

BMJ Open Maternal socioeconomic status and neonatal mortality in OECD countries: a systematic review and meta-analysis protocol

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ABSTRACT

Introduction Socioeconomic inequalities in neonatal mortality are observed globally but gaps remain in the evidence from current reviews, specifically: a wider range of socioeconomic indicators at the individual, household and area level than previous reviews, and alternative time frames to define neonatal mortality. Thus, a comprehensive updated review of the literature is required, focusing on multiple measures of socioeconomic status and alternative time frames, to assess the relationship between maternal socioeconomic status and neonatal mortality in high-income countries.

Methods and analysis Three different search approaches will be used: electronic searching of three databases, grey literature searching and reference list checking. First, the three databases Medline, Scopus and Web of Science will be searched using relevant synonyms and adapted terms from medical subject heading terms (MeSH) in Medline for maternal socioeconomic status and neonatal mortality identified from previous systematic reviews on inequalities in adverse pregnancy outcomes. Second, grey literature will be searched by entering the relevant terms into Google. Title, abstract and full text screening will be conducted by the review team against the inclusion and exclusion criteria, with at least 10% checked by a second reviewer to assess for any bias and errors. We will also conduct the kappa statistic for inter-rater reliability. Third, the reference lists of included studies will be reviewed for any additional studies that meet the criteria. Data will be extracted using a data extraction form and extracted studies will be assessed using the Liverpool Quality Assessment Tool. A narrative synthesis will be conducted and, where appropriate, meta-analysis will be performed. If the data allow, subgroup analysis by neonatal care population and specific gestational ages will be performed.

Ethics and dissemination Ethical approval is not required as all studies in this systematic review will be publicly available. The findings of this review will be presented at conferences and disseminated in peer-reviewed publications.

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STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This systematic review will consolidate existing literature across wider definitions of maternal socioeconomic status and alternative time frames of neonatal mortality.
- ⇒ We will use rigorous methods, reported in line with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols checklist.
- ⇒ Including all Organisation for Economic Co-operation and Development countries will allow for a larger number of studies to be included should a meta-analysis be conducted.
- ⇒ Advances in neonatal care are likely to have had an impact on neonatal mortality and morbidity; therefore, restricting data to 2000 onwards ensures the review is relevant to current clinical practices and populations.
- ⇒ As alternative time frames of neonatal mortality will be included, some populations, such as neonatal care populations, might be subject to selection bias as they might not be representative of the general population.

INTRODUCTION

Socioeconomic inequalities in neonatal mortality are observed globally. A systematic review of global literature published in 2021 (with almost half of the data included from high-income countries) identified an association between high parental education and low neonatal mortality across multiple countries. Balaj *et al*¹ showed a 21.3% reduction in the risk of neonatal mortality when mothers have 16 years of completed education compared with mothers with 0 years. A recent UK systematic review by Thomson *et al*² also found there were significantly increased odds of neonatal mortality in babies born to women from lower levels of occupation/social class compared with the highest level in the UK and Ireland (OR 1.39, 95% confidence interval [CI] 1.22

to 1.57).² In an earlier systematic review within the UK by Weightman *et al*,³ babies born to women living in the most deprived quintile had 1.61 (95% CI 1.08 to 2.39) times the odds of neonatal mortality compared with women living in areas of the most advantaged quintile. The recent Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK (MBRRACE-UK) report revealed a two-fold higher neonatal mortality rate (NMR) in the most deprived areas compared with the least deprived areas in the UK (2.50 vs 1.03 per 1000 live births).⁴ However, there are several gaps in the evidence base, which include the lack of synthesis of studies across different measures of maternal socioeconomic status (SES), limitations of restricting neonatal mortality to one time frame, and a lack of investigation of the relationship between maternal SES and neonatal mortality according to preterm or neonatal unit populations.

The relationship between maternal SES and neonatal mortality may vary based on the measure of SES used, but published reviews have not synthesised the latest evidence across different indicators of maternal SES. Balaj *et al*¹ captured global data on inequalities in neonatal mortality with a focus on parental education. The UK-focused review by Thomson *et al*² included other individual measures such as income and occupation but excluded area-level measures of deprivation, which are commonly used as proxies for family SES.⁵ Weightman *et al*³ included both individual and area-based measures but only included studies up to 2011. This suggests current evidence gaps exist with the need to synthesise contemporary evidence across a broad range of maternal socioeconomic indicators.

