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Mortality of ethnic minority groups in the United Kingdom: a systematic review protocol

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Abstract

Introduction

Growing ethnic diversity in the United Kingdom has made it increasingly important to determine the presence of ethnic health inequalities. There has been no systematic review that has drawn together research on ethnic differences in mortality in the United Kingdom.

Methods

All types of observational studies that compare all-cause mortality between major ethnic groups and the White majority population in the United Kingdom will be included. We will search Medline (Ovid SP), Embase (Ovid SP), Scopus and ISI Web of Science and search the grey literature through conference proceedings and online thesis registries. We will conduct forward and backward citation tracking of identified references and consult with experts in the field to identify further publications and ongoing or unpublished studies. Two reviewers will independently screen studies and extract data. Two reviewers will independently assess the quality of included studies using the Newcastle-Ottawa Scale. If at least two studies are located for each ethnic group and studies are sufficiently homogeneous we will conduct a meta-analysis. If insufficient studies are located or if there is high heterogeneity we will produce a narrative summary of results.

Ethics and dissemination

As no primary data will be collected, formal ethical approval is not required. The findings of this review will be disseminated through publication in peer reviewed journals and conference presentations.

PROSPERO registration number TBA (submitted 06/08/2019)

Strengths and limitations of this study

- We will include all studies comparing all-cause mortality between pre-specified ethnic groups and the White majority population in the United Kingdom
- We will conduct an extensive and sensitive search of online databases and a thorough search for unpublished studies
- Lack of data on both country of birth and ethnicity in a large number of studies may reduce our ability to conduct the planned subgroup analyses comparing the health of UK-born and overseas-born ethnic minority group members

For peer review only

Introduction

Growing ethnic diversity in the United Kingdom (UK)¹ and the need to comply with legislation ensuring health for all^{2,3} has made it increasingly important to determine the presence of health differences by ethnicity. Mortality is an important measure of overall health status and mortality differences by ethnicity and migration status are a frequent topic of research both in the UK and other countries^{4,5,6}. Despite this, there remains little consensus on how mortality differs by ethnicity in the UK, particularly in UK-born ethnic minority individuals^{4,7}. Part of the difficulty in understanding mortality differences between ethnic minority groups in the UK arises from variability in how ethnicity is defined in studies, with some studies using self-reported ethnicity and others using proxy measures such as country of birth or ancestry. The use of country of birth has some limitations in that it will a/ include people born overseas that are not a member of the ethnic group of interest such as White British born in India and b/ limit ethnic minority individuals to the overseas born, a population in which the healthy migrant effect is an important driver of observed health differences.

The lack of consensus around mortality differences by ethnicity in the UK is also influenced by the complexity of the comparisons, as observed mortality differences will be impacted by a number of factors including the ethnic group under study, the ethnic group being compared to and the time period. Methodological and quality differences between studies could also contribute to different findings, particularly when comparing data from cohort studies to that of unlinked census and registry-based studies. This complexity underlies the importance of conducting a systematic review that draws together all of the different pieces of research on mortality differences by ethnicity in the UK and synthesises them in a rigorous manner. A systematic review will help to provide clarity on health inequalities in terms of mortality in the UK and provide guidance for policies promoting health equity.

To the best of our knowledge, there has been no other systematic review of the relationship between ethnicity and all-cause mortality in the UK. To address this gap, we have developed a protocol for a systematic review that will identify, appraise and synthesise the evidence comparing all-cause mortality rates between major ethnic groups and the White majority population in the UK.

Research question

The aim of this systematic review is to answer the following question: how do all-cause mortality rates differ between major ethnic groups and the White majority population in the UK? The population (P) is defined as the population of the UK, the 'risk factor' of interest (I term) is being a member of an ethnic minority population, the comparator (C term) is being a member of the White majority population and the outcome (O) is mortality.

Methods and analysis

Protocol design and registration

This protocol has been prepared according to the Preferred Reporting Items for Systematic reviews and Meta-analysis Protocols (PRISMA-P) statement and checklist (see online supplementary appendix 1)⁸. The protocol has also been registered in the PROSPERO international prospective register of systematic reviews (<http://www.crd.york.ac.uk/PROSPERO>) (number TBA). Any amendments to the protocol will be submitted to PROSPERO to establish a record of any changes and will be reported in the final published systematic review.

Patient and public involvement

No members of the public have been involved in the research design process. We will produce plain language summaries of our results for dissemination to members of the public.

Eligibility criteria

Population

The population will be restricted to that of the UK and can include studies on samples in any country or region within the UK. Studies will be limited to those on population-based samples. Studies restricted to populations with a specific disease such as diabetes will be excluded.

Ethnicity

Ethnicity can be defined by self-report or by proxy measures such as country of birth, country of birth of parents or ancestry. Table 1 shows the ethnic groups considered for inclusion in the study. These are based on ethnicity classifications used in the 2011 censuses of England and Wales, Scotland and Northern Ireland⁹⁻¹¹. Ethnic groups selected for inclusion represent at least 0.5% of the population in any one of these three censuses. The exceptions are broad non-specific categories such as 'other White' and 'other Western European' that were considered to be too heterogeneous to be meaningful and can have varying definitions depending on the sample. Where possible, we selected ethnic group classifications from the three UK censuses that were the most specific and narrowly defined rather than a larger composite group (for example, Indian and Pakistani British/Scottish as separate categories rather than the combined South Asian British/Scottish category). However, we selected broader groupings when more narrowly defined groupings were not available (e.g. Caribbean rather than Jamaican, African rather than Ghanaian). When broader groupings are used to define ethnic categories, we have provided in the second column of Table 1 details of what other more specific groupings will be included under the umbrella of this broader category. In contrast, when smaller more specific groupings are used, we provide in column two, details of

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3 what broader, less specific groupings would also be accepted in studies where only
4 these broader groupings are used.
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7 Studies that group multiple and extremely diverse ethnic groups together as one
8 single category (such as all non-white ethnic minorities) will be excluded. Due to
9 frequently observed differences in mortality between South Asians and East
10 Asians^{4,7} we will also not include data from studies using the composite group of
11 Asian, where this group combines South Asians and East Asians as one category.
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14 **Comparators**

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16 The comparator group is the ethnic majority population which could include any of
17 the following groups in the UK depending on the location of the study:
18

- 19 • White British – the majority population for the UK
- 20 • White English/Welsh – the majority population for studies in England and
- 21 Wales
- 22 • White Scottish – the majority population for studies in Scotland
- 23 • White Irish – the majority population for studies in Northern Ireland
- 24 • White – with all White or all White British ethnic groups included together
- 25 • Rest of the population – all other ethnic groups apart from the ethnic group(s)
- 26 of interest in the study
- 27
- 28
- 29
- 30

