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Socioeconomic deprivation as a risk factor for stillbirth: a case-control study

Thesis presented by

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List of Acronyms and Abbreviations

aOR – Adjusted Odds Ratio

aRR – Adjusted Rate Ratio

BIMD – Bavarian Index of Multiple Deprivation

BMI – Body Mass Index

CSO – Central Statistics Office, Ireland

CUMH – Cork University Maternity Hospital

DoE – Department of Environment Index (UK)

DPO – Data Protection Officer

ENAP – Every Newborn Action Plan

ENND – Early Neonatal Death

G – Grams

GDPR – General Data Protection Regulation

HSE – Health Service Executive

ICS – Social Deficiency Index (Brazil)

IMD – Index of Multiple Deprivation

iPMS – Integrated Patient Management System

IUD – Intrauterine Death

JBI – Joanna Briggs Institute

LFD – Late Fetal Death

LIGG – Local Information Governance Group

LNND – Late Neonatal Death

MDI – Multiple Deprivation Index (Chile)

MN-CMS – Maternal and Newborn Clinical Management System

MRN – Medical Record Number

Nbr – Number

NND – Neonatal Death

NPEC – National Perinatal Epidemiology Centre

NPRS – National Perinatal Reporting System

NZDep – New Zealand Deprivation Index

ONS – Office National Statistics

OR – Odds Ratio

PCC – Population, Concept, Context framework

PMNCA – Perinatal Mortality National Clinical Audit

PMR – Perinatal Mortality Rate

PRISMA-SCr – Preferred Reporting Items for Systematic Reviews and Meta-Analyses, Scoping Review Extension

ROI – Republic of Ireland

RR – Rate Ratio

SA – Small area

SB – Stillbirth

SDGs – Sustainable Development Goals

SDH – Social Determinant's of Health

SDI – Social Deprivation Index (Brazil)

SESI – Socioeconomic Status Indicator (Argentina)

SPSS – Statistical Package for the Social Sciences

TDS – Townsend deprivation score

UK – United Kingdom

UNIGME – United Nations Inter-agency Group for Child Mortality Estimation

WHO – World Health Organisation

WIMD – Welsh Index of Multiple Deprivation

Declaration

This is to certify that the work I am submitting is my own and has not been submitted for another degree, either at University College Cork or elsewhere. All external references and sources are clearly acknowledged and identified within the contents. I have read and understood the regulations of University College Cork concerning plagiarism and intellectual property.

Signed:  Date: 20/03/2024

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Abstract

Introduction:

Stillbirth (SB) is a devastating outcome for families. Identifying and addressing risk factors is of crucial importance. Level of deprivation has been linked to adverse perinatal outcomes. This thesis aims to comprehensively examine the relationship between area-level deprivation and the risk of SB by conducting a scoping review of international literature and a case-control study using an Irish based cohort.

Methods:

Guided by the Joanna Briggs Institute methodology and PRISMA-ScR framework, this scoping review focused on studies examining SB in upper-middle and high-income countries using composite geographical indices of deprivation. A systematic search across six scientific databases was performed. The screening process, involving title, abstract, and full text reviews, followed specified inclusion criteria. Data extraction and synthesis were carried out and presented in a narrative summary.

An observational case-control study was conducted, matching cases of SB (n=127) with a control cohort of live births (n=266). A ratio of 2 controls to 1 case was identified. Retrospective data over four years (2018-2021) was collected from a tertiary university maternity unit in the Republic of Ireland. The study employed the Pobal HP Deprivation Index to categorise small areas into levels of deprivation, ranging from affluence to deprivation. Variables, including maternal age, parity, BMI, booking visit gestation were identified as confounding factors. Statistical analysis was conducted using SPSS and included; frequency tables to present the distribution of certain variables, Chi-squared tests to identify associations between deprivation and the confounding factors with risk of SB, T-tests and logistic regression for crude and multivariate analysis on the relevant confounding factors, including odds ratio calculations, to identify any significant differences in the risk of SB across the deprivation levels and categories of the confounding factors.

Results:

A total of 29 studies were included in the scoping review, from 9 countries (the majority UK-based; n=20, followed by the Netherlands; n=2 and Brazil; n=2). A range of deprivation indices were utilised internationally (n=18), the UK's Index of Multiple

Deprivation (IMD) was the most commonly used (n=8), followed by the Townsend and Jarman indices (n=6 and n=3, respectively). Income, employment, education and access to services were some of the most common factors included in the indices. Results show an association between SB rates and areas identified as being more deprived, with 22 of the 29 studies (75.9%) showing positive correlations.
The results of the case-control study demonstrated no statistically significant correlation between level of deprivation and risk of experiencing SB within our sample (p-value 0.288). When readjusted into quintiles of deprivation, a slightly higher representation of SB was noted in the more deprived levels, though not significant. When examined by cause of death, there was a significant association between deprivation and placental causes of death (p-value 0.045). BMI was consistently associated with risk of SB, while booking visit gestation and maternal age also showed associations.

Conclusion:

This comprehensive investigation into the relationship between area-level deprivation and SB risk provides important insights. The complex nature of measuring deprivation and of SB aetiology is demonstrated. The scoping review suggests that countries and regions should consider assessing deprivation when evaluating their SB rates, as this could offer valuable information for care programme development to impact deprived areas. While the case control study demonstrates the need for further national research to understand the relationship between deprivation and adverse perinatal outcome in the Irish context. Ultimately, using the evidence to guide and inform local policy and resource management will aid in tackling the inequalities in healthcare provision, thus encouraging equal and quality maternity care. Tailored initiatives have the potential to enhance healthcare services, clinical practice, and ultimately improve maternal and perinatal outcomes.

Thesis Introduction

The occurrence of stillbirth (SB) is a difficult and distressing event for families. It remains a poignant indicator reflecting not only individual tragedies but also broader systemic challenges within the realm of maternity care and public health, despite advancements in medical science and healthcare infrastructure. Sadly, the UN Inter-agency Group for Child Mortality Estimation (UN IGME) has highlighted that globally, "one stillbirth occurs every 16 seconds".[1] The Lancet SB series highlights the significant psychosocial and economic impact of SB on families, caregivers, communities and society, affecting nations as a whole.[2-4] While a large focus is on the substantial inequality within low-income countries, it's noted that SB rates between high-income countries also varies widely, which suggests that further reduction in rates is possible.[1,5] The literature identified that marginalised populations in all countries demonstrate the highest SB risk.[6,7] Important risk factors that the Lancet SB series identified included advance maternal age (>35 years), infection, non-communicable diseases, and nutrition and lifestyle choices.[5] Aswell as factors such as obesity, smoking and suboptimal antepartum engagement with services being lifestyle factors highly associated the SB in high-income countries.[6] Considering the global health burden, SB research remains largely unsupported.[2] There is currently a global call to action to achieve a reduction in SB rates and equity gaps, through the United Nations' Global Strategy for Women's, Children's and Adolescents' Health 2016–2030[8] and the Every Newborn Action Plan (ENAP), which was endorsed by 194 WHO Member States.[9] The WHO's framework of social determinants of health (SDH) are described as the non-medical conditions that affect health outcomes such as those in which people are born, grow and live.[10] This framework is useful in gaining a better understanding of health disparities. The SDH highlight elements such as income, education, employment, housing and access to services as an important factor in health and equity.[10] These socioeconomic determinants are closely linked with the broader concept of deprivation. The indicators considered when measuring level of deprivation consistently align with the factors within the SDH framework,[11] demonstrating the link between socioeconomic determinants, deprivation and health inequality.

Deprivation is a concept that can be considered as multidimensional. It was originally defined by Townsend in 1987 as "observable and demonstrable disadvantage relative to the local community or the wider society or nation to which an individual, family or group belongs".[12] Socioeconomic deprivation has been long associated with health inequalities, impacting physical and mental health.[13] For example, those from less advantaged areas have been found to have "substantially higher mortality rates".[14] There is also strong evidence demonstrating that level of deprivation is linked to poor perinatal outcomes, such as small for gestational age or intrauterine growth restriction, preterm birth, low birth weight, SB, neonatal death and infant mortality.[15-18] One study in particular found that rates of mortality due to very preterm birth was nearly twice that in the most deprived areas compared with the least.[19] The infants born into areas identified as more deprived have continually shown to be at increased risk of perinatal death.[20] MBRRACE-UK identified an almost a two-fold risk of SB and over 70% excess risk of neonatal death.[20]

As highlighted, the nature of deprivation is complex and multifaceted. It encompasses a range of socioeconomic factors (e.g. income, education, employment, and access to resources). Evidence suggests that to truly understand its impact on health, it must be measured through comprehensive indices that capture these various dimensions. Deprivation indices, which are tools designed to measure and categorise deprivation,[11] have been developed internationally to encompass the multifaceted aspect of deprivation by considering several socioeconomic factors in the construction of the index. Applying the measurement to a geographical area or small defined area can support the examination of socioeconomic disparities and outcomes for a particular locality or population,[21,22] thus facilitating targeted resource allocation to areas in greater need.[12] An established deprivation index available in Ireland is the Pobal HP Deprivation Index for Small Areas (SA).[23] This index is developed using Census data to calculate the level of affluence or disadvantage for small geographical areas in the Republic of Ireland (ROI), comprising of fourteen indicators categorised into Demographic Profile, Social Class Composition and Labour Market Situation.[24] The index is used widely to provide insight into socioeconomic conditions, guiding and informing policy at national level. For example, Ireland's Central Statistics Office (CSO) used this index to identify that those living in the most deprived areas have the lowest

life expectancy.[25] This supports Ireland's Sláintecare Implementation Strategy & Action Plan 2021- 2023 by the Department of Health, which emphasised the importance of targeted investments in deprived regions to foster healthy communities.[26] Stating that enabling "an area-based approach to developing healthy communities, with a particular focus on targeted investment in areas of deprivation" was a pertinent issue in which to allocate budget funds to.[26] There is a strong body of evidence that examines deprivation and its influence on health outcomes using individual measures of deprivation, such as income [27-30], education [31-33] and employment.[34,35] However, focusing on these single indicators might overlook the broader social and environmental factors that contribute to how deprivation impacts health. It is argued that individual indicators of deprivation may only service as proxies for other underlying factors.[11] Deprivation is influenced by a variety of interrelated factors (e.g. community resources, neighbourhood conditions, access to healthcare, among others) and the socioeconomic characteristics of its residents.[36] These factors influence public policies and structural inequities, making it challenging to measure and incorporate each factor individually. Thus, deprivation indices have become more widely adopted by health equity researchers to address the multifactorial impact of deprivation on health outcomes.[11,36] The complex interplay between these variables further highlights the multidimensional nature of deprivation.[12]