To date, most studies have only examined neonatal mortality within 28 days of birth, excluding deaths occurring later outside of this time frame.² This potentially excludes large contributors to mortality in preterm babies such as necrotising enterocolitis; therefore, alternative time frames of interest warrant consideration, such as death before 36 and 40 weeks' post-menstrual age (PMA) or death occurring before discharge from the neonatal unit.⁶ PMA is often used for preterm infants when they are still receiving care before discharge or death and is typically translated to corrected gestational age on discharge.⁷ Broadening the definition of neonatal mortality would be beneficial to include studies that employ alternative time frames of interest to capture important causes of mortality that occur while a baby is still preterm and in the neonatal unit.

The relationship between maternal SES and neonatal mortality may vary according to gestational age; however, this has not been examined in previous systematic reviews. For example, in a national birth cohort study in England and Wales, there was no variation between deprivation fifths for any case of death or immaturity-related death in babies born before 32 weeks.⁸ By contrast, a recent US study found that neighbourhood deprivation was a risk factor for neonatal intensive care unit mortality in extremely preterm

infants and suggested more research to understand the mechanisms underlying this association.⁹ Extracting and synthesising global data on the association between deprivation and neonatal mortality, while taking into account gestational age, would thus expand the currently limited body of knowledge.

Babies admitted to neonatal units due to extreme prematurity, severe illness or major congenital anomalies are at the highest risk of mortality and contribute significantly to the NMR.¹⁰ Current research into the relationship between maternal SES and neonatal mortality in specific neonatal care populations has been limited, with no synthesis of the evidence on inequalities in this population in a systematic review. As babies receiving neonatal care are more susceptible to adverse outcomes including mortality, synthesising the current evidence for this specific population and examining mortality up to neonatal discharge as described above would be of interest to policymakers.

Lastly, in each of the reviews by Thomson *et al*² and Weightman *et al*,³ only three studies were pooled for meta-analyses, both indicating high heterogeneity. To increase the likelihood of identifying more studies for such analyses, the geographical scope should be broadened. Countries within the Organisation for Economic Co-operation and Development (OECD) offer a degree of comparability in key health outcomes and typically provide universal or near-universal coverage of core health services.¹¹ While widening the search globally may increase the number of eligible studies included, low-income and middle-income countries may differ drastically in terms of healthcare systems and population characteristics. Consequently, inclusion of only OECD countries could increase the number of studies included while allowing for more feasible data synthesis and meta-analysis.

As a result of these limitations, a comprehensive updated review of the literature is required, focusing on multiple measures of SES and alternative time frames on neonatal mortality across high-income countries. Therefore, the main aim of this systematic review is to assess the relationship between maternal SES and neonatal mortality in high-income countries. A secondary aim is to explore this relationship in populations admitted to neonatal intensive care units. Where data allow, we will also assess this relationship stratified by gestational age and/or time frame of mortality outcome. To achieve this, we will include a broader range of maternal socioeconomic indicators (individual, household and area-level) and expand the definition of neonatal mortality to capture deaths in neonatal units. Collecting data on gestational age may further clarify how prematurity moderates socioeconomic inequalities in neonatal mortality. Finally, by focusing on OECD countries, we aim to enhance comparability of healthcare systems and increase the pool of data available for meta-analysis.

Table 1 PECOS framework

Term	Study term
Population	Women and their babies, born in high-income countries
Exposure	Maternal socioeconomic status, measured at the individual, household or area level
Comparator	There will be no restriction on comparator as studies may use different classifications
Outcome	Neonatal mortality
Study design	Cross-sectional Case-control Retrospective cohort Prospective cohort Ecological

METHODS AND ANALYSIS

This protocol has been developed in collaboration with experts in neonatal medicine, health inequalities and systematic reviews. This protocol was reported in line with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols checklist.¹²

This study started in April 2023 when the first searches occurred, but, due to other projects, this was paused and the searches were updated in September 2025. The initial results will be presented in a PhD thesis in February 2026, but it is anticipated that this study will not be completed for publication until July 2026.

Inclusion and exclusion criteria

The main question of this review is: In high-income countries, what is the impact of low vs high maternal SES on neonatal mortality?

The Population, Exposure, Comparator, Outcome and Study design framework (table 1)¹³ will help determine the inclusion and exclusion criteria.

This study will include observational studies (cross-sectional, case-control, retrospective and prospective cohort, ecological) reporting quantitative results and analysis of data on the relationship between SES and neonatal mortality (difference in rates, relative risk, OR) between babies born to women of a low SES and babies born to women of a high SES in OECD countries. This will include univariable and/or multivariable analyses where the estimate of interest is the total effect of maternal SES associated with the risk of neonatal mortality, possibly adjusted for confounders.