31 **Outcome**

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33 The outcome will be the all-cause mortality rate comparison by ethnicity which can
34 be presented as a standardised mortality ratio (SMR), relative risk (RR) or hazard
35 ratio (HR). Studies providing age adjusted beta coefficients will be included and the
36 beta coefficients exponentiated. Studies that provide absolute measures of effect will
37 also be included if sufficient information is provided to estimate relative measures.
38 We will include outcomes adjusted for or stratified by a/ age and sex; b/ age, sex and
39 socioeconomic status (SES); c/ all other confounders.
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44 **Study types**

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46 Due to the frequent under-representation of ethnic minority populations in cohort
47 studies¹², we will include all observational study types that meet our PICO inclusion
48 criteria. This will include:
49

- 50 • Cross-sectional registry-based studies (unlinked numerator and denominator)
- 51 • Longitudinal registry-based studies (unlinked numerator and denominator)
- 52 • Cohort studies – including those involving data linkage
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Table 1. Ethnic groups considered for inclusion in the systematic review

Census category ethnic group	Composite/specific ethnic groups and synonyms to be accepted
British/White British	White
English/White English	White
Scottish/White Scottish	White
Irish/White Irish	White
Polish	Eastern European
Indian/British Indian/Indian Scottish	South Asian
Pakistani/British Pakistani/Pakistani Scottish	South Asian
Bangladeshi/British Bangladeshi	South Asian/other South Asian
Chinese/British Chinese/Chinese Scottish	East Asian
African/British African/African Scottish	Black/African origin/Any ethnic group with an origin from any specific sub-Saharan African country (e.g. Ghanaian)
Caribbean	Black/African Caribbean/West Indian/Any ethnic group with predominantly African ancestry from any specific Caribbean country (e.g. Jamaican)
Black Irish/Black Scottish/Black British	Black/African origin
White and Black Caribbean	Mixed background
White and Asian	Mixed background

Search strategy

We will conduct searches of Medline (Ovid SP), Embase (Ovid SP), Scopus and ISI Web of Science (which includes ISI conference proceedings). We will conduct further searches of the grey literature through EThOS (the British Library e-theses online service) and ProQuest dissertations and theses: UK and Ireland. We will additionally search the NICE website and conduct searches on Google given that some material is likely to be published as government reports more readily available from the internet than in published journals. Searches will be carried out from inception to the

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3 date of the search with no language or other restrictions. We will attempt to contact
4 the authors of relevant studies where additional data may be available on mortality
5 by ethnic subgroups. We will also perform forward and backward citation tracking of
6 identified relevant articles. We will contact experts in the field for additional studies
7 not located as part of the comprehensive search. We will also contact chief
8 investigators of cohort studies in the UK where data on ethnicity and mortality are
9 likely to have been collected but have not been published. The search strategy was
10 developed by FFS in consultation with a medical librarian with expertise in
11 conducting searches for systematic reviews. The Medline search strategy is provided
12 in Supplementary Appendix 2.
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17 **Data management**

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19 Search results will be exported into Endnote X8.2 for screening purposes. An excel
20 spreadsheet will be used to document the selection process and will document the
21 total number of references located by each database, the total number of references
22 identified after removal of duplicates, the total number of references identified via
23 grey literature searches and the number of references selected at each stage of the
24 screening process and reasons for exclusion.
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28 **Selection process**

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30 Two authors (FFS and NN) will independently screen titles and abstracts for possible
31 selection into the study. Any article identified by at least one author will be included
32 in the list of full text articles to review in the second stage of article selection. Two
33 authors (FFS and NN) will then independently review full text versions of articles
34 selected in the screening stage to confirm their eligibility for inclusion.
35 Disagreements will be resolved by consensus or when necessary, consultation with
36 a third reviewer (RSB). For studies that use overlapping datasets such as registry-
37 based studies that have overlapping time periods, the study with data over the
38 longest period will be included. If the time periods are of equivalent length, we will
39 select the study that includes the most recent time period.
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45 **Data extraction**

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47 Data will be extracted by two authors (FFS and NN) independently. Data will be
48 entered into a data extraction form that will be pilot tested by the two authors prior to
49 commencing data extraction. Extracted information will include: study citation, study
50 design, study location and setting, ethnic group(s) included and method of
51 ascertainment of ethnicity, comparison group, participant characteristics (n, mean
52 age, sex, SES) in each group, participation rates/losses/linkage rates in each group,
53 method of outcome ascertainment, number of events in each group, the measure of
54 effect for mortality comparison (SMR, HR, RR) and the confidence interval or
55 standard error. We will extract the following effect measures if available: a/
56 SMR/HR/RR adjusted for age and stratified by or adjusted for sex; b/ HR/RR
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3 adjusted for age and SES and stratified by or adjusted for sex; c/ HR/RR adjusted for
4 other confounders. After completion of independent data extraction, the two authors
5 will review both sets of extracted data together to check for errors and
6 disagreements. Any disagreements will be resolved by consensus with the help of an
7 additional author (EM) if necessary. Finalised data will be collated into an excel
8 spreadsheet. For studies with missing data or with some outcome data not
9 disaggregated by sex or particular ethnic groups, contact will be made with original
10 authors requesting the raw data if available. Contact will also be made with
11 investigators of major cohort studies in the UK where data on ethnicity and mortality
12 have likely been collected but not reported in publications.
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17 **Risk of bias assessment of individual studies**

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19 Study quality will be appraised independently by two authors (FFS and EM).
20 Disagreements will be resolved by consensus or when necessary, consultation with
21 a third reviewer (RSB). The quality of included studies will be appraised using a
22 modified version of the Newcastle-Ottawa scale¹³ (Supplementary Appendix 3). The
23 risk of bias table will be grouped according to study type. For cross-sectional studies,
24 only the first three questions under selection, the single question under comparability
25 and the first question under outcome will be used. Some further specific details on
26 the use of the Newcastle-Ottawa scale in this systematic review are as follows:
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31 The Newcastle-Ottawa Scale will be scored using a similar approach to the
32 Cochrane risk of bias tool, where a judgement will be made about the risk of bias
33 being high, low or unclear. A low risk of bias will be equivalent to receiving stars for
34 particular items as recommended in the manual for the Newcastle-Ottawa Scale.
35 However, this modified approach will allow us to distinguish between studies that
36 likely have a high risk of bias due to serious methodological flaws and those with
37 unclear risk of bias due to inadequate reporting or lack of information about the
38 likelihood of particular biases such as salmon bias¹⁴ in a particular ethnic group.
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42 Other differences in the use of this scale will be as follows: in terms of comparability,
43 we will only assess if the study adjusts for/stratifies by age and sex. In terms of
44 ascertainment of exposure, the ideal method of exposure assessment will be self-
45 reported ethnicity which will be given a low risk of bias assessment. Proxy measures
46 for ethnicity such as country of birth will also receive a low risk of bias rating if there
47 is good evidence that this is an accurate measure of ethnicity in the specific
48 instance. As the accuracy of country of birth as a proxy measure varies by ethnic
49 group¹⁵, in studies that include a number of different ethnic groups a judgement of
50 risk of bias will be made for each ethnic group included in the study and provided as
51 a supplementary file, but only a summary judgement for the study overall will be
52 displayed in the main risk of bias table. The summary judgement will be based on
53 the average risk of bias for exposure ascertainment across all included ethnic
54 groups.
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3 We will add an additional domain of other bias to incorporate the problem of
4 numerator/denominator mismatch that can occur in unlinked registry-based studies.
5 The likelihood of this bias being present will be judged according to publications
6 reporting the likelihood of this bias in UK data for specific ethnic groups in addition to
7 the information provided in the included studies. For studies using data linkage,
8 reported linkage rates will be used as part of the judgement of numerator-
9 denominator bias. Similar to exposure ascertainment, numerator-denominator bias
10 may differ between ethnic groups, and when this is likely a risk of bias judgement will
11 be made for each ethnic group separately, but only a summary judgement for the
12 study overall will be displayed in the main table.
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17 **Quality of evidence for individual ethnic groups**

