Mortality among people who have experienced homelessness: protocol for a systematic review and meta-analysis

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ABSTRACT
Introduction Homelessness is a major contributor to health inequalities. People who experience homelessness are at markedly increased risk of multiple and complex health morbidities which likely increase their susceptibility to early, preventable death. Despite this, the mortality burden in this group remains poorly understood, limited in part by insufficient synthesis of data at a global level. This systematic review will synthesise international literature examining rates of risk and protective factors for mortality among people who have experienced homelessness.

Methods and analysis We will search MEDLINE, PsycINFO, Embase and PubMed for peer-reviewed cohort studies examining mortality among people who have experienced homelessness. No study eligibility restrictions will be placed on the date, country of origin, or language of publications, or age of the sample. We will assess the quality of included studies using the Methodological Standards for Epidemiological Research scale. Our measures of mortality will include: (A) incidence—all cause and cause-specific, expressed as a crude mortality rate (CMR) per 1000 person-years, with 95% CI; and (B) all cause and cause-specific, indirectly standardised mortality ratios (SMRs) with 95% CI. Associations between risk and protective factors and all-cause and cause-specific mortality will be reported using pooled relative risk ratios with 95% CI. Where there are sufficient data, the influence of subgroup and methodological factors on CMRs, SMRs and predictive factors will be examined using meta-regression.

Ethics and dissemination This study does not require institutional ethics review or approval as it will synthesise findings from published studies that have previously been granted relevant ethics approvals. Study findings will be disseminated through a peer-reviewed journal article, conference and seminar presentations. A plain language summary will be distributed through the authors’ academic and professional networks.

STRENGTHS AND LIMITATIONS OF THIS STUDY
⇒ The global systematic review will be conducted and reported in line with best practice guidelines (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols 2015) and is registered with PROSPERO (CRD42021272937).
⇒ Our methods have been specified a priori, and a comprehensive search strategy across four key health, medicine and biomedical databases has been developed in consultation with a research librarian.
⇒ If sufficient data are available, our planned meta-analysis will permit reliable estimation of the pooled risk for mortality (crude mortality rates and standardised mortality ratios), and its potentially modifiable (risk and protective) factors (relative risk ratios), among people who have experienced homelessness.
⇒ While global in scope, it is anticipated that reviewed studies will predominantly come from high-income countries and will be published in English language, limiting the representativeness and generalisability of the derived estimates.
⇒ Most reviewed studies are expected to be observational and, as such, we may have limited capacity to draw causal inferences.

INTRODUCTION
International estimates suggest that over 1.6 billion people are inadequately housed, with over 100 million people worldwide having no housing. This is likely to be an underestimate given vast differences in global socioeconomic, structural, cultural and political contexts. People who have experienced homelessness face health inequalities and are at markedly increased risk for preventable morbidity and premature mortality. The large and increasing number of people who experience homelessness worldwide presents a strong imperative for understanding the extent and nature of the health burden in this group, including mortality. Yet, our understanding of mortality among people who experience homelessness is limited.

To our knowledge, there are only two prior systematic reviews of mortality among homeless people. A review and meta-analysis by Aldridge et al. analysed mortality outcomes across four groups experiencing social exclusion from studies published between January 2005 and October 2015. Of the 337 studies they reviewed, only 3 included measures...
of mortality for homeless people. The Aldridge study\(^2\) confirmed excess mortality associated with experiencing homelessness but it was limited by the small body of evidence reviewed meaning that neither pooled crude mortality rates (CMRs) nor pooled standardised mortality ratios (SMRs) for mortality among homeless people could be calculated. A more recent systematic review\(^6\) analysed data from eight studies examining mortality rates among homeless people, all set within the USA and published between 2009 and 2019. These studies analysed selected samples, such as data collected from samples based on community-based shelter records or convenience samples of homeless people participating in healthcare programmes, and most studies focused on adults. A meta-analysis was not conducted as a part of this review.