Additionally, there are some documented limitations in using income alone as a measure of disadvantage, for example.[37] Income does not account for savings, assets, accumulated debt, or other non-cash benefits which can significantly impact living standards. Nor does it account for individuals on the same income level requiring different levels of need.[37]

Therefore, composite measures that encompass the various socioeconomic factors are arguably more accurate at measuring the level and effects of deprivation on health.[11,38] By incorporating multiple socioeconomic factors, these indices offer a more comprehensive understanding of deprivation's effects on perinatal health, making them a more appropriate choice for assessing risk in this thesis.

While the concept of deprivation is linked with health inequalities, measuring deprivation and its impact on perinatal health outcomes is not currently employed routinely in the Irish maternity care system.[39,40]

This thesis aims to comprehensively examine the relationship between area-level deprivation and the risk of SB by conducting a scoping review of international literature in Chapter 1 and a case-control study using an Irish based cohort for Chapter 2.

The scoping review aims to consolidate and synthesise existing knowledge, examining the global landscape and highlighting prevailing patterns and gaps in research concerning this important issue. This review focuses on the use of composite measures of deprivation to assess SB risk. Drawing on the insights obtained from the international literature, this thesis then focuses the investigation within the Irish population. Examining data from a cohort within a large hospital in the Republic of Ireland (ROI), this study adopts a case-control methodology. Cases were designated as instances of SB and controls as live births to assess the influence of area-level deprivation on SB risk. A validated deprivation index tool will be used to measure the level of deprivation prevalent in different geographic areas, categorised into small areas (SA).

The choice of this methodology, with a specific focus on a hospital-based cohort in Ireland, is deliberate. Ireland, despite its advancements in healthcare, has seen consistent SB rates showing minimal decline over recent years, as reported by the National Perinatal Epidemiology Centre (NPEC).[41] This case-control study seeks to fill the gap in the literature pertaining to the Irish context, providing a nuanced understanding of how socioeconomic deprivation at an area level might contribute to the occurrence of SB in this specific setting.

By employing a multidimensional approach that amalgamates findings from international literature and empirical data from an Irish hospital, this thesis aims not only to enhance the understanding of this issue but also to offer actionable insights for policy formulation and targeted interventions aimed at mitigating the occurrence of SB. The ultimate goal is to contribute meaningfully to the discourse surrounding public health strategies, fostering a more inclusive and equitable environment that supports healthier pregnancies and reduces the incidence of SB in Ireland.

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Chapter 1: Scoping Review

Area-level deprivation as a risk factor for stillbirth in upper-middle and high-income countries: a scoping review

1.1 Introduction

Although perinatal mortality has decreased in recent years in high-income countries, relative reduction in areas of socioeconomic deprivation is not matched, leading to widening inequalities.[1-3] This demonstrates that deprivation can disproportionately affect the health outcomes of certain groups, contributing to unfair health disparities. As discussed in the "Thesis Introduction" section of this manuscript, there is a body of evidence linking single-variable socioeconomic markers of deprivation with perinatal mortality. However, this might not entirely capture the multifaceted nature of deprivation. Aggregate-level indicators, provided by area-based deprivation indices, allow for a more comprehensive understanding of the various factors that contribute to socioeconomic disadvantage.[4] Globally, many countries have developed their own specific area-based deprivation measures, incorporating various socioeconomic factors. This can provide important information about geographical disparities and the associated health outcomes.[5] For example, the UK currently uses the 'Indices of Multiple Deprivation (IMD)' for England, Scotland, Wales, and Northern Ireland. This encompasses 7 domains of deprivation: Income, Employment, Education Skills and Training, Health and Disability, Crime, Barriers to Housing and Services and Living Environment.[6] Similarly, other high-income countries such as the US and Canada use the Area Deprivation Index (ADI)[4] and the Canadian Index of Multiple Deprivation (CIMD)[7] to capture these multifaceted socioeconomic conditions. There is also a 'European Deprivation Index (EDI)' that is, however, not established for use in all European countries.[8] Therefore a standardised approach to the use of deprivation indices across Europe is not currently available. However, one European study found socioeconomic inequalities across perinatal health using different measures of socioeconomic status.[9] While some studies have examined the association between deprivation and risk of SB, as can be seen in systematic reviews and meta-analysis,[10,11] no review has specifically investigated the evidence available between the association

of aggregate level indicators and incidence of SB. Therefore, this scoping review aims to examine and provide a descriptive overview of the international literature available on the relationship between area-level deprivation, based on composite measures specifically, and SB in upper-middle and high-income countries.

1.2 Methods

A scoping review was carried out in order to map the body of evidence on the topic,[12] including identifying the characteristics of area-level deprivation indices and examining their association with risk of SB. This scoping review was conducted in accordance with the defined methodology provided by Joanna Briggs Institute (JBI) guide for scoping reviews,[13] including use of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Scoping Review extension (PRISMA-ScR)(Appendix A and B).[14] The review question for this piece was developed based on the Population Concept Context (PCC) framework recommended by JBI for scoping reviews.[13]

1.2.1 Eligibility criteria

The population focus for this review include studies that examine SB, the definition of which were according to the definition in the country of the study. Studies that did not report on SB alone were not included for review, e.g. where perinatal mortality is reported.

The concept for this review is area-level deprivation and its impact on SB outcomes. Only studies that focus on SB in relation to level of deprivation were reviewed. Only studies that used geographical indices of deprivation encompassing composite measures were included. Literature that looks at single-variable indicators of deprivation were not included for this review.

Specific areas classified in terms of level of deprivation in all upper-middle and high-income countries, according to the classification of the World Bank Index at the time of the year of publication of the study[15], is the context for this review.

For selected reviews (i.e. scoping, systematic or meta-analyses), the included studies in that review were screened but the review itself was excluded. No further restrictions were included regarding study design, year of publication, language or type/status of publication. This ensured all relevant literature was identified in keeping with the scoping review approach.

1.2.2 Search strategy and review selection process

The following databases were searched to identify all relevant studies on the review topic: Pubmed, EMBASE, CINAHL and Medline via EBSCO host, Web of science and

Scopus. Appendix C provides one example of the full electronic search strategy terms used for each of these databases. This search strategy was adapted per database depending on the specific searching rules for each one. The search was carried out between the period of 07/05/2023 to the 02/06/2023. All search results were then uploaded onto Rayyan web application to facilitate screening process, whereby the title of each search result was screened for any clearly inappropriate studies. As demonstrated in the flow diagram below (Figure 1.1), Pubmed, EMBASE and Web of Science followed the same process while for CINAHL and Medline via EBSCO Host and Scopus, duplicates were first removed prior to title screen. Due to volume of results in Scopus database, the Rayyan AI tool was used to refine the search results in line with the process.[16,17] Firstly, duplicates retrieved in this database were removed (n=34) and then 500 studies were title screened. The remaining studies were then rated for relevance with those rating below 2.5 stars excluded, as deemed a reliable threshold.[18] The remaining studies that were rated >2.5 stars (n= 1,632) were manually screened by title.

A total of 4,079 studies were identified as appropriate for the abstract screening stage. Rayyan's duplication detector was utilised again at this point and each possible duplication of studies was reviewed, with duplicate studies being removed (n= 1,956). The studies were divided into two groups and two reviewers then independently completed an abstract screening, identifying those that met the eligibility criteria as previously outlined. Rayyan's computed ratings functionality was utilised again for the abstract screening stage after 300 studies were initially screened manually. Following abstract screening, a full text screening of the studies selected (n=165 divided among the two reviewers) was undertaken. This involved specific evaluation against the eligibility criteria of this scoping review. As a quality control measure, and to ensure consistency and reduction of possible bias, throughout the screening process a random selection of 10% of studies were reviewed by both reviewers. If there was disagreement on the appropriateness of a study for inclusion, these would be discussed by the two reviewers to resolve any conflicting decisions and reach a mutual consensus. Consultation with a third reviewer was sought where necessary.

Once the full text review was completed, 27 studies were identified for inclusion in this review. Reference list searching was undertaken on these 27 studies and a further 2

studies were identified as relevant for inclusion. Where systematic reviews included met the eligibility criteria, the included studies in that review were also screened but the review itself was excluded from the final data extraction table. In total, 29 studies were identified for inclusion for the purpose of this scoping review.