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19 We will examine the quality of the body of evidence for mortality differences for each
20 ethnic group using GRADE criteria¹⁶. This will include consideration of risk of bias
21 assessment (with consideration given to the specific risk of bias assessment for
22 individual ethnic groups in terms of exposure ascertainment, linkage rates etc),
23 inconsistency of results, indirectness of evidence, imprecision and publication bias.
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26

27 **Data synthesis**

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29 Data synthesis will be carried out by author SKS using a random effects model. We
30 will only conduct quantitative synthesis if we locate at least two studies for a
31 particular ethnic group and if there is sufficient homogeneity to enable meaningful
32 synthesis as detailed below in the section on subgroup analysis and investigation of
33 heterogeneity. In the absence of a quantitative synthesis we will provide a narrative
34 synthesis of results by ethnic group. Quantitative synthesis of age adjusted results
35 will be stratified by sex and ethnic group. We will conduct additional quantitative
36 synthesis of results adjusted for age and SES also stratified by sex and ethnic group
37 if available data permits. If data extracted are adjusted for rather than stratified by
38 sex, we will summarise this additional data narratively and provide the results in the
39 appendices. If extracted effect measures are adjusted for other potential
40 confounders in addition to age and sex such as health behaviours and comorbidities
41 we will summarise this information narratively and provide the data in the
42 appendices.
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49 Given the likely diversity in measures of effects used between unlinked registry
50 studies and cohort studies we will treat standardised mortality ratios, hazard ratios
51 and relative risks as equivalent measures of effect. As event rates are likely to be
52 low in population-based samples including in the non-exposed group, the hazard
53 ratio and relative risk should be equivalent¹⁷. In addition, as the proportion of most
54 ethnic minority populations included in the analysis will range between 0.5-2.5%, the
55 standardised mortality ratio is less likely to be a biased representation of the relative
56 risk as the exposure rate (ethnicity) is low¹⁸. However, given that the standardised
57 mortality ratio can be biased when both age-specific mortality ratios and population
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3 age distribution differs between ethnic groups¹⁹, we will include consideration of
4 difference in effect measures in our assessment of heterogeneity as discussed
5 below. We will screen for publication bias using a funnel plot and Begg's test²⁰ if at
6 least 10 studies are located for a particular quantitative synthesis. We will also
7 investigate publication bias by sub-group analysis comparing results of published
8 and unpublished data if sufficient data are available.
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12 Where data sources for a single ethnic group include disparate time periods, we will
13 arrange studies by date and then conduct a random-effects cumulative meta-
14 analysis to examine how comparative mortality estimates evolve over time. If data is
15 available on both country of birth and self-reported ethnicity from included studies,
16 we will conduct subgroup analyses within ethnic groups by country of birth (UK- vs
17 overseas-born). The need for this subgroup analysis is based on the need to account
18 for the healthy migrant effect as a potential underlying cause of observed differences
19 in mortality rates and the importance of understanding if there are differences in
20 mortality between overseas-born and UK-born ethnic minority group members. We
21 also plan subgroup analyses based on different comparison populations (e.g. White
22 British, White Scottish, White Irish). This is due to frequently poorer observed health
23 in White Scottish and White Irish populations compared to White British populations⁴.
24 Therefore, using the White Scottish or White Irish populations as the comparator
25 group in studies based in Scotland or Northern Ireland, could alter the pattern of
26 observed ethnic differences. If sufficient high-quality cohort studies are located, we
27 will also conduct sensitivity analyses restricted to these high-quality studies with
28 results from cross-sectional studies and unlinked registry studies removed. If high
29 heterogeneity is observed, we will investigate whether this is reduced by conducting
30 the prespecified subgroup and sensitivity analyses listed below.
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37 **Investigation of heterogeneity**

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40 We will assess for the presence of heterogeneity using Cochran's Q and the I²
41 Statistic²¹. If we observe an I² value of 50% or more, we will explore possible
42 explanations for the observed heterogeneity in subgroup and sensitivity analyses as
43 follows:
44
45

46 **Subgroup analyses**

- 47 1. Method of ethnicity ascertainment between studies – country of birth vs self-
48 reported ethnicity vs other methods.
- 49 2. Definition/included groups in one major ethnic group – e.g. South Asian vs
50 subgroups of Indian, Pakistani, Bangladeshi.
- 51 3. Comparison population – e.g. White majority population in England and Wales vs
52 White Scottish population in Scotland.
- 53 4. Measure of effect – standardised mortality ratio vs hazard ratio or relative risk.
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58 **Sensitivity analyses**

1. Study design – non-cohort studies removed.
2. Risk of bias – within cohort studies only, studies with high risk of bias will be removed.

If any of the above are identified as a plausible explanation of the observed heterogeneity, we will conduct a quantitative synthesis at the subgroup level if sufficient studies are available. If insufficient studies are available, we will summarise the results of studies narratively.

In addition to the abovementioned subgroup analyses that will be conducted to investigate heterogeneity, if sufficient data are available, we will also conduct the following subgroup analyses:

Additional subgroup analyses

1. UK-born versus overseas-born within each ethnic group to examine the contribution of the healthy migrant effect to observed differences in mortality by ethnicity.
2. Published versus unpublished results within each ethnic group to examine the presence of publication bias.

Ethics and dissemination

To our knowledge, the proposed systematic review will be the first to systematically collect and synthesise evidence on mortality differences between the major ethnic groups in the UK. The results of the review will provide important evidence about health inequalities and provide important guidance for policies promoting health equity. It is also likely that the review will identify important gaps in the knowledge base such as a lack of research in particular ethnic groups or insufficient evidence in terms of differences in mortality between UK-born and overseas-born members of particular ethnic minority groups.

On completion of the review, we will implement a robust knowledge translation strategy that will include publication in peer-reviewed journals with selection of an open access format where possible, presentation of results at relevant conferences, and production of plain language summaries for dissemination of results to members of the public.