A high-income country is defined as being a member of the OECD. OECD membership reflects not only economic status but also broadly comparable health system structures and policy environments. This will include studies reporting whole population data and hospital settings. As we are also interested in this relationship in a neonatal unit setting and stratified by gestational age, we will also include studies reporting babies admitted for neonatal care and studies reporting preterm babies.

Included studies are those published from 1 January 2000 onwards, including data from 1 January 2000 onwards, and published in the English language. Studies that are published from 1 January 2000 and include data before 2000 and from 2000 onwards will be reviewed on a case-by-case basis, assessing the proportion of data included from 1 January 2000 onwards. Including studies and data only from 2000 onwards was due to advances in neonatal care, which have had an impact on neonatal mortality and morbidity. As a result, this systematic review aims to capture data on current populations and practices.

Exclusions apply to studies published from 1 January 2000 onwards that present only data from before 1 January 2000 or studies for which the country was not yet part of the OECD at the time of the study (online supplemental file p3). Any literature reviews or case studies will be excluded. The full inclusion and exclusion criteria (box 1) will be used for the first stage of screening titles and abstracts and the second stage of full-text screening.

Exposure

The exposure of interest is maternal SES, measured at the individual, household or area level. While we acknowledge that SES is a complex construct, often derived from multiple demographic variables, we aim to capture any measure of SES. Examples of this include occupation, education, income, household income and area-level measures of deprivation linked to individual maternal postcode such as index of multiple deprivation and social deprivation index.

Outcome

The primary outcome of interest is neonatal mortality. Accepted definitions include death within 28 days of birth, death before 36 weeks' PMA, death before 40 weeks' PMA, or death of baby before discharge from the neonatal unit.

Search strategy

The search strategy will be developed with the review team and a Systematic Review Information Specialist (MMaden). Three different systematic approaches will be used to identify as much literature as possible. The first approach involves electronic database searching. Electronic searching of three databases will be performed: Medline, Scopus, Web of Science. MeSH terms in Medline will be used and then these terms will be converted into equivalent free-text terms for Scopus and Web of Science. Databases most relevant to the research question and subject area in Web of Science will be selected as they are likely to yield the highest number of relevant papers.

Search terms will be identified from initial scoping searches and comprised outcomes specific to neonatal mortality and socioeconomic terms. Although these terms will not be exhaustive, they will be selected to represent current clinical and policy discourse.

Relevant synonyms for maternal SES neonatal mortality will be identified from previous systematic reviews focused

Box 1 Inclusion and exclusion criteria

Inclusion criteria

1. Studies reporting neonatal mortality using population-based studies or routine data on neonates (crude and/or adjusted for confounders). Definitions may include death within 28 days of birth, death before 36 weeks' post-menstrual age, death before 40 weeks' post-menstrual age (for preterm babies) or death of baby before discharge from the neonatal unit.
2. Studies measuring maternal socioeconomic status (SES) at the individual, household or area level. Examples of this include occupation, education, income, household income, deprivation of area of residence (score or level) or insurance status. This may include using paternal occupation or income as a proxy for the household.
3. Comparison of the first two inclusion criteria, that is, comparison in the maternal SES between those babies who survived and those babies who died within 28 days of being born (or an equivalent measure of neonatal mortality).
4. Population within studies is women and their babies born in Organisation for Economic Co-operation and Development (OECD) countries at the time of the study.
5. Studies reporting on human subjects.
6. Observational studies (cross-sectional, case-control, cohort prospective and retrospective, ecological) reporting quantitative results.
7. Studies published from January 2000 and including data from 1 January 2000 onwards.
8. Studies published in English Language.

Exclusion criteria

1. Unrepresentative population sample or study conducted in a subgroup of the population, for example, only in specific ethnic groups or in twin population.
2. Studies where maternal SES is categorised as whole country-level income.
3. Studies where maternal SES is not defined as a separate exposure, for example, only adjusted for maternal SES.
4. Studies that do not report any data on neonatal mortality (stillbirth not to be included).
5. Studies conducted outside of an OECD country or were not at OECD country at the time of the study or combined multiple countries together including those outside of an OECD country.
6. News articles, editorials, case studies, systematic reviews.
7. No full text available.

on inequalities in adverse pregnancy outcomes. Terms will be combined using Boolean operators and proximity operators will also be applied where necessary. The exact terms will be used for Scopus and Web of Science; however, due to differences in function and design, some adaptations may be necessary, such as proximity operators changes. An example of the terms that will be used in Medline can be found in the online supplemental files p1 and 2.