1.2.3 Data extraction and synthesis

Data was extracted from the 29 relevant studies. A data extraction table was adapted for use in this review.[19] The extracted information was organised and synthesised as outlined in Table 1.1 and 1.2. Data items on the study characteristics were extracted, including a) the year the study was published, b) country of the study, c) how the SB population was defined, d) sample size, e) period covered, and f) the area-level deprivation index utilised. These were included in Table 1.1. Further data on the study design and methodological approaches employed, and the evidence pertaining to the impact of deprivation on SB outcomes was recorded and displayed in Table 1.2. The results of this synthesis are presented in a narrative summary within the review, providing a comprehensive overview of the existing literature in relation to the impact of area-level deprivation on the risk of SB.

1.3 Results

A total of 29 studies were included for review following the screening process.

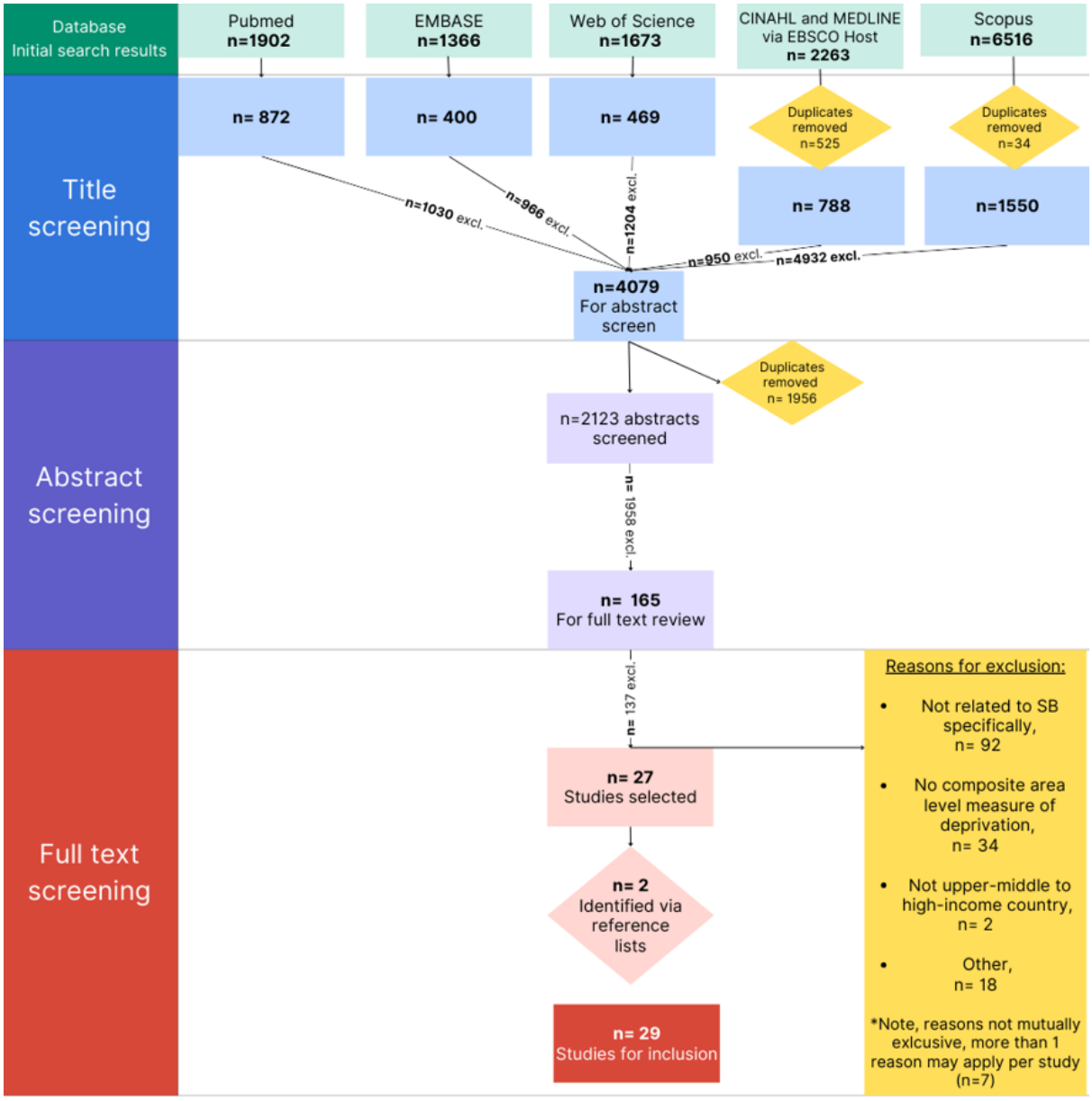

Figure 1.1: Flow diagram of scoping review selection process

Table 1.1 outlines the information extracted from each of these studies, in chronological order from earliest to most recently published study.

Table 1.1: Data extraction of study characteristics

Ref	Year	Country	Population	SB Sample size (n)	Period covered	Index
20	1998	UK	SB undefined*	80,835	1981-1992	Townsend/Carstairs like' index
21	1999	UK	SB undefined*	553	1993-1995	TDS
22	2000	UK	Fetal death after 24 weeks gestation	Nbr SB not reported; SB rates reported from 364 English local authorities	1995	Jarman and TDS
23	2000	UK	Fetal death after 28 weeks gestation until 1992, then from 24 weeks gestation	46,572	1950-1993 Cumbria; 1981-1992 England and Wales	TDS, DoE score and Jarman
24	2000	UK	SB undefined*	1,214	1991-1993	TDS
25	2001	UK	Fetal death after 28 weeks gestation until 1992, then from 24 weeks gestation due to congenital anomaly	10,954 (SB and NND)	1986-1996	Carstairs
26	2001	UK	Fetal death after 20 weeks gestation	1,146	1993-1998	TDS
27	2004	UK	Fetal death after 24 weeks gestation	3,150	1994-1996	TDS
28	2004	New Zealand	Late fetal deaths (LFD) from 28 weeks gestation	4,477	1980-1999	NZDep
29	2004	UK	Fetal death after 24 weeks gestation	342	1996-1998	Jarman score
30	2009	UK	Fetal death after 24 weeks gestation	2,699	1994-2003	Carstairs-Morris score
31	2009	UK	Fetal death after 24 weeks gestation	Nbr SB not reported; SB rates reported for each 17 West Midlands primary care trusts.	2006-2008	IMD
32	2011	UK	Intrauterine death (IUD), gestation unspecified	190	2002-2004	IMD
33	2011	The Netherlands	Fetal death after 22 weeks gestation	37	2002-2006	Dutch index of deprivation
34	2012	UK	Fetal death after 28 weeks gestation	3,259	1992-2008	Carstairs
35	2012	UK	Fetal death after 24 weeks gestation	20,433	2000-2007	IMD

36	2013	The Netherlands	Fetal death after 22 weeks gestation	5,927	2002-2006	Deprived neighborhoods determined by Dutch government
37	2014	UK	Fetal death after 24 weeks gestation, including multiple pregnancies	32,475	1997-2008	IMD
38	2016	UK	Fetal death after 24 weeks gestation	20,433	1997-2008	IMD
39	2018	Argentina	Fetal death of an infant weighing 500g or more, if weight unknown, gestation after 22 weeks included	Nbr SB not reported; SB rates reported for each of the 525 geographic areas of Argentina	2007-2014	SESI
40	2019	Sweden	Fetal death after 22 weeks gestation	524	2013-2017	National Operations Department report
41	2020	Brazil	Fetal death after 22 weeks gestation	2,210	2006-2010 and 2011-2015	SDI
42	2020	Germany	Fetal death of an infant weighing 500g or more	2,473	2009-2016	BIMD
43	2021	UK and Australia	Fetal death after 24 weeks gestation, excluding congenital anomaly	3,725 UK; 2,431 Australia	1993-2015	WIMD and the Index of Relative Socio-Economic Disadvantage for Western Australia
44	2021	Brazil	Fetal death after the 22 weeks gestation, or fetuses weighing 500 g or more, or height from 25 cm identified as avoidable	12,337	2010-2017	ICS
45	2021	UK	Fetal death after 24 weeks gestation	4,505	2015-2017	IMD
46	2021	UK	Fetal death after 28 weeks gestation	287	2014-2016	IMD
47	2023	Chile	Fetal death after 20 weeks gestation	181	2009-2016	MDI
48	2023	UK	Fetal death after 24 weeks gestation, excluding congenital anomaly	551	2006-2020	IMD

Notes: *uses ONS data, SB after 24 weeks gestation. Acronyms used; Deprivation indices: Townsend deprivation score (TDS), Department of Environment Index (DoE) UK, New Zealand Deprivation Index (NZDep), Index of Multiple Deprivation (IMD), Socioeconomic status indicator (SESI) Argentina, Social deprivation index (SDI) Brazil, Bavarian Index of Multiple Deprivation (BIMD), Welsh Index of Multiple

Deprivation (WIMD), Social Deficiency Index (ICS) Brazil, Multiple Deprivation Index (MDI) Chile. Population: Stillbirth (SB), Neonatal Death (NND).

The years of the included studies ranged from 1998-2023. Therefore, while no filter by year was added to the search strategy, the studies identified for inclusion remained from within the last 25 years. One publication had a study period of one year,[22] two publications had 2 different time periods studied [23,41] and the remainder of publications covered one study period ranging from 2-22 years (average 8 years).

A total of nine countries were included, with the majority of studies originating from the United Kingdome (UK) (n=20). The Netherlands and Brazil each contributed 2 studies, while the other six countries had 1 study each included in this review (Table 1.1).