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9 Cochrane Collaboration, 2011.
10

11 **Authors' contributions**

12
13
14 The protocol was drafted by FFS in consultation with the other authors in terms of
15 ethnic groups to be included, literature search strategy, risk of bias assessment and
16 data synthesis. All authors approved the final version of the protocol.
17

18 **Funding statement**

19
20
21 Open access fees were covered by financial support from the School of Public
22 Health Academic Support Scheme. The School of Public Health had no role in
23 developing the protocol.
24

25 **Competing interests**

26
27
28 None of the authors declare any competing interests
29

30 **Word count** 3507
31

32 **Supplementary files**

33
34 Appendix 1: PRISMA-P checklist
35

36 Appendix 2: Example search strategy in Ovid MEDLINE
37

38 Appendix 3: Newcastle-Ottawa scale
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PRISMA- P 2015 Checklist

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input type="checkbox"/>	n/a
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	<input checked="" type="checkbox"/>	<input type="checkbox"/>	2 (awaiting confirmation of registration from Prospero, submitted 06/08/2019)
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	14
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input checked="" type="checkbox"/>	<input type="checkbox"/>	5
Support					
Sources	5a	Indicate sources of financial or other support for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	14
Sponsor	5b	Provide name for the review funder and/or sponsor	<input checked="" type="checkbox"/>	<input type="checkbox"/>	14
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input checked="" type="checkbox"/>	<input type="checkbox"/>	14
INTRODUCTION					

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
Rationale	6	Describe the rationale for the review in the context of what is already known	<input checked="" type="checkbox"/>	<input type="checkbox"/>	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	4
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	5-7
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	<input checked="" type="checkbox"/>	<input type="checkbox"/>	7,8
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Supplementary Appendix 2
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8, 9
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8,9
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8, 9
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8, 9
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	<input checked="" type="checkbox"/>	<input type="checkbox"/>	9-11
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	<input checked="" type="checkbox"/>	<input type="checkbox"/>	10-12

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	10-12
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	11,12
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	<input checked="" type="checkbox"/>	<input type="checkbox"/>	11,12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	11,12
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	10

Appendix 2

Medline (Ovid SP) search

#	Search Terms
1	exp United Kingdom/
2	england*.mp.
3	scotland*.mp.
4	northern ireland.mp.
5	wales.mp.
6	united kingdom.mp.
7	britain.mp.
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	exp Ethnic Groups/
10	exp Minority Groups/
11	exp "Transients and Migrants"/
12	exp "Emigrants and Immigrants"/
13	polish.mp.
14	indian.mp.
15	pakistan*.mp.

16	bangladesh*.mp.
17	chinese.mp.
18	african.mp.
19	caribbean.mp.
20	black.mp.
21	mixed.mp.
22	ethnic*.mp.
23	9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24	exp Mortality/
25	exp Death/
26	mortal*.mp.
27	24 or 25 or 26
28	8 and 23 and 27

Appendix 3

Newcastle-Ottawa quality assessment scale with modifications and assessment criteria described

Question	Risk of bias assessment	Criteria for risk of bias assessment
Selection		
1. Representativeness of the exposed sample	Low	Representative of members of the respective ethnic minority group (census-based whole population sample or cross-sectional/cohort study with high participation rates)
	High	Selected group such as nurses, volunteers
	Unclear	No description of derivation of exposed sample
2. Selection of non-exposed sample	Low	Drawn from the same community as the exposed sample/similar participation rates as the exposed sample
	High	Drawn from a different source to the exposed sample
	Unclear	No description of derivation of exposed sample
3. Ascertainment of exposure	Low	Self-reported ethnicity. Proxy measures of ethnicity (country of birth, country of birth of parents, ancestry) if evidence they are accurate measures of ethnicity
	High	Proxy measures of ethnicity that are not accurate measures of self-reported ethnicity
	Unclear	Method of exposure ascertainment not described OR proxy measure used and no data available on accuracy as a measure of self-reported ethnicity
4. Demonstration that outcome of interest was no present at start of study*	Low	Outcome not present at start of study
	High	Outcome present at start of study
	Unclear	Unable to determine if outcome present at start of study
Comparability		
1. Comparability of cohorts on the basis of the design or analysis	Low	Effect measures are adjusted/stratified by age and sex
	High	Effect measures are not adjusted/stratified by age and sex
	Unclear	Unclear if effect measures have been adjusted for age/sex
Outcome		
1. Assessment of outcome	Low	Independent blind assessment of outcome or record linkage
	High	Self-report
	Unclear	Method of outcome assessment not described

2. Was follow-up long enough for outcomes to occur*	Low	At least 24 months of follow-up or shorter period with high event rates (older population)
	High	Less than 24 months of follow-up and low event rates
	Unclear	Length of follow up not reported
3. Adequacy of follow up*	Low	No or small loss to follow up, losses even between comparison groups
	High	Large loss to follow up that has potential to change estimate of effect (determined by worst-case best-case analysis) OR losses uneven between comparison groups
	Unclear	Losses not reported
Other bias		
1. Numerator-denominator bias/linkage rates	Low	Low proportion of migrants in ethnic group <20% OR evidence that missed overseas deaths are low OR high rates of data linkage that are equal between comparison groups
	High	High proportion of migrants in ethnic group AND evidence that likelihood of missed overseas deaths is high and likely to change reported estimates, OR high rates of unlinked participants that differs by ethnic group
	Unclear	No information on proportion of migrants in ethnic group, likelihood of missed overseas deaths, or rates of data linkage

*Not assessed in cross-sectional studies

Peer review only

Fiona Stanaway

From: CRD-REGISTER <irss505@york.ac.uk>
Sent: Tuesday, 6 August 2019 12:11 PM
To: Fiona Stanaway
Subject: PROSPERO acknowledgement of receipt [146143]

Dear Registrant,

Thank you for submitting details of your systematic review for registration in PROSPERO.

We will check the information supplied to

- make sure that your systematic review is within scope
- ensure that the fields have been completed appropriately.

PLEASE NOTE THAT THESE CHECKS DO NOT CONSTITUTE PEER REVIEW OR IMPLY APPROVAL OF YOUR SYSTEMATIC REVIEW METHODS.

We will let you know when your record has been published on PROSPERO, or alternatively ask for further information or clarification. If your application is rejected we will advise you of the reasons for non-publication (usually this will be if your review is out of scope).

With the current very high demand for registration, we aim to respond within 10 working days for UK submissions and 20 working days for submissions outside the UK.

We will process your application as soon as possible. During this time the record will be locked and you will not be able to access it.

Please note that this does not stop you working on your review.

Yours sincerely,
PROSPERO Administrator
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BMJ Open

Mortality of ethnic minority groups in the United Kingdom: a systematic review protocol

Journal:	<i>BMJ Open</i>
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Primary Subject Heading:	Public health
Secondary Subject Heading:	Epidemiology
Keywords:	EPIDEMIOLOGY, PUBLIC HEALTH, STATISTICS & RESEARCH METHODS

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Mortality of ethnic minority groups in the United Kingdom: a systematic review protocol

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Abstract

Introduction

Growing ethnic diversity in the United Kingdom has made it increasingly important to determine the presence of ethnic health inequalities. There has been no systematic review that has drawn together research on ethnic differences in mortality in the United Kingdom.