In addition, the grey literature will be searched by entering the terms “neonatal death” “neonatal mortality”, “socioeconomic”, “income”, “deprivation” and “social position” in the Google/Google Scholar search engine. As no Boolean operators are available in Google Scholar, the grey literature searching will be split into six searches to account for SES and neonatal mortality synonyms. This

was agreed through consultation with a Systematic Review Information Specialist (MMaden). To prevent excessive time being spent on reviewing the grey literature searches, while still ensuring key papers could be captured, the first 50 results of each search will be assessed after combining search results in Endnote.

Finally, for backward citation searching, the reference lists of studies found through screening will be checked for any studies meeting the inclusion criteria that were not previously found through electronic database searching.

Data management

The studies from the database searches will be combined and duplicates removed in EndNote V.X9 (V.3.3). After auto-deduplication, the remaining studies will be exported to Rayyan, where manual removal of remaining duplicates will be conducted before screening occurs. This same process will also occur for the grey literature.

All identified studies from the database searches and grey literature searches will be stored in Rayyan. Rayyan will be used for all abstract and full-text screening among the reviewers.

Abstract screening

Blinding will be turned on in Rayyan throughout abstract and full-text screening to reduce bias between reviewers. Abstract and title screening will be conducted by the main reviewer (SS) and a random sample (of at least 10%) will be screened by a secondary reviewer (NG), with cross-checking for any discrepancies. Any discrepancies will be re-examined until there is agreement. Full double screening may not be feasible due to the expected large number of studies; therefore, the kappa statistic will be calculated to assess for inter-rater reliability. To calculate the kappa statistic, in Excel a 2×2 contingency table of screening outcomes between the main and secondary reviewer for the sample of studies will be developed. The observed agreement and expected agreement will be calculated, for which Cohen's kappa will then be calculated.¹⁴ A detailed description of this method can be found in the online supplemental file p4.

The inclusion and exclusion criteria will be piloted on 20 studies between the main and secondary reviewer (SS and NG). Due to the large number of synonyms for both exposure and outcome, there will be a vast number of studies initially included. Amendment of the search strategy to reduce the number of searches may prove difficult as key papers previously identified may be missed. While this review is only aimed at investigating populations from an OECD country, no restrictions on country will be made for the search strategy. The lead author (SS) will screen all abstracts and titles based on country first and then 10% of that sample will be screened by the secondary reviewer (NG) on abstract and title. This is purely to reduce the load as a large volume of studies is expected for the first stage of screening.

Full text screening

Full texts of all studies that were included from abstract and title screening will be sourced and uploaded into Rayyan. A team of reviewers will conduct the full-text screening (SS, NG, GM, SDT, MMadden). For each reviewer, a random sample of 10% will be screened by a secondary reviewer (either SS or NG). Any discrepancies will be re-examined until there is agreement. Again, the kappa statistic will be calculated.

Risk of bias assessment

Risk of bias and critical appraisal of studies included after full-text screening will be conducted by the lead author (SS), using an appropriate tool such as the Liverpool Quality Assessment Tool (LQAT). A pilot of the tool on two or three studies will first be conducted by the lead author (SS) and secondary reviewer (NG) to ensure that the quality assessment tool is appropriate for the studies included. The LQAT was adapted from the Newcastle-Ottawa scale to accommodate multiple study designs¹⁵ and has been used in large systematic reviews and meta-analyses and has been appraised against other quality assessment tools.^{15 16} Characteristics of each study that will be assessed include ascertainment of exposure/outcome of interest and comparability of groups.¹⁷ A secondary reviewer (NG) will assess a proportion of the studies to check for discrepancies. Any discrepancies will be discussed and resolved by an independent reviewer (OBE).

If the data allow, forest plots may be created to display risk of bias judgements of included studies in the meta-analysis.¹⁸ Sensitivity analysis may also be conducted, which will involve including/excluding studies based on risk of bias results into the meta-analysis to test the robustness of the results.¹⁹ Funnel plots of included studies may also be used to describe publication bias visually.²⁰

Data extraction, analysis and synthesis

The review team will use a prepiloted data extraction file using Microsoft Excel to extract relevant data from each included study. Data will be organised for ease of comparison and tabulation. We will extract data on study characteristics: aim, study design, country (or countries), population, sample size, year of publication, year(s) of data collection/study observation period, gestational ages included, setting (neonatal intensive care unit/neonatal unit/or general population), maternal SES indicator(s), measure of neonatal mortality, SES indicator level, type of SES measure, statistical analyses, controlled covariates. A separate tab will collect results to account for studies that may have more than one row of results, for example where additional measures of SES were used. Information collected for results includes SES definition, outcome measure, definition of outcome measure, whether outcome was adjusted or unadjusted, potential overadjustment, key results and direction of relationship. A direct acyclic graph will be used to support extraction, particularly with decisions around adjusted effect measures to

avoid potential overadjustment,²¹ which can be found in the online supplemental file p5).