When extracting information on study population, the sample size included SB numbers specifically, where obtainable. Sample size ranged from 37 to 80,835 within the included studies. One study reported SB numbers together with neonatal death[25] and three studies did not report the number of SB examined. For these studies, SB rates were reported from the geographical areas studied. [22,31,39]

The SB population was defined as per the country of study with 14 studies identifying this as fetal death from 24 weeks. [20-22,24,27,29-31,35,37,38,43,45,48] A total of 6 studies defined SB as fetal death from 22 weeks, [33,36,39-41,44] one of which used the definition of a birthweight over 500g and only if the weight is unknown should a gestation of 22 weeks be used.[39] One study that defined SB as having a gestation over 22 weeks also included a birthweight over 500g or height from 25cm.[44] Three studies focused on "late fetal death" or fetal death from 28 weeks gestation.[28,34,46] A further 2 studies [23,25] originally used the definition of gestational age over 28 weeks up until 1992 when the legislation changed in the UK[49].The definition of 24 weeks gestation was then used for the remainder of the study period. The study period for these 2 studies were 1950-1993/1981-1992 and 1986-1992, respectively. Another2 studies defined SB as fetal death from 20 weeks,[26,47] and one study only defined SB as "intrauterine death", with no gestation or weight specified.[32]

A wide range of deprivation indices were utilised internationally (n=18). The UK based deprivation indices were the most frequently used, with UK's Index of Multiple Deprivation (IMD) utilised in a total of 8 studies.[31,32,35,37,38,45,46,48] Followed by the Townsend deprivation score (TDS) (n=6) [21-24,26,27] and Jarman index (n=3).[22,23,29] The Carstairs socioeconomic deprivation score was used in 2 of the studies included,[25,34]

with a further 2 studies using a variation of this index ("Carstairs-Morris scores"[30] and a "Townsend/Carstairs like"[20] index). The remaining 12 indices were used once each within the included studies. Further detail regarding the measures and domains used for each deprivation index identified in the included studies is provided in Appendix D. The number of measures or components used to constitute each index ranged from 3-18. The most common measures included across the indices used were employment, housing, education, income, crime/safety, access to facilities/service and health, as demonstrated in Figure 1.2.

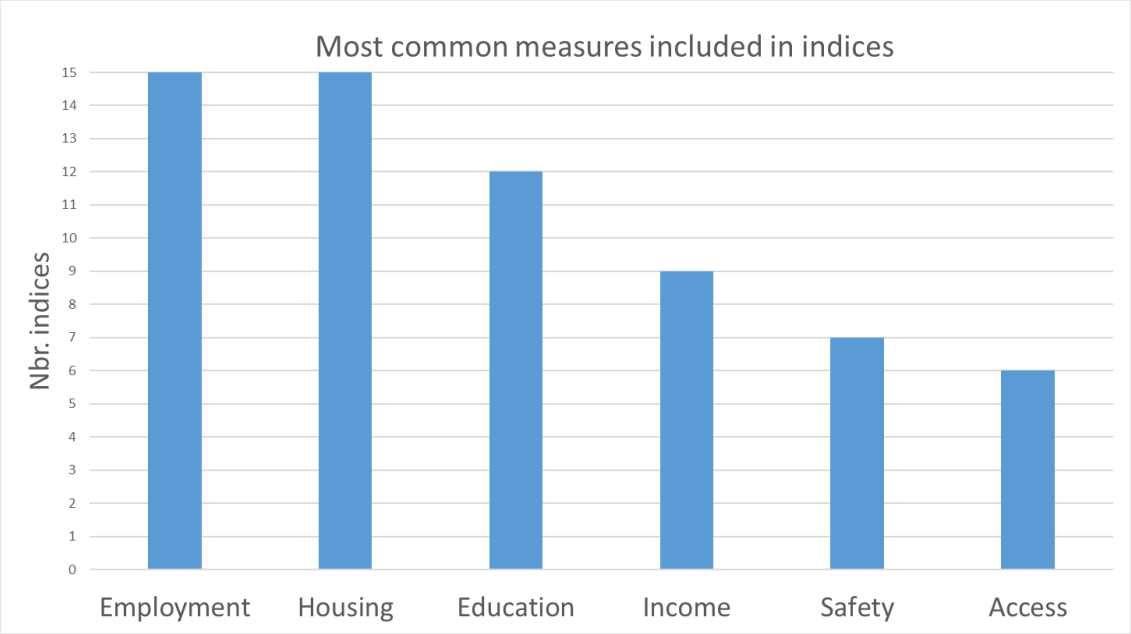

Figure 1.2: Bar chart of most common measures included in deprivation indices

Only two included indices partially considered ethnicity. The Jarman score references "ethnic minorities"[50] and the National Operations Department Report Sweden references "foreign-born individuals".[40] Some of the included studies in this review reference the varying effect that ethnicity had on SB risk, in the context of deprivation. One study noted that even when the risk of SB decreased with lower deprivation, this outcome varied across the two ethnic groups examined.[36] Another study identified that women of 'non-White' ethnicities were more at risk of SB than White women in the same socioeconomic groups.[45] Adjustments for personal/social factors such as smoking, BMI and deprivation had little effect, demonstrating the clear correlation with ethnicity alone.[45]

Table 1.2 provides further detail on the study design, methodology and the evidence of impact of deprivation on SB for each of these studies.

Table 1.2: Data extraction of design, methods, and impact

Ref	Year	Study design	Methods	Evidence of impact
20	1998	Prospective census follow up using the Office for National Statistics Longitudinal Study	The risk of SB was calculated, using multiple logistic regression models, adjusted for personal/household circumstances.	The deprivation gradient is indeterminate for SB, therefore the association in inconclusive.
21	1999	Cross-sectional study	Trends in SB rates tested by chi-squared test for trend. Association SB rate - Townsend score studied with logistic regression.	Statistically significant relationship between SB and higher deprivation when TDS used as a continuous variable.
22	2000	Cross-sectional study	Simple linear regression studied association SB rates - deprivation indicators. Pearson's correlation measured strength of relationship.	Variability in SB explained by deprivation was not statistically significant (less than 10%).
23	2000	Time-trend analysis	Inequality of SB risk between social strata measured by relative index of inequality, estimated with logistic regression.	The risk of SB in less advantaged areas was significantly higher in the earlier time periods (1950–1975), but not subsequently for Cumbria. England/ Wales showed consistent differences across the time periods.
24	2000	Retrospective cohort study	Crude rates for cause specific deaths calculated for each level of deprivation and relative risk was measured.	Focusing exclusively on Wigglesworth classification B (Antepartum events) to consider primarily only SB, however SB may be included in other classifications (A,C and D) that are not considered for this review. The RR from least to most deprived quintile was 1.81.
25	2001	Population based study	Extended perinatal mortality analysed across deprivation quintiles and time using Nptrend. Poisson regression for relative risk. Analysis repeated for SB alone.	Reported as extended perinatal mortality rate but analysis for SB separately did not alter results, showing increased in mortality of non-chromosomal anomalies with increased deprivation but the opposite for chromosomal.
26	2001	Population based ecological study	Poisson regression analysis estimated the magnitude of effect for associations. Relative risk of death between most and least deprived enumeration districts was derived.	SB significantly associated with TDS, the magnitude of effect was 4.3% (41% across the whole range).

27	2004	Cross-sectional study	Cross sectional data collected from one region. Multiple regression analysis and Principle Components Analysis studied impact of deprivation on SB. Sensitivity analyses performed to confirm the results.	Association between SB and TDS does not appear statistically significant.
28	2004	Observational study	Trend analysis of crude late fetal death using logistic regression to fit generalised linear models. Multivariate logistic regression calculated odd ratios.	Persistence of a modest socioeconomic gradient in LFD when all causes are considered together with an OR of 1.48 for the most deprived decile.
29	2004	Case-control study	Conditional logistic regression analyses with forward stepwise regression.	Results were not statistically significant. Deprivation was not an important factor in explaining SB's in this health authority.
30	2009	Population based retrospective cohort study	Multiple logistic regression modelling was used to derive odds ratios.	OR 1.56 for SB least to most deprived, aOR 1.32 adjusted for maternal and infant factors. The SB rate increased from 3.8 per 1000 in the least deprived group to 5.9 per 1000 in the most deprived group.
31	2009	Epidemiological analysis for Clinical report	Analysis of SB rates for each trust in the West Midlands; comparison across deprivation quintiles. Completed as part of regional report.	SB rates in the most deprived quintile are consistently higher, OR 1.5. strong correlation shown between IMD score and SB rate.
32	2011	Retrospective data analysis	Retrospective data collected and analysed.	Strong correlation between the IMD and the distribution of IUDs, with IUD more concentrated in areas with high deprivation.
33	2011	Population based prospective cohort study	Comparisons using Independent Student's t, Mann–Whitney U, and chi-square test. Crude Relative Risk estimated for all outcomes. Multivariable logistic regression analysis applied.	Substantially higher number of intrauterine fetal deaths in deprived neighbourhoods (20/2,779 versus 17/4,580), RR 1.94.
34	2012	Retrospective cohort study	Risk of SB analysed with Logistic regression models. Comparisons made by Kruskal-Wallis test.	There was a linear association between rates of antepartum SB and socioeconomic deprivation score. OR 1.75, aOR 1.53-1.34
35	2012	Population based study	Poisson regression models estimated relative deprivation gap in rates of SB.	Rates were twice as high in the most deprived area compared to the least (RR 2.1) with no evidence of change over time. Deprivation gap for all causes but mechanical events.