Methods

All types of observational studies that compare all-cause mortality between major ethnic groups and the White majority population in the United Kingdom will be included. We will search Medline (Ovid SP), Embase (Ovid SP), Scopus and ISI Web of Science and search the grey literature through conference proceedings and online thesis registries. We will conduct forward and backward citation tracking of identified references and consult with experts in the field to identify further publications and ongoing or unpublished studies. Two reviewers will independently screen studies and extract data. Two reviewers will independently assess the quality of included studies using the Newcastle-Ottawa Scale. If at least two studies are located for each ethnic group and studies are sufficiently homogeneous we will conduct a meta-analysis. If insufficient studies are located or if there is high heterogeneity we will produce a narrative summary of results.

Ethics and dissemination

As no primary data will be collected, formal ethical approval is not required. The findings of this review will be disseminated through publication in peer reviewed journals and conference presentations.

PROSPERO registration number CRD42019146143

https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019146143

Strengths and limitations of this study

- We will include all studies comparing all-cause mortality between pre-specified ethnic groups and the White majority population in the United Kingdom
- We will conduct an extensive and sensitive search of online databases and a thorough search for unpublished studies
- We will examine the extent to which country of birth and socio-economic status contribute to ethnic inequalities in mortality
- Lack of data on both country of birth and ethnicity in a large number of studies may reduce our ability to conduct the planned subgroup analyses comparing the health of UK-born and overseas-born ethnic minority group members

Introduction

Growing ethnic diversity in the United Kingdom (UK)¹ and the need to comply with legislation ensuring health for all^{2,3} has made it increasingly important to determine the presence of health differences by ethnicity. Mortality is an important measure of overall health status and mortality differences by ethnicity and migration status are a frequent topic of research both in the UK and other countries^{4,5,6}. Despite this, there remains little consensus on how mortality differs by ethnicity in the UK, particularly in UK-born ethnic minority individuals^{4,7}. Part of the difficulty in understanding mortality differences between ethnic minority groups in the UK arises from variability in how ethnicity is defined in studies, with some studies using self-reported ethnicity and others using proxy measures such as country of birth or ancestry. The use of country of birth has some limitations in that it will a/ include people born overseas that are not a member of the ethnic group of interest such as White British born in India and b/ limit ethnic minority individuals to the overseas born, a population in which the healthy migrant effect is an important driver of observed health differences.

The lack of consensus around mortality differences by ethnicity in the UK is also influenced by the complexity of the comparisons, as observed mortality differences will be impacted by a number of factors including the ethnic group under study, the ethnic group being compared to and the time period. Methodological and quality differences between studies could also contribute to different findings, particularly when comparing data from cohort studies to that of unlinked census and registry-based studies. There has also been very little exploration and as a result, limited consensus on what the underlying drivers of mortality differences by ethnicity in the UK might be. Place of birth (in particular being born overseas compared to being born in the UK) is likely an important predictor of mortality differences as well as socioeconomic status (SES). However, results can be conflicting for the influence of socioeconomic status on the health of ethnic minority persons, particularly in terms of the relationship between SES and mortality in migrants^{4,6}.

This complexity and lack of consensus underlies the importance of conducting a systematic review that draws together all of the different pieces of research on mortality differences by ethnicity in the UK and synthesises them in a rigorous manner. A systematic review will help to provide clarity on health inequalities in terms of mortality in the UK and provide guidance for policies promoting health equity.

To the best of our knowledge, there has been no other systematic review of the relationship between ethnicity and all-cause mortality in the UK. To address this gap, we have developed a protocol for a systematic review that will identify, appraise and synthesise the evidence comparing all-cause mortality rates between major ethnic groups and the White majority population in the UK.

Research question

1
2
3 The aim of this systematic review is to answer the following question: how do all-
4 cause mortality rates differ between ethnic minority groups and the White majority
5 population in the UK? The population (P) is defined as the population of the UK, the
6 'risk factor' of interest (I term) is being a member of an ethnic minority population, the
7 comparator (C term) is being a member of the White majority population and the
8 outcome (O) is mortality.
9

11 **Methods and analysis**

12 **Protocol design and registration**

13
14
15
16 This protocol has been prepared according to the Preferred Reporting Items for
17 Systematic reviews and Meta-analysis Protocols (PRISMA-P) statement and
18 checklist (see online supplementary appendix 1)⁸. The protocol has also been
19 registered in the PROSPERO international prospective register of systematic
20 reviews (<http://www.crd.york.ac.uk/PROSPERO>) (number TBA). Any amendments to
21 the protocol will be submitted to PROSPERO to establish a record of any changes
22 and will be reported in the final published systematic review.
23
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25

26 **Patient and public involvement**

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28 No members of the public have been involved in the research design process. We
29 will produce plain language summaries of our results for dissemination to members
30 of the public.
31
32

33 **Ethics and dissemination**

34
35 As no primary data will be collected, formal ethical approval is not required. The
36 findings of this review will be disseminated through publication in peer reviewed
37 journals and conference presentations.
38
39

40 **Eligibility criteria**

41 **Population**

42
43 The population will be restricted to that of the UK and can include studies on
44 samples in any country or region within the UK. Studies will be limited to those on
45 population-based samples. Studies restricted to populations with a specific disease
46 such as diabetes will be excluded as mortality rates in these population sub-groups
47 would be higher and not able to be meaningfully combined with those based on the
48 whole population.
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53 **Ethnicity**

54
55 Ethnicity can be defined by self-report or by proxy measures such as country of birth,
56 country of birth of parents or ancestry. Table 1 shows the ethnic groups considered
57 for inclusion in the study. These are based on ethnicity classifications used in the
58 2011 censuses of England and Wales, Scotland and Northern Ireland⁹⁻¹¹. Ethnic
59
60

1
2
3 groups selected for inclusion represent at least 0.5% of the population in any one of
4 these three censuses. The exceptions are broad non-specific categories such as
5 'other White' and 'other Western European' that were considered to be too
6 heterogeneous to be meaningful and can have varying definitions depending on the
7 sample. Where possible, we selected ethnic group classifications from the three UK
8 censuses that were the most specific and narrowly defined rather than a larger
9 composite group (for example, Indian and Pakistani British/Scottish as separate
10 categories rather than the combined South Asian British/Scottish category).
11 However, we selected broader groupings when more narrowly defined groupings
12 were not available (e.g. Caribbean rather than Jamaican, African rather than
13 Ghanaian). When broader groupings are used to define ethnic categories, we have
14 provided in the second column of Table 1 details of what other more specific
15 groupings will be included under the umbrella of this broader category. In contrast,
16 when smaller more specific groupings are used, we provide in column two, details of
17 what broader, less specific groupings would also be accepted in studies where only
18 these broader groupings are used.
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25 Studies that group multiple and extremely diverse ethnic groups together as one
26 single category (such as all non-white ethnic minorities) will be excluded. Due to
27 frequently observed differences in mortality between South Asians and East
28 Asians^{4,7} we will also not include data from studies using the composite group of
29 Asian, where this group combines South Asians and East Asians as one category.
30
31
32