Several international studies from Denmark\(^7,8\) Sweden,\(^9\) Ireland,\(^10\) Scotland\(^11\) \(^12\) and the Netherlands,\(^13\) which were either not included in prior reviews or published after the Aldridge review, used data linkage to estimate mortality among those who are homeless or have experienced homelessness. Data linkage addresses issues of low power in small retrospective studies and, if appropriately designed, permits the comparison of mortality rates between people experiencing homelessness and the general population. Among the findings of these European and Scandinavian studies are that (1) rates of mortality were greater among those who experienced homelessness than in the general population, with suicide and overdose among the leading causes and that (2) at least one recorded episode of homelessness is associated with increased risk of death. Stratified by sex, SMRs among those who have experienced homelessness are higher for females than males; and stratified by age, SMRs are generally higher for younger than for older people.\(^7,10\) \(^13\)-\(^17\)

There is now an important opportunity to synthesise the international literature and quantify the association between homelessness and mortality. This is because at present, knowledge of the extent and causes of premature death relative to the general population, and the contribution of associated risk and protective factors, limits effective, comprehensive responses. Accordingly, the aim of this systematic review is to synthesise the peer-reviewed evidence to investigate: (A) the incidence of all-cause and cause-specific mortality among people who have experienced homelessness; (B) how these rates compare to age-matched and sex-matched general populations and (C) historical (static) and potentially modifiable factors that are associated with all-cause and cause-specific mortality among people who have experienced homelessness. These factors may be associated with increased (risk) or decreased (protective) mortality rate.

### METHODS AND ANALYSIS

**Protocol and registration**

This systematic review and meta-analysis will be conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis for Protocols 2015.\(^18\) \(^19\) This protocol is registered with the International Prospective Register of Systematic Reviews (PROSPERO; CRD42021272937).

**Search strategy**

We will search the following electronic health, medicine and biomedical databases of peer-reviewed research: MEDLINE, PsycINFO, Embase and PubMed, using variations and combinations of database-specific controlled subject vocabulary (ie, MESH terms and subject headings) relating to homelessness and mortality. This method will ensure uniformity in search terms across each database. Given that no restrictions will be placed on the date of publication, databases will be searched from their inception until the date of the search. The MEDLINE search strategy is presented in **table 1**. The search strategy was developed in consultation with a research librarian at the Royal Children’s Hospital (RCH) Melbourne, Australia.

<table>
<thead>
<tr>
<th>Table 1 MEDLINE Search Strategy</th>
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<tbody>
<tr>
<td>1 exp “Homeless Persons/</td>
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<tr>
<td>2 (Homeless* or street-youth* or street-sleeper* or runaway* or unhoused or no-fixed-abode or unhoused or temporary-housing or insecure-housing or street-sleeper* or emergency-housing).tw,kf.</td>
</tr>
<tr>
<td>3 exp Mortality/</td>
</tr>
<tr>
<td>4 suicide/ or suicide, completed/</td>
</tr>
<tr>
<td>5 mo.fs.</td>
</tr>
<tr>
<td>6 (mortalit* or death* or dying or fatal* or decease*).tw,kf.</td>
</tr>
<tr>
<td>7 risk*.tw,kf,hw.</td>
</tr>
<tr>
<td>8 (predict* or associat* or likelihood).tw,kf.</td>
</tr>
<tr>
<td>9 exp cohort studies/</td>
</tr>
<tr>
<td>10 (longterm or long-term or repeat* or serial or longitudinal* or follow-up or followup or cohort* or retrospective* or prospective*).tw,kf.</td>
</tr>
<tr>
<td>11 (1 or 2) and (3 or 4 or 5 or 6) and (7 or 8) and (9 or 10)</td>
</tr>
<tr>
<td>12 limit 11 to (case reports or comment or editorial or guideline or letter or practice guideline)</td>
</tr>
<tr>
<td>13 11 not 12</td>
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</table>

**Inclusion criteria**

Eligible peer-reviewed studies are prospective and/or retrospective cohort studies, as defined by the Cochrane study design guide,\(^26\) which report at least one estimate of mortality among a sample of people who have experienced homelessness, or provide sufficient information to permit calculation of such an estimate. The types of homelessness and causes of mortality that will be considered for inclusion are described below (see the Participants and Outcome measure sections, respectively). Study eligibility will not be restricted by the date or the country of origin, or the age of the sample. No restrictions will be placed on the language of publications. Where identified, the abstracts of non-English publications will be translated into English and reviewed for eligibility.

**Exclusion criteria**

Case reports, cross-sectional studies and case–control studies will be excluded, as will commentaries, editorials,
practice guidelines and letters. Dissertations, conference abstracts and grey literature (book chapters, government reports/guidelines) will also be excluded. Previous reviews of the literature will be excluded; however, the reference lists of any previous reviews will be screened to identify additional eligible studies not identified in our search strategy.