36	2013	Epidemiological analysis	Multiple logistic regression analysis analysed association between deprived neighbourhoods and fetal mortality.	The excess risk for perinatal mortality in a deprived neighbourhood is 21%, mainly through foetal mortality
37	2014	Population cohort study	Poisson regression models, including interactions, explored trends over time.	Births from most deprived decile showed higher rates of SB for singletons and twins.
38	2016	Population based study	Cause-specific analysis of all SB and live births, poisson regression models estimate relative deprivation gap.	Rates of SB were twice as high in the most deprived decile as in the least deprived, the deprivation gap was wide and constant over time.
39	2018	Descriptive ecological study	The principle components of geographic areas were analysed, and the fetal mortality ratios was calculated. A Poisson regression analysis was performed, the slope index of inequality and the Kunst and Mackenbach relative index of inequality was calculated.	The fetal mortality ratio is higher in areas identified as having a very unfavourable socioeconomic status. However, the deprivation gap narrowed between the period studied.
40	2019	Population based register study	Associations investigated with logistic regression and risk estimates.	Living in a deprived neighborhood was associated with SB (deprived OR 1.62, 95% CI 1.17-2.26, severely deprived OR 1.56, 95% CI 1.11-2.19). After accounting for individual maternal and social risk factors the risk did not remain.
41	2020	Ecological study	Descriptive spatial analysis using distribution of coefficients. Scan statistics used for exploratory spatial analysis.	There was a presence of clusters of fetal death in areas of greater social deficit.
42	2020	Cross-sectional study	Logistic regression calculating ORs (95% CIs) for SB with and without adjustment for potential confounders.	Increased deprivation was associated with lower SB rates - overall trend, linear increase per quintile: 0.95 (95% CI 0.92 to 0.98)
43	2021	International retrospective cohort study	Multivariate Poisson regression analysis evaluated interaction between cohort and time period.	Rates suggest SB more likely in more deprived areas, but not statistically significant.
44	2021	Ecological study	Factor analysis by main components for the elaboration of the social need index. Spatial analysis applying the local empirical Bayesian estimator and Moran's spatial autocorrelation was verified.	Avoidable fetal mortality was higher among the strata of greater social need/ increased as social deprivation increased. Rates of 8.0, 8.1, 8.8 and 10.7 from the lowest to highest deprivation.

45	2021	Cohort study	Logistic regression models estimated associations, adjusting for relevant factors. Sensitivity analysis done for SB.	Risk of SB increased with socioeconomic deprivation, from 0.29% in the least socioeconomically deprived group to 0.47% in the most deprived group.
46	2021	Case-control study	Data collected via questionnaire. Multivariable analysis adjusting for social and behavioural factors.	Those living in the most deprived quintile had an increased risk of SB compared with the least deprived quintile (adjusted odds ratio [aOR] 3.16; 95% CI 1.47–6.77).
47	2023	Retrospective cohort study	Temporal trend analysis with log binomial regression models, and spatial analysis.	Numbers of SB were rare and so no correlation was found with neighborhood deprivation.
48	2023	Prospective observational study	Logistic regression analysis determined whether deprivation provided a significant independent contribution to SB, after adjusting for maternal risk factors	Unadjusted analysis shows a correlation between SB and deprivation (OR 1.57), however, this did not remain after adjusting for ethnicity and other maternal risk factors.

Notes: Acronyms used; Townsend deprivation score (TDS), Index of Multiple Deprivation (IMD), Stillbirth (SB), Late Fetal Death (LFD), Rate ratio (RR), Odds ratio (OR), Adjusted odds ratio (aOR)

A range of study designs were noted in the included studies. The most frequent study designs included retrospective cohort studies (n=7)[24,30,34,37,43,45,47], cross-sectional studies (n=4)[21,22,27,42] and ecological designs (n=4)[26,39,41,44].

A positive correlation between the increased risk of SB for areas identified as more deprived was seen in 22 of the 29 studies (75.9%) (Table 1.2).[21,23-26,28,30-41,44-46,48] Three of these were conditional on other factors. For example, one study[23] identified higher SB rates in less advantaged areas over both time periods studied for both areas – England and Cumbria, but in the later time period the inequality was no longer statistically significant for the Cumbria area. Also, for two studies,[40,48] while deprived areas were associated with SB, the risk did not remain after adjusting for maternal and social risk factors. Variation was noted throughout the studies in adjusting for other factors.

The remaining seven studies either showed inconclusive or negative association between increased deprivation and SB risk. For 6 of these 7 studies, although differences may have been noted between the deprivation levels, the results were not deemed to be of statistical significance.[20,22,27,29,43,47] One study showed decreased SB rate with increasing deprivation, opposing the majority of the evidence.[42]

Table 1.3 outlines studies selected for their presentation of odds ratios (OR) or rate ratios (RR) to assess the effect of deprivation on SB, aiming to quantify the level of association reported in the literature. The range of deprivation is also included to provide context for the extent of the disparities between studies. A total of 18 studies were identified as having used similar methodologies and presentation of results, which is examined further in Table 1.3. The remaining studies were excluded due to heterogeneity in the analysis methods or presentation of results.

Table 1.3: Study results quantifying risk of stillbirth in relation to deprivation

Ref	Year	Range of deprivation	Effect for positive association*
			Odd ratios (OR)/ Adjusted Odds Ratios (aOR)
21	1999	Septiles	OR 1.45 (95% CI 1.06 to 1.97)
28	2004	Deciles	OR 1.48 (95% CI 1.29 to 1.71)
30	2009	Quintiles	aOR 1.32 (95% CI 1.16 to 1.50)
31	2009	Quintiles	OR 1.5 (CI 95% 1.4 to 1.7)
34	2012	Categories 1-7	aOR 1.34 (95% CI 1.17 to 1.54)
46	2021	Quintiles	aOR 3.16 (95% CI 1.47 to 6.77)
			Rate ratios (RR)/ Adjusted Rate Ratios (aRR)
23	2000	Quintiles for 3 deprivation indices	RR 1.36 (95% CI 1.28 to 1.45)[a]
33	2011	Deprived neighbourhood yes/no	RR 1.94 (95% CI 1.02 to 3.69)
35	2012	Deciles	RR 2.1 (95% CI 2.0 to 2.2)
36	2013	Deprived neighbourhood yes/no	RR 1.53 (95% CI 1.40 to 1.67)
37	2014	Deciles	RR 2.41 (95% CI 2.25 to 2.58)[b]
38	2016	Deciles	RR 2.1 (95% CI 2.0 to 2.2)
39	2018	Quintiles	RR 1.4 (95% CI 1.31 to 1.52)
Ref	**Year**	**Range of deprivation**	**Effect for negative/inconclusive association***
			OR/ aOR
20	1998	9 categories	aOR 1.00 (95% CI 0.93 to 1.08)
40	2019	3 categories, non-exposed/ deprived/ severely deprived	aOR 0.79 (95% CI 0.46 to 1.37)[c]
42	2020	Quintiles	aOR 0.86 (95% CI 0.74 to 1.01)
48	2023	Quintiles	aOR 1.03 (95% CI 0.75 to 1.43)[d]
			RR/ aRR
23	2000	Quintiles for 3 deprivation indices	RR 1.10 (95% CI 0.71 to 1.71)[e]
43	2021	Quintiles	aRR 37-38 weeks: 1.26 (0.94, 1.69) and 39-41 weeks: 1.18 (0.93, 1.50)[f]
			aRR 37-38 weeks: 1.28 (0.14, 1.79) and 39-41 weeks: 1.26 (0.92, 1.71)[g]

Notes: *Unless otherwise stated, the effect represents the comparison of the most deprived versus the least deprived areas.

a TDS for England/Wales

b Applies to singletons (study presented results for singleton and multiple births)

c Applies to severely deprived category. Crude rate showed positive association between deprivation and SB, but risk did not remain after adjustment

d Crude rate showed positive association between deprivation and SB, but risk did not remain after adjustment

e TDS for Cumbria

f Wales, term infants only

g Western Australia, term infants only

For quantifying results, where indicated, the most recent time period was selected. Adjusted rates were preferred in an attempt to obtain the most representative result. There were 13 studies that identified a positive association between higher levels of deprivation and SB. A further 6 studies identified a negative or inconclusive association. One study is included across both sections as the different areas studied had varying results.[23] Positive association demonstrated a range of OR/aOR of 1.32 to 3.16 and RR 1.36 to 2.41. Negative or inconclusive correlation demonstrated a range 0.79 to 1.03 OR, and 1.10 to 1.26 RR/aRR (Figure 1.3).