33 **Comparators**

34 The comparator group is the ethnic majority population which could include any of
35 the following groups in the UK depending on the location of the study:
36
37

- 38 • White British – the majority population for the UK
- 39 • White English/Welsh – the majority population for studies in England and
40 Wales
- 41 • White Scottish – the majority population for studies in Scotland
- 42 • White Irish – the majority population for studies in Northern Ireland
- 43 • White – with all White or all White British ethnic groups included together
- 44 • Rest of the population – all other ethnic groups apart from the ethnic group(s)
45 of interest in the study
46
47
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49

50 **Outcome**

51 The outcome will be the all-cause mortality rate comparison by ethnicity which can
52 be presented as a standardised mortality ratio (SMR), relative risk (RR) or hazard
53 ratio (HR). Studies providing age adjusted beta coefficients will be included and the
54 beta coefficients exponentiated. Studies that provide absolute measures of effect will
55 also be included if sufficient information is provided to estimate relative measures.
56 We will include outcomes adjusted for or stratified by a/ age and sex; b/ age, sex and
57 SES; c/ all other confounders.
58
59
60

Study types

Due to the frequent under-representation of ethnic minority populations in cohort studies¹², we will include all observational study types that meet our PICO inclusion criteria. This will include:

- Cross-sectional registry-based studies (unlinked numerator and denominator)
- Longitudinal registry-based studies (unlinked numerator and denominator)
- Cohort studies – including those involving data linkage

For peer review only

Table 1. Ethnic groups considered for inclusion in the systematic review

Census category ethnic group	Composite/specific ethnic groups and synonyms to be accepted
British/White British	White
English/White English	White
Scottish/White Scottish	White
Irish/White Irish	White
Polish	Eastern European
Indian/British Indian/Indian Scottish	South Asian
Pakistani/British Pakistani/Pakistani Scottish	South Asian
Bangladeshi/British Bangladeshi	South Asian/other South Asian
Chinese/British Chinese/Chinese Scottish	East Asian
African/British African/African Scottish	Black/African origin/Any ethnic group with an origin from any specific sub-Saharan African country (e.g. Ghanaian)
Caribbean	Black/African Caribbean/West Indian/Any ethnic group with predominantly African ancestry from any specific Caribbean country (e.g. Jamaican)
Black Irish/Black Scottish/Black British	Black/African origin
White and Black Caribbean	Mixed background
White and Asian	Mixed background

Search strategy

We will conduct searches of Medline (Ovid SP), Embase (Ovid SP), Scopus and ISI Web of Science (which includes ISI conference proceedings). We will conduct further searches of the grey literature through EThOS (the British Library e-theses online service) and ProQuest dissertations and theses: UK and Ireland. We will additionally search the NICE website and conduct searches on Google given that some material is likely to be published as government reports more readily available from the internet than in published journals. Searches will be carried out from inception to

1
2
3 August 2, 2019 with no language or other restrictions. Database searches will be
4 repeated prior to publication to identify new articles published since the initial search.
5 We will attempt to contact the authors of relevant studies where additional data may
6 be available on mortality by ethnic subgroups. We will also perform forward and
7 backward citation tracking of identified relevant articles. We will contact experts in
8 the field for additional studies not located as part of the comprehensive search. We
9 will also contact chief investigators of cohort studies in the UK where data on
10 ethnicity and mortality are likely to have been collected but have not been published.
11 The search strategy was developed by FFS in consultation with a medical librarian
12 with expertise in conducting searches for systematic reviews. The Medline search
13 strategy is provided in Supplementary Appendix 2.
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18 **Data management**

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21 Search results will be exported into Endnote X8.2 for screening purposes. An excel
22 spreadsheet will be used to document the selection process and will document the
23 total number of references located by each database, the total number of references
24 identified after removal of duplicates, the total number of references identified via
25 grey literature searches and the number of references selected at each stage of the
26 screening process and reasons for exclusion.
27
28

29 **Selection process**

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32 Two authors (FFS and NN) will independently screen titles and abstracts for possible
33 selection into the study. Any article identified by at least one author will be included
34 in the list of full text articles to review in the second stage of article selection. Two
35 authors (FFS and NN) will then independently review full text versions of articles
36 selected in the screening stage to confirm their eligibility for inclusion.
37 Disagreements will be resolved by consensus or when necessary, consultation with
38 a third reviewer (RSB). For studies that use overlapping datasets such as registry-
39 based studies that have overlapping time periods, the study with data over the
40 longest period will be included. If the time periods are of equivalent length, we will
41 select the study that includes the most recent time period.
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46 **Data extraction**

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49 Data will be extracted by two authors (FFS and NN) independently. Data will be
50 entered into a data extraction form that will be pilot tested by the two authors prior to
51 commencing data extraction. Extracted information will include: study citation, study
52 design, study location and setting, ethnic group(s) included and method of
53 ascertainment of ethnicity, comparison group, participant characteristics (n, mean
54 age, sex, SES) in each group, participation rates/losses/linkage rates in each group,
55 method of outcome ascertainment, number of events in each group, the measure of
56 effect for mortality comparison (SMR, HR, RR) and the confidence interval or
57 standard error. We will extract the following effect measures if available: a/
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3 SMR/HR/RR adjusted for age and stratified by or adjusted for sex; b/ HR/RR
4 adjusted for age and SES and stratified by or adjusted for sex; c/ HR/RR adjusted for
5 other confounders. After completion of independent data extraction, the two authors
6 will review both sets of extracted data together to check for errors and
7 disagreements. Any disagreements will be resolved by consensus with the help of an
8 additional author (EM) if necessary. Finalised data will be collated into an excel
9 spreadsheet. For studies with missing data or with some outcome data not
10 disaggregated by sex or particular ethnic groups, contact will be made with original
11 authors requesting the raw data if available. Contact will also be made with
12 investigators of major cohort studies in the UK where data on ethnicity and mortality
13 have likely been collected but not reported in publications.
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18 **Risk of bias assessment of individual studies**