Participants
Definitions of homelessness vary internationally, however, it is generally considered within a typology of housing instability. For this review, people experiencing homelessness include those who are currently, or report a history of (A) being unsheltered (eg, living directly on the streets or in spaces not intended for habitation); and/or (B) residing in emergency shelter (eg, crisis housing, refuge) and/or (C) residing in temporary accommodation (eg, couch-surfing, short-term accommodation such as a rooming or boarding house). Those who are, or have, experienced homelessness may or may not have sought assistance from a specialist homelessness service. Studies of people whose residence is (or has been) threatened due to financial insecurity or poor living standards, and who do not report being unsheltered, residing in an emergency shelter, or residing in temporary accommodation, will be excluded. Studies will only be included where there is a subgroup that (A) is identifiable as experiencing homelessness; (B) meets the inclusion criteria and where (C) their rate of mortality can be disaggregated from the full study sample.

Outcome measure
Included studies will report on mortality as an outcome to be eligible for inclusion. Studies of mortality during or after a period of homelessness will be included. There will be no restrictions on the time frame in which mortality is examined after a period of homelessness. Causes of mortality will depend on those reported within the retrieved studies but may include communicable diseases (eg, SARS-CoV-2, HIV, tuberculosis, pneumonia), non-communicable diseases (eg, diabetes, diseases of the circulatory or respiratory system, cancer) and external causes (eg, intentional or unintentional injury). Mortality that results from legal intervention (ie, where a person dies because of interactions with a law enforcement officer in the course of duty, or death in custody) will be included, consistent with the international literature.

Study selection
Publication details and abstracts for each of the studies identified through the search of electronic databases will be imported into Endnote reference management software. Duplicates will be removed. Next, all remaining eligible studies will be imported into Covidence systematic review management software for screening. All remaining articles will undergo title and abstract screening. To ensure that the inclusion and exclusion criteria are consistently applied and in line with current best practice guidelines, the titles and abstracts of all identified studies will be independently screened by two authors (JH and RB). A random sample of 10% of these titles and abstracts will first be screened by RB (and inter-rater reliability (Cohen’s kappa statistic calculated)), before the remaining 90% of retrieved abstracts are screened. To achieve consensus, a third author (JY) will examine the titles and abstracts of any studies where there is disagreement between the two authors. Inter-rater reliability (Cohen’s kappa statistic) will be calculated for the full title and abstract screening process. If reliability is low (<0.40), the author team will review and revise the eligibility criteria and double-code a second random 10% of retrieved studies and Cohen’s kappa statistic recalculated. If applicable, the revised eligibility criteria will be used to guide a revised screening process.

Following title and abstract screening, the full-text version of all remaining potentially eligible studies will be reviewed by two authors (JH and RB) according to the inclusion and exclusion criteria. Any conflicts will be resolved by consensus with a third author (JY). The original study author(s) will be contacted twice via email where further clarification on the study is needed to determine its eligibility for inclusion. Where there is no reply received from the authors, the study will be excluded. In

Table 2: Fields for inclusion in the data extraction form

<table>
<thead>
<tr>
<th>Study information</th>
<th>Exposed/non-exposed conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author(s) and year of publication</td>
<td>No of deaths (all-cause and cause specific)</td>
</tr>
<tr>
<td>Study country of origin</td>
<td>Total person-time</td>
</tr>
<tr>
<td>Study design (eg, data linkage, survey data, prospective)</td>
<td>Incidence of all-cause and cause-specific mortality (CMRs, with 95% CI)</td>
</tr>
<tr>
<td>Year(s) of study</td>
<td>Cause(s) of death</td>
</tr>
<tr>
<td>Study Setting</td>
<td>All-cause and cause-specific standardised mortality ratios (SMRs, with 95% CIs) including the noting variable ratios were standardised on</td>
</tr>
<tr>
<td>Sample size</td>
<td>Predictors of mortality with effect sizes (eg, RRR, OR, HR, including 95% CIs)</td>
</tr>
<tr>
<td>Sample characteristics (eg, population-based, age, sex, homelessness status, race, ethnicity, reference population, other demographic characteristics of interest)</td>
<td>Significance levels (p values)</td>
</tr>
<tr>
<td>Type of homelessness (ie, unsheltered, residing in emergency shelter, residing in temporary accommodation)</td>
<td>Subgroup analysis results</td>
</tr>
<tr>
<td>Length of follow-up</td>
<td>Risk and protective factors</td>
</tr>
<tr>
<td>Age at time of death</td>
<td>Measures of bias/sensitivity analyses</td>
</tr>
<tr>
<td>Source(s) of mortality data</td>
<td>Statistical methods used</td>
</tr>
<tr>
<td>Attrition rates/loss to follow-up</td>
<td>Funding sources declared</td>
</tr>
<tr>
<td>Conflicts of interest declared</td>
<td>CMR, crude mortality rate; RRR, relative risk ratio; SMR, standardised mortality ratio.</td>
</tr>
</tbody>
</table>
the case where two (or more) eligible studies analyse the same data, only the study with the longer time frame (ie, follow-up duration) will be included.