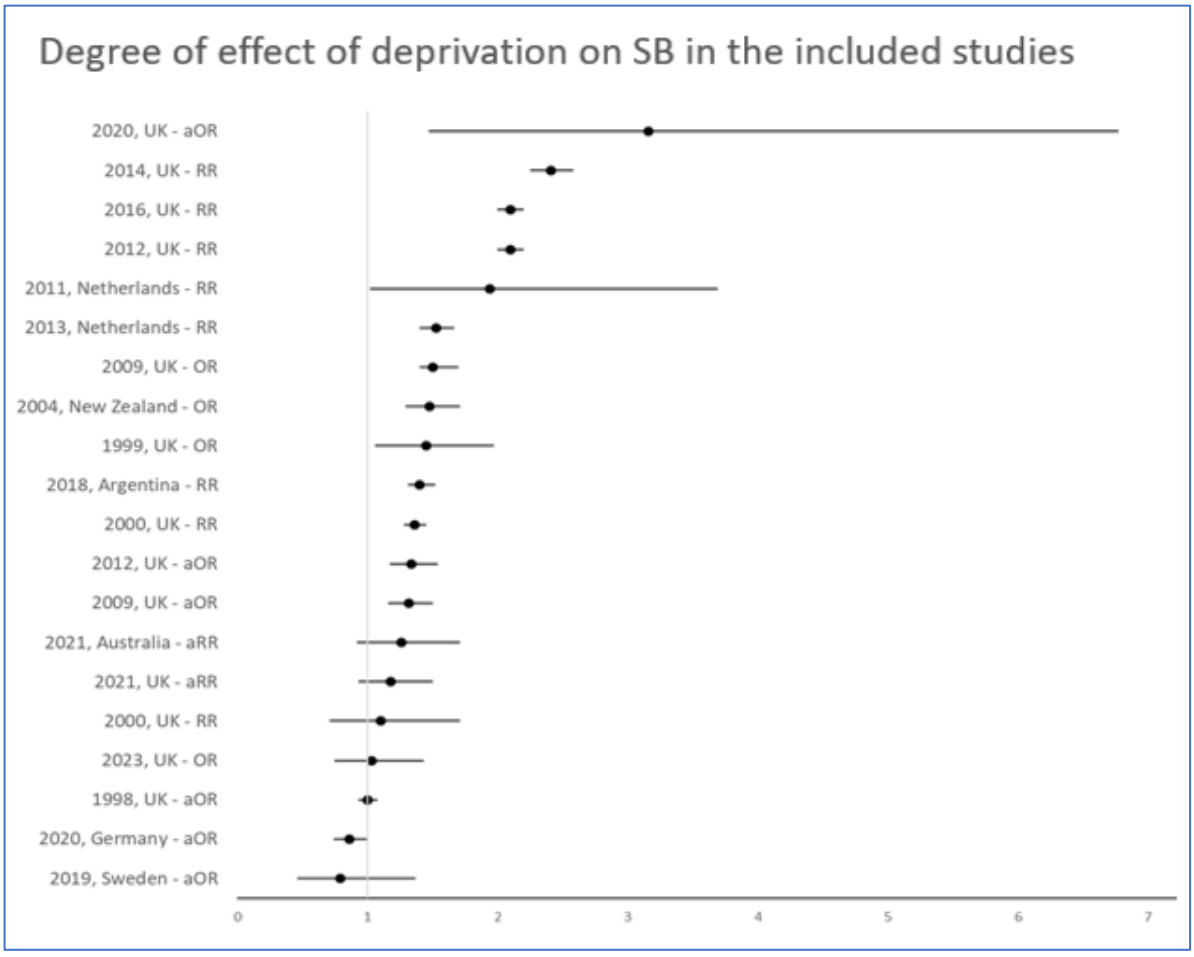

Figure 1.3: Forest plot demonstrating degree of effect of deprivation on stillbirth (SB) in the included studies*

Notes: *These figures are derived from the studies where the results were presented in OR/RR, therefore not all studies are represented.

1.4 Discussion

This scoping review provides a descriptive overview of the international literature on the relationship between area-level deprivation, based on composite measures, and SB risk in upper-middle and high-income countries. The evidence predominantly demonstrates that an individual's level of deprivation does affect their risk of having a SB, with those living in more deprived areas having an increased risk of SB. This is evidenced in 75.9% of the studies included in this review. This finding highlights the critical role that socioeconomic factors play in perinatal health outcomes.

Area-level deprivation is a multidimensional concept, encompassing a range of factors that extend beyond an individual's control,[51-53] which is also seen within in this review. This is linked closely with the World Health Organisation's Social Determinant's of Health (WHO SDH) which are described as "non-medical factors that influence health outcomes", including the conditions that people are born in and live in. SDH were found to be one of the most important influences on health, possibly even more so than lifestyle choices.[54] This is evident also in this scoping review as the risk of SB remained higher for those living in more deprived areas even after adjusting for specific maternal factors.[30,34,46] The WHO SDH model outlines elements such as income, education, employment, housing and access to services as having an influence on health and equity.[54] This is clearly reflected in the area-level deprivation indices identified by this review, where such aspects were components of the indices which showed an impact on the risk of SB. (Appendix D, Figure 1.2). However, it is worth noting that two studies from within this scoping review did demonstrate a reduction in SB risk after adjusting for individual maternal factors.[40,48] Thus, further research could be useful in determining a clear measure of the increase in the risk that maternal factors have on perinatal outcomes specifically, in the context of deprivation.

Although the literature identified in this review was published within the last 25 years, it is interesting to note that the majority (19 of 29 included papers) were published after 2008, the year in which the WHO released the "Closing the Gap in a Generation" report.[55] This report has put further emphasis on the SDH and their impact on global health status and inequalities, highlighting that across all countries lower socioeconomic status has a direct negative impact on health outcomes. The report put out a call for action, advocating for interventions that address health disparities.[54,55]

This has potentially created an increased awareness of the impact that SDH can have on health, which was reflected in the timeline of the publications within this review. The wide range of deprivation indices employed in the reviewed studies highlights the level of complexity that is involved in adequately measuring deprivation. As outlined in the findings, the various deprivation indices applied included numerous components of deprivation. These ranged from income, employment and education to housing, overcrowding, safety or even access to sanitation. This reflects the intricate nature of deprivation as a concept and the highly complex and multifaceted nature it holds. As highlighted by one included study,[22] one index may be more suitable and provide a more accurate measure of deprivation of one area than another, depending on the characteristics of the area being studied. This might explain the wide variety of deprivation indices used throughout the studies in this review, even from studies within the same country, e.g. the UK. Nonetheless, the use of aggregate indices in this study assists in providing a more comprehensive assessment of deprivation by capturing a broad range of socioeconomic factors. While single measures (such as income or education level)[56-60] offer insights into specific aspects of socioeconomic status, they may not fully reflect the cumulative impact of multiple deprivation factors on health outcomes.[35] Therefore, composite indices were deemed more suitable for capturing the complex, multidimensional nature of deprivation, which is essential for informing targeted interventions.

There are some similarities or consistencies of the components within most of the indices which are generally accepted as important markers of deprivation, such as income, employment, education, among others.[61] It is also important to note that there is variation specific to the country or community. Such adjustments might ensure further appropriateness and tailoring of the deprivation measure to the culture and environment to where it applies. This was the case for the Chilean Multiple Deprivation index (MDI) which considers the Mapuche population, an indigenous community of Chile.[47] Some indices were noted to have more basic measures surrounding access to facilities, such as the Social Deprivation Index (SDI) of Brazil.[41] This index includes factors such as having a main network water supply or a garbage removal service, for example. This underscores the importance of context specific measures to accurately reflect the socioeconomic disparities. Further research could

be useful in scrutinizing the components and validity of the available indices internationally, and the appropriateness of their use in measuring health outcomes. A universally accepted systematic approach to the development and validation of deprivation indices that could be used and applied internationally could be of benefit.[61]

The majority of indices included in this review were validated, confirming the accuracy and reliability of their use. This is evident in the indices such as the Index of Multiple Deprivation (used in UK, Welsh and German studies included), the Townsend and Carstairs indices, for example. However not all indices appear to have gone through a validation process and were possibly developed for the purpose of that particular study. This is evident for the Socioeconomic status indicator (SESI) Argentina[39] and the "Townsend-Carstairs like" index.[20] Although these models do reflect many of the measures used in validated indices, utilising census-based information from the country of study, it could be argued that they lack the rigorous validation and are therefore less reliable in measuring the outcomes in relation to deprivation. Validating a deprivation index involves verifying whether it adequately reflects the reality of what's being measured.[62] Hence, it is essential that area-level deprivation indices are adequately validated to ensure their accuracy in capturing the multifaceted aspects of deprivation within different communities.

Despite the large body of evidence available on the association of ethnicity and deprivation,[63-66] ethnicity was not a consistent measure included in the indices, as highlighted in the findings. Only a limited number of studies examined the effect of ethnicity and those that did grouped ethnicity with a range of other maternal factors including smoking and BMI, among others.[33,40,45,46] Only one study examined ethnicity specifically.[36] Each of these studies demonstrated that risk of SB was reduced when adjusted for factors including ethnicity. Further evidence demonstrates ethnicity as an important factor in risk of perinatal mortality.[63,67,59,68] Hence, ethnicity might be of relevance for the adequate measure of deprivation and its impact on health outcomes. Future studies examining deprivation and the association with health should also explore the effect of ethnicity to gain a more comprehensive understanding of this intricate relationship.

While it is evident that a higher level of deprivation is associated with an increased risk of SB, there is variation in how SB is defined throughout the studies. SB is generally described as fetal death from a specific gestation (20/22/24/28 weeks gestation), with some definitions including birthweight and/or height. The lack of consensus in defining SB is clear in the literature and a strong body of evidence recommends an international review of perinatal mortality definitions.[69,70] The Lancet SB series has called for a global classification system.[71] The lack of a standard SB definition affects the ability to effectively analyse the available literature on this topic, hampers the standardised reporting and comparison of SB and neonatal death rates and, ultimately, impacts clinical care.[70] National policies on bereavement supports and entitlements are generally founded on these specific definitions. Therefore, impacting access to maternity leave benefits, parental leave and assistance towards funeral arrangements.[72] Consequently, families face significant disparities in recognition and entitlements based on the classification of their loss, sometimes leading to a lack of formal recognition of their baby at the state level.[70] This profoundly impacts overall wellbeing, the grieving process and possible future pregnancies.[73]

It is interesting to note the large proportion of studies that were UK based, 20 of the 29 studies, therefore leading much of the research in this area in relation to deprivation and SB risk. This is evidenced also in the use of deprivation measures in national maternity reports, such as those published by MBRRACE-UK.[67] This could be an example to be followed in other countries, to expand the body of research in this area, and possibly incorporate into health service analyses and reports.