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21 Study quality will be appraised independently by two authors (FFS and EM).
22 Disagreements will be resolved by consensus or when necessary, consultation with
23 a third reviewer (RSB). The quality of included studies will be appraised using a
24 modified version of the Newcastle-Ottawa scale¹³ (Supplementary Appendix 3). The
25 risk of bias table will be grouped according to study type. For cross-sectional studies,
26 only the first three questions under selection, the single question under comparability
27 and the first question under outcome will be used. Some further specific details on
28 the use of the Newcastle-Ottawa scale in this systematic review are as follows:
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30
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32 The Newcastle-Ottawa Scale will be scored using a similar approach to the
33 Cochrane risk of bias tool, where a judgement will be made about the risk of bias
34 being high, low or unclear. A low risk of bias will be equivalent to receiving stars for
35 particular items as recommended in the manual for the Newcastle-Ottawa Scale.
36 However, this modified approach will allow us to distinguish between studies that
37 likely have a high risk of bias due to serious methodological flaws and those with
38 unclear risk of bias due to inadequate reporting or lack of information about the
39 likelihood of particular biases such as salmon bias¹⁴ in a particular ethnic group.
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44 Other differences in the use of this scale will be as follows: in terms of comparability,
45 we will only assess if the study adjusts for/stratifies by age and sex. In terms of
46 ascertainment of exposure, the ideal method of exposure assessment will be self-
47 reported ethnicity which will be given a low risk of bias assessment. Proxy measures
48 for ethnicity such as country of birth will also receive a low risk of bias rating if there
49 is good evidence that this is an accurate measure of ethnicity in the specific
50 instance. As the accuracy of country of birth as a proxy measure varies by ethnic
51 group¹⁵, in studies that include a number of different ethnic groups a judgement of
52 risk of bias will be made for each ethnic group included in the study and provided as
53 a supplementary file, but only a summary judgement for the study overall will be
54 displayed in the main risk of bias table. The summary judgement will be based on
55 the average risk of bias for exposure ascertainment across all included ethnic
56 groups.
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3 We will add an additional domain of other bias to incorporate the problem of
4 numerator/denominator mismatch that can occur in unlinked registry-based studies.
5 The likelihood of this bias being present will be judged according to publications
6 reporting the likelihood of this bias in UK data for specific ethnic groups in addition to
7 the information provided in the included studies. For studies using data linkage,
8 reported linkage rates will be used as part of the judgement of numerator-
9 denominator bias. Similar to exposure ascertainment, numerator-denominator bias
10 may differ between ethnic groups, and when this is likely a risk of bias judgement will
11 be made for each ethnic group separately, but only a summary judgement for the
12 study overall will be displayed in the main table.
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17 **Quality of evidence for individual ethnic groups**

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19 We will examine the quality of the body of evidence for mortality differences for each
20 ethnic group using GRADE criteria¹⁶. This will include consideration of risk of bias
21 assessment (with consideration given to the specific risk of bias assessment for
22 individual ethnic groups in terms of exposure ascertainment, linkage rates etc),
23 inconsistency of results, indirectness of evidence, imprecision and publication bias.
24
25
26

27 **Data synthesis**

28
29 Data synthesis will be carried out by author SKS using a random effects model¹⁷.
30 Analyses will be conducted in STATA version 16.0 (StataCorp, College Station, TX).
31 We will only conduct quantitative synthesis if we locate at least two studies for a
32 particular ethnic group and if there is sufficient homogeneity to enable meaningful
33 synthesis as detailed below in the section on subgroup analysis and investigation of
34 heterogeneity. In the absence of a quantitative synthesis we will provide a narrative
35 synthesis of results by ethnic group. Quantitative synthesis of age adjusted results
36 will be stratified by sex and ethnic group. We will conduct additional quantitative
37 synthesis of results adjusted for age and SES also stratified by sex and ethnic group
38 if available data permits. If data extracted are adjusted for rather than stratified by
39 sex, we will summarise this additional data narratively and provide the results in the
40 appendices. If extracted effect measures are adjusted for other potential
41 confounders in addition to age, sex and SES, such as health behaviours and
42 comorbidities, we will summarise this information narratively and provide the data in
43 the appendices.
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50 Given the likely diversity in measures of effects used between unlinked registry
51 studies and cohort studies we will treat standardised mortality ratios, hazard ratios
52 and relative risks as equivalent measures of effect. As event rates are likely to be
53 low in population-based samples including in the non-exposed group, the hazard
54 ratio and relative risk should be equivalent¹⁸. In addition, as the proportion of most
55 ethnic minority populations included in the analysis will range between 0.5-2.5%, the
56 standardised mortality ratio is less likely to be a biased representation of the relative
57 risk as the exposure rate (ethnicity) is low¹⁹. However, given that the standardised
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3 mortality ratio can be biased when both age-specific mortality ratios and population
4 age distribution differs between ethnic groups²⁰, we will include consideration of
5 difference in effect measures in our assessment of heterogeneity as discussed
6 below. We will screen for publication bias using a funnel plot and Begg's test²¹ if at
7 least 10 studies are located for a particular quantitative synthesis. We will also
8 investigate publication bias by sub-group analysis comparing results of published
9 and unpublished data if sufficient data are available.
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13 Where data sources for a single ethnic group include disparate time periods, we will
14 arrange studies by date and then conduct a random-effects cumulative meta-
15 analysis²² to examine how comparative mortality estimates evolve over time. If data
16 is available on both country of birth and self-reported ethnicity from included studies,
17 we will conduct subgroup analyses within ethnic groups by country of birth (UK- vs
18 overseas-born). The need for this subgroup analysis is based on the need to account
19 for the healthy migrant effect as a potential underlying cause of observed differences
20 in mortality rates and the importance of understanding if there are differences in
21 mortality between overseas-born and UK-born ethnic minority group members. We
22 also plan subgroup analyses based on different comparison populations (e.g. White
23 British, White Scottish, White Irish). This is due to frequently poorer observed health
24 in White Scottish and White Irish populations compared to White British populations⁴.
25 In addition, there is some evidence that the health of non-White minority groups can
26 differ between countries in the UK. If sufficient high-quality cohort studies are
27 located, we will also conduct sensitivity analyses restricted to these high-quality
28 studies with results from cross-sectional studies and unlinked registry studies
29 removed. If high heterogeneity is observed, we will investigate whether this is
30 reduced by conducting the prespecified subgroup and sensitivity analyses listed
31 below.
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39 **Investigation of heterogeneity**

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41 We will assess for the presence of heterogeneity using Cochran's Q and the I²
42 Statistic²³. If we observe an I² value of 50% or more, we will explore possible
43 explanations for the observed heterogeneity in subgroup and sensitivity analyses as
44 detailed below. If sufficient studies are available, we will consider the use of meta-
45 regression in our exploration of causes of heterogeneity. The first two subgroup
46 analyses listed below will be conducted regardless of the presence or absence of
47 statistical heterogeneity.
48
49
50

51 **Subgroup analyses**

- 52 1. UK-born versus overseas-born within each ethnic group to examine the
53 contribution of early life environment to observed differences in mortality by
54 ethnicity.
- 55 2. Published versus unpublished results within each ethnic group to examine the
56 presence of publication bias.
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Subgroup analyses to explore heterogeneity

1. Method of ethnicity ascertainment between studies – country of birth vs self-reported ethnicity vs other methods.
2. Definition/included groups in one major ethnic group – e.g. South Asian vs subgroups of Indian, Pakistani, Bangladeshi.
3. Comparison population/geographic location – e.g. White majority population in England and Wales vs White Scottish population in Scotland.

