2)</td>
<td>--</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>29 (1)</td>
<td>--</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injury, poisoning and certain</td>
<td>98 (3)</td>
<td>44 (13)</td>
<td>--</td>
<td></td>
<td></td>
</tr>
<tr>
<td>external causes</td>
<td>Other</td>
<td>207 (7)</td>
<td>61 (18)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figures

Figure 1. Flowchart of included studies

Records identified through database searching from 1 January 2005 and 1 October 2015 (n = 7946)

Records excluded duplicates (n = 1274)

Records screened (n = 6672)

Articles excluded on title and abstract (n = 5901)

Full text articles assessed for eligibility (n = 711)

Full text articles excluded (n = 293)

Studies meeting inclusion criteria (n = 418)

Excluded because of overlapping data with other studies (n = 81)

Studies included in quantitative synthesis (n = 337)
Figure 2. Geographical spread of existing data from high-income countries on homeless populations.

Included countries: Australia, Austria, Belgium, Canada, Chile, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hong Kong, Hungary, Ireland, Israel, Italy, Japan, Latvia, Lithuania, Luxembourg, Netherlands, New Zealand, Norway, Poland, Portugal, Puerto Rico, Russia, Singapore, South Korea, Spain, Sweden, Switzerland, Taiwan, United Kingdom, United States, Uruguay.

Figure 3. Treemap summarising amount of data by ICD-10 chapter and summary estimates of SMR
| SMR | 0.91 | 23.53 |

Note: Size of box indicates number of data points included (e.g. Infectious and parasitic disease = 953; Disease of Nervous system = 43). SMR used is summary estimate for ICD-10 chapter for both sexes combined. Boxes without labels are 1=Genitourinary; 2=Musculoskeletal; 3=symptoms, signs and abnormal clinical and laboratory findings; 4=Ear and Mastoid process; and 5=Eye and Adnexa. Grey boxes (with an SMR of '0') indicate that none of the studies included in this review reported SMR.

Commented [D8]: There was still one label missing. Looking at the ICD10 chapters, I'm guessing it's diseases of the blood?

Commented [RA9]: ? Blood – to check and update before submission
Figure 43. Standardised Mortality Ratios for all-cause mortality

Note: Weights are from random effects analysis. Several studies contribute multiple rows of data due to different: SUD groups included (Arendt and Pavarin); countries (Bargagli); or time periods (Merrall).
Figure 54. Standardised Mortality Ratios by ICD-10 category (excluding those due to injury and external causes).

Note: Weights are from random effects analysis. SMRs greater than 60 are excluded for presentational purposes. Several studies contribute multiple rows of data due to different: outcomes (Graham; Pavarin; Karimina; Randall and Gibson) and time periods included (Merrall).
Figure 65. Standardised Mortality Ratios due to injury and external causes

Note: Weights are from random effects analysis. SMRs greater than 60 are excluded for presentational purposes. Several studies contribute multiple rows of data due to different: outcomes (Nielsen; Graham; Bjornaas; Gibson; Kariminia and Degenhardt) SUD groups included (Pavarin); or time periods (Merrall).

Commented [DL10]: This might not be necessary given the log axis. Do we need to add anything in?