Ultimately, the literature compiled in this review provides an invaluable resource for healthcare practitioners, researchers, and policymakers seeking to develop evidence-based strategies to address SB inequalities. It highlights the need for area-specific interventions that would support and encourage access to care and resources in more deprived areas through tailored initiatives, such as those suggested in the Marmot review.[74] This review advised the channelling of public expenditure on policies aimed at reducing health inequalities through acting on SDH.[74] It is evident from the literature that interventions must target the wider population of an area to make the required improvements,[45] especially considering the disproportionately higher risk of SB in more deprived groups. Addressing these disparities requires an intersectional

approach involving collaboration between maternity services, public health professionals, and policymakers.[41,45] Supporting universal access to maternity care is also shown to be an important action that addresses disparities in SB risk influenced by level of deprivation.[75,76] Prioritising these care initiatives have the potential to reduce SB rates and ensure the well-being of families and their infants.

While deprivation, based on place of residence, is shown to increase an individual's risk of experiencing SB, this is a complicated and complex relationship with many factors involved and warrants further investigation.

1.4.1 Strengths, limitations and further research

The scoping review has a strength in its innovation, being one of the few comprehensive reviews analysing the literature on the association between deprivation indices and SB. It also addresses a timely and relevant topic within the field.

The rigorous methodology provided by the JBI guide for scoping reviews[13] was adhered to, allowing for reliability and transparency. The screening process considered a large number of studies from a wide range of scientific journals and an inclusive variety of search terms. Thus, ensuring a comprehensive search of the available published literature on the topic. The Rayyan AI tool was utilised in order to more efficiently manage the large volume of studies initially retrieved, while maintaining accuracy in identifying relevant literature.[16,17] This method of assisting in the review process has been tested and found to be efficient in excluding ineligible studies.[16-18] Although it was noted that inconsistent terminology within the literature may have had an impact, one study in particular achieved a 98-99% sensitivity rates using a threshold of <2.5 for exclusion.[18] Utilising this Rayyan AI tool was a strength of the scoping review as it supported a systematic approach to the selection of papers. Application of the inclusion and exclusion criteria, and labelling of the reasons for exclusion, allowed for clarity and traceability of the process. It also promoted a methodical and structured collaboration between the reviewers, including use of the blind feature, which reduced bias from one author to another, promoting a more independent review. This combination of features not only improved time management and practicality but also strengthened the overall accuracy and reliability of the study selection process.

While the screening process was extensive, it was challenging to describe the extent of the effect in the included studies due to the inconsistency in analysis and reporting techniques used within the studies. While a range of effect was noted between 0.79 to 3.16, as demonstrated in the results, this was based on studies that used different study designs and deprivation indices, with varying levels of categories (e.g. quintiles vs. deciles). The use of crude and adjusted rates was also varied across the studies. As a scoping review, the aim is to provide a broad overview of the literature.[19,77] While this allowed for a comprehensive exploration of the topic, it could be argued that the depth of the analysis was therefore limited. A systematic review of the topic, including quality assessment and meta-analysis, may provide a more robust and precise estimation of the degree of effect observed.[78] However, the available data was not appropriate to complete this type of review and analysis due the variance in definitions and reported parameters used throughout the studies identified.

The scope of this review also did not include grey literature searching. While peer-reviewed literature ensures a high standard of evidence, grey literature may have provided further insight on this issue.[19,77]

As noted during the screening process of this review, there is a volume of evidence on other aspects of perinatal and infant mortality on deprivation that was beyond the scope of this review. Further research in this area would be useful.

1.5 Conclusion

In conclusion, the findings of this scoping review highlight the significant impact of area-level deprivation on SB rates in upper-middle and high-income countries. The evidence consistently points to a positive correlation between higher levels of deprivation and an increased risk of SB. These findings emphasise the critical importance of understanding and addressing the multifaceted nature of deprivation and its role as a social determinant of perinatal health.

Countries and regions should consider assessing deprivation when evaluating their SB rates as this could offer valuable information for care programme development to impact deprived areas. The development and implementation of focused initiatives aimed at reducing SB among those at higher deprivation related risk would be beneficial. Using the evidence to guide and inform local policy and resource management will aid in tackling the inequalities in healthcare provision, thus encouraging equality in maternity care. These initiatives have the potential to enhance healthcare services, clinical practice, and ultimately improve maternal and perinatal outcomes.

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Chapter 2: Case-control Study

Socioeconomic deprivation as a risk factor for stillbirth: a case-control study

2.1 Introduction

Equity is described by the World Health Organisation (WHO) as "the absence of unfair, avoidable or remediable differences among groups of people".[1] Equity in health is described as providing every individual the opportunity to attain their highest level of health.[1,2] Unfortunately, global health inequalities continue to be seen.[3] One 2013 WHO review of European member states found significant health disparities in countries with higher levels of disadvantage.[4] Life expectancy demonstrated a difference of 17 years for men and 12 years for women, and children were more likely to die before the age of five.[4] Addressing these disparities is fundamental for ensuring optimal wellbeing across populations.[5] However, health inequality is a complex concept that considers many diverse factors and interdependencies.[6,7] Thus, understanding inequality and its effect on health outcomes is the first step in tackling these disparities.

The WHO's framework of social determinants of health (SDH)[8] highlights how non-medical factors like income, education, and housing influence health outcomes, which is closely aligned to the concept of deprivation.[9] As demonstrated in the scoping review carried out in Chapter 1, various indices have been developed and are available for use primarily in the context of public health. For example, the 'Index of Multiple Deprivation (IMD)' is the official measure of deprivation in England.[10] Seven domains of deprivation are examined for the IMD, each of which are separately weighted and combined into one single index, encompassing the following: Income, Employment, Health and Disability, Education Skills and Training, Crime, Barriers to Housing and Services and Living Environment.[10] This is used widely used to measure health outcomes in relation to deprivation, including its use by the United Kingdom's (UK) Office of National Statistics. For example, to measure inequality in life expectancy,[11] among others. Adapted versions are also available for Scotland, Wales and Northern Ireland to reflect the unique characteristics and priorities of each region.[12]

Similarly, New Zealand's Deprivation Index (NZDep) is a small-area index developed using Census data, aggregating nine socioeconomic variables. This index includes factors related to receiving government benefits, income below a threshold, not living in own home, single-parent families, unemployment, qualifications, bedroom occupancy, access to a telephone and access to a car.[13] The NZDep is used by the nation's Ministry of Health for the Annual Health Survey that examines a wide range of health outcomes for the country.[14]

Deprivation is associated with and is used to measure an extensive range of overall health outcomes. Furthermore, the literature consistently demonstrates the impact of level of deprivation on perinatal health outcomes.[15-18] Also identified in the literature are other possible contributing factors associated with both deprivation and adverse perinatal health outcomes, such as ethnicity, parity, maternal age, and smoking status. Body Mass Index (BMI) is also continually evidenced in the literature as having links with both deprivation and adverse perinatal outcome.[19,20] Access to care, such as the gestation at which one attends their first antenatal appointment (booking visit), is another potential confounding factor. With individuals from areas identified as more socioeconomically deprived being more likely to attend their booking appointment later in their pregnancies,[21] which is also seen as a contributing factor to poor perinatal outcome.[22,23]

While Ireland has similarly low rates of SB to other developed countries,[24] reports from the National Perinatal Epidemiology Centre (NPEC) highlight the worryingly static rates of stillbirth (SB) in the ROI.[20] As identified over a decade ago, there is a potential impact of Ireland's limited social spending to be a contributing factor in adverse health outcomes for those experiencing higher deprivation levels.[25] International evidence demonstrates a gap in the literature examining the effect that deprivation has on risk of SB in the country.[26] The scoping review completed in Chapter 1 also found no studies pertaining to level of deprivation on the risk of SB in the Irish context, demonstrating a clear gap in the literature.

The Institute of Public Health in Ireland recently released a report that stated that while SB rates nationally were reducing in the past few decades, the relative reduction in those from lower socioeconomic groups is not matched which is leading to widening inequalities.[27] However, the socioeconomic status in this report is measured by

occupation alone, which as discussed previously, might not fully capture the multifaceted experience of deprivation.

Therefore, this research aims to identify if there is an association between an individual's level of deprivation, based on their area of residence, and the risk of experiencing SB in an Irish cohort.

2.2 Methods

2.2.1 Study design

An observational design was utilised for this research project. A case-control study was conducted, matching cases of SB with a control cohort of live births. A ratio of 2 controls to 1 case was identified.

This case-control study used retrospective data over four years which includes births from January 1st 2018 to December 31st 2021, using clinical records from a tertiary university maternity unit in the ROI for chart review and secondary data analysis.

Ethical approval for this study was obtained via the Clinical Research Ethics Board, University College Cork (Appendix E).

2.2.2 Data sources

The study was conducted in Cork University Maternity Hospital (CUMH), a tertiary referral maternity care centre and university hospital part of the HSE South/South West hospital group.

A list of MRNs ('Medical Record Number', a unique reference number) for the SB cases was provided by the NPEC Perinatal Mortality Audit co-ordinator for the CUMH, who is a co-investigator of this project. This was used to obtain the relevant data points from the maternity clinical records for the cases. The clinical hospital maternity notes were accessed via the electronic health record called the Maternal and Newborn Clinical Management System (MN-CMS). Once the required data had been collected, the list of MRNs was securely destroyed.

Further data for the SB cases was collected from the NPEC Perinatal Mortality National Clinical Audit (PMNCA), including some audit specific variables for the cases, such as main cause of death. The data in the CUMH maternity clinical records (access via MN-CMS) for the SB cases were then crosschecked with the data submitted for the NPEC Perinatal Mortality Audit. This ensured that no cases were missed and allowed for the triangulation of data using the NPEC's standardised and validated dataset, as consolidated with the National Perinatal Reporting System (NPRS).

Data for the control group was also accessed via the MN-CMS, where information from the selected live births was retrieved.