Sensitivity analyses

1. Study design – non-cohort studies removed.
2. Risk of bias – within cohort studies only, studies with high risk of bias will be removed.
3. Measure of effect – hazard ratio vs relative risk or standardised mortality ratio.

If any of the above are identified as a plausible explanation of the observed heterogeneity, we will conduct a quantitative synthesis at the subgroup level if sufficient studies are available. If insufficient studies are available, we will summarise the results of studies narratively.

Ethics and dissemination

To our knowledge, the proposed systematic review will be the first to systematically collect and synthesise evidence on mortality differences between the major ethnic groups in the UK. The results of the review will provide important evidence about health inequalities and provide important guidance for policies promoting health equity. It is also likely that the review will identify important gaps in the knowledge base such as a lack of research in particular ethnic groups or insufficient evidence in terms of differences in mortality between UK-born and overseas-born members of particular ethnic minority groups.

On completion of the review, we will implement a robust knowledge translation strategy that will include publication in peer-reviewed journals with selection of an open access format where possible, presentation of results at relevant conferences, and production of plain language summaries for dissemination of results to members of the public.

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Authors' contributions

RB and FFS conceived the idea for the study. FFS, NN, SKS, EM and RB planned and designed the study protocol in terms of ethnic groups to be included, literature search strategy, risk of bias assessment and data synthesis. FFS wrote the first draft with all authors contributing critical insights and comments of specific elements (NN search strategy and data management, EM risk of bias assessment, SKS statistical analysis and data synthesis, and RB categorisation of ethnicity and need for comparison between UK-born and foreign-born populations). All authors have approved and contributed to the final version of the protocol.

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Competing interests

None of the authors declare any competing interests

Word count 3507

Supplementary files

Appendix 1: PRISMA-P checklist

Appendix 2: Example search strategy in Ovid MEDLINE

Appendix 3: Newcastle-Ottawa scale

PRISMA- P 2015 Checklist

This checklist has been adapted for use with protocol submissions to *Systematic Reviews* from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 4:1

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input type="checkbox"/>	n/a
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	<input checked="" type="checkbox"/>	<input type="checkbox"/>	2 (awaiting confirmation of registration from Prospero, submitted 06/08/2019)
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	14
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input checked="" type="checkbox"/>	<input type="checkbox"/>	5
Support					
Sources	5a	Indicate sources of financial or other support for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	14
Sponsor	5b	Provide name for the review funder and/or sponsor	<input checked="" type="checkbox"/>	<input type="checkbox"/>	14
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input checked="" type="checkbox"/>	<input type="checkbox"/>	14
INTRODUCTION					

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
Rationale	6	Describe the rationale for the review in the context of what is already known	<input checked="" type="checkbox"/>	<input type="checkbox"/>	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	4
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	5-7
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	<input checked="" type="checkbox"/>	<input type="checkbox"/>	7,8
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Supplementary Appendix 2
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8, 9
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8,9
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8, 9
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8, 9
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	<input checked="" type="checkbox"/>	<input type="checkbox"/>	9-11
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	<input checked="" type="checkbox"/>	<input type="checkbox"/>	10-12

Section/topic	#	Checklist item	Information reported		Page number(s)
			Yes	No	
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	10-12
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	11,12
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	<input checked="" type="checkbox"/>	<input type="checkbox"/>	11,12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	11,12
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	10

Appendix 2

Medline (Ovid SP) search

#	Search Terms
1	exp United Kingdom/
2	england*.mp.
3	scotland*.mp.
4	northern ireland.mp.
5	wales.mp.
6	united kingdom.mp.
7	britain.mp.
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	exp Ethnic Groups/
10	exp Minority Groups/
11	exp "Transients and Migrants"/
12	exp "Emigrants and Immigrants"/
13	polish.mp.
14	indian.mp.
15	pakistan*.mp.

16	bangladesh*.mp.
17	chinese.mp.
18	african.mp.
19	caribbean.mp.
20	black.mp.
21	mixed.mp.
22	ethnic*.mp.
23	9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24	exp Mortality/
25	exp Death/
26	mortal*.mp.
27	24 or 25 or 26
28	8 and 23 and 27

Appendix 3

Newcastle-Ottawa quality assessment scale with modifications and assessment criteria described

Question	Risk of bias assessment	Criteria for risk of bias assessment
Selection		
1. Representativeness of the exposed sample	Low	Representative of members of the respective ethnic minority group (census-based whole population sample or cross-sectional/cohort study with high participation rates)
	High	Selected group such as nurses, volunteers
	Unclear	No description of derivation of exposed sample
2. Selection of non-exposed sample	Low	Drawn from the same community as the exposed sample/similar participation rates as the exposed sample
	High	Drawn from a different source to the exposed sample
	Unclear	No description of derivation of exposed sample
3. Ascertainment of exposure	Low	Self-reported ethnicity. Proxy measures of ethnicity (country of birth, country of birth of parents, ancestry) if evidence they are accurate measures of ethnicity
	High	Proxy measures of ethnicity that are not accurate measures of self-reported ethnicity
	Unclear	Method of exposure ascertainment not described OR proxy measure used and no data available on accuracy as a measure of self-reported ethnicity
4. Demonstration that outcome of interest was no present at start of study*	Low	Outcome not present at start of study
	High	Outcome present at start of study
	Unclear	Unable to determine if outcome present at start of study
Comparability		
1. Comparability of cohorts on the basis of the design or analysis	Low	Effect measures are adjusted/stratified by age and sex
	High	Effect measures are not adjusted/stratified by age and sex
	Unclear	Unclear if effect measures have been adjusted for age/sex
Outcome		
1. Assessment of outcome	Low	Independent blind assessment of outcome or record linkage
	High	Self-report
	Unclear	Method of outcome assessment not described

2. Was follow-up long enough for outcomes to occur*	Low	At least 24 months of follow-up or shorter period with high event rates (older population)
	High	Less than 24 months of follow-up and low event rates
	Unclear	Length of follow up not reported
3. Adequacy of follow up*	Low	No or small loss to follow up, losses even between comparison groups
	High	Large loss to follow up that has potential to change estimate of effect (determined by worst-case best-case analysis) OR losses uneven between comparison groups
	Unclear	Losses not reported
Other bias		
1. Numerator-denominator bias/linkage rates	Low	Low proportion of migrants in ethnic group <20% OR evidence that missed overseas deaths are low OR high rates of data linkage that are equal between comparison groups
	High	High proportion of migrants in ethnic group AND evidence that likelihood of missed overseas deaths is high and likely to change reported estimates, OR high rates of unlinked participants that differs by ethnic group
	Unclear	No information on proportion of migrants in ethnic group, likelihood of missed overseas deaths, or rates of data linkage

*Not assessed in cross-sectional studies