Data extraction
Data will be extracted from the included studies by the lead author, using a prespecified data extraction form (standardised Excel form). Data extraction fields are presented in table 2. Data extracted from the included studies will be checked by a second author (RB) to identify and correct any errors. Any conflicts will be resolved by consensus with a third author (JY).

Risk of bias assessment
Study quality will be assessed using the Methodological Standards for Epidemiological Research (MASTER) scale. Two authors (JH and RB) will independently assess each study, with any ambiguity to be resolved by consensus through discussion with a third author (JY). Studies classified as being of low quality will be retained in the review and a sensitivity analysis conducted restricting the meta-analyses to those studies which are above the median MASTER score (see the Data synthesis and statistical analysis section).

Data synthesis and statistical analysis
A detailed descriptive synthesis of all included studies will be conducted, including study identification information (eg, author(s), year of publication, study country of origin), study characteristics (eg, sample size, mean age, sex, length of follow-up), study design (retrospective or prospective; sampling frame) and source(s) of mortality data. The statistical analysis strategy will be led by the author team and developed in consultation with a biostatistician at the Murdoch Children’s Research Institute, Melbourne, Australia. Where there are sufficient data within the included studies (ie, CMRs, SMRs and predictive factors), a meta-analysis will be conducted to produce pooled estimates. It is likely that most, if not all, included studies will be observational, meaning there is no specific exposure to be reviewed. Our measures of mortality will include: (A) incidence of all-cause and cause-specific mortality, expressed as pooled CMRs per 1000 person-years, with 95% CI and (B) all-cause and cause-specific, indirectly SMRs with 95% CI. Associations between risk and protective factors and all-cause and cause-specific mortality will be reported using pooled relative risk ratios with 95% CI. Where CMRs are not reported in an included study, they will be calculated wherever possible, using the method outlined by Zlozdre and Fazel. We will pool SMRs which compare an exposure (homelessness) to the general population (no homelessness). We will generate a funnel plot and use Egger’s test to assess potential publication bias.

Where the data permit, our analyses will be stratified by whether participants were homeless at the time of death. The proportion of total variation across study estimates due to heterogeneity will be examined using the I² statistic; an I² of at least 50% will be considered indicative of substantial heterogeneity. Subject to the availability of sufficient data in the included studies, the influence of subgroups and methodological factors on the CMRs, SMRs and/or risk/protective factors will be examined using meta-regression. To further understand potential sources of heterogeneity and where the data permit, subgroup analyses will be conducted by sex, age, study country of origin, study design (ie, retrospective, prospective), type of homelessness (eg, being unsheltered or residing in emergency shelter or residing in temporary accommodation), and length of time homeless. Sensitivity analyses will be conducted which exclude studies assessed as being low quality (based on quality assessment scores below the median on the MASTER scale) to examine the potential effect of study quality on outcome measures.

Patient and public involvement
There was no patient or public involvement in the design of the study. There will be no patient or public involvement in the conduct, reporting or dissemination plans of this study. Within the author team, however, there is lived experience of homelessness.

ETHICS AND DISSEMINATION
This study will analyse the findings of published studies that have already obtained ethics approval, meaning that it does not require institutional ethics review or approval. Despite recognition that people who are homeless, or have experienced periods of homelessness, have poor health outcomes and reduced life chances, efforts to address health inequality and improve health outcomes among this group have long been neglected in health policy. Thus, we will disseminate our findings to academic researchers, key stakeholders in health and other service systems working with people who have experienced homelessness, and policy makers in Australia and internationally. We will publish the findings of our study in an appropriate peer-reviewed journal. We will present our findings at national and international symposia and through seminar presentations. We will also disseminate our findings via a plain language summary distributed among our academic and professional networks, including a link to the main publication. A link to the published review will be circulated via social media.

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REFERENCES