The data extraction file will be piloted by the review team (SS, NG, GM, SDT, MMadden) to ensure similar data items are being extracted and to achieve coherence in understanding key definitions. Any discrepancies will be resolved by an independent reviewer (OBE). Any missing or supplementary data not available may be requested from study authors if appropriate. At least 10% of the extracted data will be checked for accuracy by at least one other reviewer. The variables in the pilot data extraction form can be found in the online supplemental file p6.

Results will be tabulated, showing key study characteristics, such as author, year, population, country, SES and neonatal mortality definitions, and main findings. Grading of extracted studies from the LQAT will also be presented. Data synthesis will include narrative synthesis describing any patterns or trends that emerged from the included studies. A harvest plot may also be conducted to describe visually the different relationships observed between maternal SES and neonatal mortality. It is anticipated, due to the differences in country populations and potential differing definitions of exposure and outcome measures, that there will be heterogeneity. As a result, meta-analysis will be dictated by the data quality by assessing variance in effect measures, bias in the evidence, as well as clinical and methodological diversity.²² If a meta-analysis is not conducted, then data synthesis methods and reporting will be aligned with the synthesis without meta-analysis reporting guidelines (SWiM).²³

To identify suitable data to be combined for a meta-analysis, key extracted data that will be considered and compared between studies include the population (including country and setting), measure of SES, measure of neonatal mortality, gestational age, effect measures and level of analysis. Where multiple studies reporting relative effect measures such as ORs and HRs are available, and they are reporting comparable exposures and outcomes, such results might be pooled. However, subgroups will be reported by type of effect measure rather than re-calculating estimates. Effect measures may differ between studies due to heterogeneity in study design, and the meta-analysis will be pooling a more consistent summary statistic.²⁴ Results from possible eligible studies for meta-analysis will be plotted on forest plots to assess heterogeneity. This will include reviewing any overlapping of CIs and performing a χ^2 test, where a p value of less than 0.10 may indicate statistical significance as well as the interpretation of I^2 , with results above 30% indicating heterogeneity.¹⁹ Any meta-analysis will be conducted in R studio.

As the data extraction form will collect any information on gestational age and settings in the included studies, if the data allow, we will assess any effect modification of the relationship between maternal SES and neonatal mortality by gestational age as well as the relationship in neonatal care settings specifically.

DISCUSSION AND IMPLICATIONS OF THE REVIEW

Our systematic review aims to provide a comprehensive overview of the relationship between maternal SES and neonatal mortality, accounting for a large number of SES measures and wider definition of neonatal mortality. Including recent studies and widening the search terms to include OECD countries will add to the body of knowledge generated by the previous systematic reviews. It will also be the first review to our knowledge that explores this relationship in both preterm and neonatal unit populations, both of which are large risk factors for adverse neonatal outcomes. Using the LQAT and SWiM for assessing the strength of the body evidence overcomes challenges of some of the issues with other quality assessment tools such as the Risk Of Bias In Non-randomized Studies - of Exposures (ROBINS-E) and Newcastle Ottawa Scale^{25 26} and also ensures systematic processes of data synthesis can occur even if meta-analysis is not possible.²³

Compared with 27 other European Union countries, the UK had stalled in progress between 1990 and 2015 in terms of neonatal mortality.²⁷ Despite previous Government targets aimed at halving the NMR by 2025, a 2023 policy progress report highlighted that neonatal death rates are off-track to meet this target.²⁸ This, alongside recent reports highlighting a widening of the deprivation gap for adverse perinatal outcomes,²⁹ highlights the importance of understanding the relationship between maternal SES and neonatal mortality to implement policies targeted at reducing that mortality, overall and differentially.

Patient and public involvement

Neither the public nor patients were involved in the development of this protocol.

ETHICS AND DISSEMINATION

Ethical approval is not required as all studies in this systematic review will be publicly available. This systematic review will be submitted for publication, and it is anticipated that the findings of this review will be presented at conferences. We will also aim to seek input from charities and organisations that work closely with bereaved families affected by neonatal loss to ensure that the dissemination of this review reflects the priorities of these families.

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Contributors All authors were involved in the conceptualisation of this project. SS drafted the protocol. DT-R, DKS and OBE reviewed the protocol and provided guidance. All authors reviewed and approved the final protocol. SS is the guarantor as the corresponding and lead author.

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