The addresses for both cases and controls were gathered from the Integrated Patient Management System (iPMS), which is a national HSE administration system for admission, discharge and transfer of patients.
The data points collected from the above sources for cases and controls, e.g. relating to maternal, obstetric and infant factors, are outlined in Appendix F. These were gathered and compiled onto the main study database from the sources outlined.

2.2.3 Study variables and measures

The following definitions were followed for SB cases and the control group of live births:

- The cases comprised of stillbirths (SB), defined as "A child born weighing 500 grams or more or having a gestational age of 24 weeks or more who shows no sign of life" as per the Stillbirths Registration Act, 1994 (Section 1).[28] SB cases were obtained within the period from January 1st 2018 to December 31st 2021. The NPEC does not consider SB whose death was diagnosed at less than 24 weeks gestation, and who had a birthweight of less than 500g, in the Perinatal Mortality Rates (PMR). This inclusion criteria was adhered to for the purpose of this study also.
- The control group comprised of live births, defined as "The complete expulsion or extraction from its mother of a product of conception weighing 500 grams or more (…) which, after such separation, breathes or shows any other evidence of life".[29] The criteria of a gestational age of 24 weeks or more was also followed for the control group. Early and late neonatal deaths were excluded from the control cohort. This refers to any live born baby who died within 28 days completed days of birth, as per the NPEC definitions.[20]

A deprivation index publicly available for the ROI identified for use in this project was the Pobal Deprivation Index.[30] This index identifies small geographical areas of the country that factor, on average, 80-100 households. A small area code and numerical score is then assigned to the area, which is calculated using the fourteen indicators that constitute the index which are weighted either positively or negatively. These fourteen indicators fall under 3 domains of Demographic Profile, Social Class Composition and Labour Market Situation and are expanded as follows:

- Demographic Profile: population change over five years, percentage aged under 15 or over 64, percentage with primary school education only, percentage with third-level education, percentage of single-parent households with children under 15 and mean number of persons per room.
- Social Class Composition: percentage with primary school education only, percentage with third-level education, percentage of households headed by professionals, managers, or farmers, percentage of households headed by semi-skilled or unskilled workers and mean number of persons per room.
- Labour Market Situation: percentage of single-parent households with children under 15, male unemployment rate and female unemployment rate.

The numerical score is then categorised into one of the eight levels of deprivation: extremely affluent, very affluent, affluent, marginally above average, marginally below average, disadvantaged, very disadvantaged and extremely disadvantaged.[31]
The individual's residence was used to identify the uniquely assigned small area code, score and category of deprivation for that particular area. The risk of SB and any confounding factors were analysed in relation to the calculation of deprivation that was provided by this index.
The sociodemographic health indictors that were examined as potential confounding factors for this study included maternal age, parity, BMI, antepartum engagement with services (i.e. booking visit gestation). Infant birthweight and gestation at delivery were also examined for the study cohort.
Further sociodemographic factors related to SB cases were collected to give further context to the characteristics of the SB population of this study. These included the individual's: marital status, employment status, ethnicity, smoking status, and previous experience of pregnancy loss. These variables were only available for the SB cohort and could not be obtained for the control cohort due to the data availability from the sources as outlined in the 'Data sources' section. Cause of death was also examined for SB cases.

2.2.4 Data collection procedures

An application was made to and approved by the Local Information Governance Group (LIGG) for Ireland South Women & Infants Directorate for the undertaking of this research project, following review by the Executive Management Committee and the CUMH Data Protection Officer (DPO) (Appendix G).

A data request was made to the NPEC for data pertaining to SB cases submitted by the CUMH for the annual NPEC PMNCA for the 4-year reporting period (Appendix H). Request to access the CUMH maternity clinical records via the MN-CMS was also submitted.

The CUMH maternity clinical records were also accessed for selection of the live births for the control group. The list of births on the MN-CMS were accessed to identify two live births per SB, as per the inclusion criteria. A randomised approach was used to identify the control cohort by randomly selecting two times the number of SB cases from each year of the study period, after removing the SB cases from the birth list. Hence, the process that was followed for the selection of the control group included extracting all births over the study years 2018-2021 with SB cases excluded. This was then listed in a Microsoft Excel document and a random number was allocated to each one using the RAND function on the Microsoft Excel program. These randomly generated numbers were then sorted in descending order. Depending on the number of SB cases per year, approximately double that amount was selected from the top of the randomly ordered live birth cohort for inclusion in the study.

The individual's address was used to identify the small area code, which indicated the level of deprivation. This was carried out for the whole cohort.

A list of the specific variables that were collected compiled onto the main study database from the sources outlined, namely the NPEC perinatal mortality audit data and the electronic health records from the MN-CMS system, are outlined in Appendix F. The same data was collected for the cases and controls, except in some instances where there were non-applicable points such as cause of death.

All data was fully anonymised on the main study database. No identifiable data (e.g. date of birth, address) was available once compiled onto this database. The individual's address was used to identify a small area of residence and the code representing this

small area was recorded, not the address. The fully anonymised dataset was kept on an encrypted UCC server with restricted access to the research team only.
General Data Protection Regulation (GDPR) regulations were adhered to throughout the project with confidentiality maintained.[32]

2.2.5 Statistical analysis

Data compiled onto the main study Excel file was then analysed using SPSS (Statistical Package for the Social Sciences) software. Characteristics of those experiencing SB was examined using frequency tables, with comparison to national statistics for available variables. Simple comparisons were conducted using Chi-squared and individual sample T-tests to compare cases and controls across the deprivation levels and covariates (including age, BMI, parity and booking visit gestation). Further comparisons were also made to examine the effect of the cause of death on the association with deprivation. Odds ratios were then calculated using logistic regression including multivariable models that adjusted for relevant confounding factors outlined above.
As some of the analysis required categorical data, the data was recoded where necessary into categories for analysis. The levels of deprivation were initially classified according to the predefined categories within the Pobal Deprivation Index.[30] Subsequently, to reflect the profile of the study cohort more accurately, this classification was transformed into quintiles utilising the ranking function in SPSS.
In order to categorise the booking visit gestation, local policy and international literature was reviewed to determine a consensus. HSE advice for booking visit gestation is 8-12 weeks,[33] with some tertiary units suggesting a gestation of up to 14 weeks for this initial visit.[34] There is some variance in the international literature for categorising booking visit gestation, however, generally a gestation of over 20 weeks is seen as late.[19,35,36] Hence, the categories chosen for booking visit gestation were 8-14 weeks, 15-19 weeks and over 20 weeks gestation. Booking visit gestation data is measured in completed weeks of gestation for the purpose of this study.
Universally accepted BMI categories were to be used for this study.[37] However, due to the small numbers in the “underweight” category, the groups were condensed into three categories of “lean” (up to 24.9kg/m2), which encompasses both underweight and average groups. This category was used in addition to “overweight” (25-

29.9kg/m2) and “obese” (30kg/m2 or more) categories, which adheres to those used for the NPEC PMNCA BMI analysis.[20]

Five maternal age categories were created, also in keeping with those used for the NPEC PMNCA,[20] of less than 25 years old, 25-29 years, 30-34 years, 35-39 years and over 40 years old.

2.3 Results

2.3.1 Characteristics of those experiencing SB

The case group was first examined using the available sociodemographic indicators. As demonstrated in Table 2.1, characteristics including ethnicity, marital status, employment status, smoking status, and previous history of pregnancy loss were examined for the individual's experiencing the SB. Maternal age, parity, BMI and booking visit gestation for this cohort will be examined later in this chapter in Table 2.10 to Table 2.14 to when analysing cases compared with controls.

Table 2.1: Socioeconomic characteristics of individuals who experienced stillbirth in this study cohort, 2018-2021

Characteristic	**Category**	**Frequency (n)**	**Percent (%)**
Year the birth occurred	2018 2019 2020 2021	30 41 31 25	23.6 32.3 24.4 19.7
Ethnic Group	White Irish Irish Traveller Other White Asian/ Asian Irish Black/ Black Irish Mixed	101 4 14 3 2 3	79.5 3.1 11 2.4 1.6 2.4
Marital Status	Married Never Married Separated/Divorced	85 40 2	66.9 31.5 1.6
Living with Partner*	No Yes	8 116	6.3 91.3
Employment status*	Employed Unemployed Home Duties Student Other	105 7 11 2 1	82.7 5.5 8.7 1.6 0.8
Smoking status*	Smoker Non-smoker	16 105	12.6 82.7
Previous pregnancy	No Yes	35 92	27.6 72.4
Previous stillbirth	No Yes	91 1	98.9 1.1
Previous pregnancy loss	No Yes	42 50	45.7 54.3

Notes: *Living with partner unknown for 3 individuals. Employment status unknown for 1 individual. Smoking status unknown for 6 individuals.

Table 2.1 highlights some characteristics of the individuals who experienced SB within this study's cohort. The majority were of white Irish ethnicity (79.5%), lived with their partner (91.3%) and were in full or part-time employment (82.7%). A total of 12.6% were documented as smokers at their initial booking visit, which is slightly higher than the percentage of the national general population of daily smokers in Ireland, reported as 8.73%.[38] Of those who had a previous pregnancy (n=92 of 127, 72.4%), 50 (54.3%) had experienced a previous pregnancy loss of <24 weeks gestation and <500g birthweight, with only 1 individual experiencing a previous SB (1.1%).

Table 2.2: Ethnicity of those experiencing stillbirth in this study cohort compared to female population

Ethnicity group*	**Stillbirth in CUMH (2018-2021); N=124 n(%)**	**15-49 year of age national female population, 2022** [39]**
White Irish	101 (79.5)	69.8%
Irish Traveller	4 (3.1)	0.7%
Other White	14 (11)	13.8%
Asian/ Asian Irish	3 (2.4)	4.6%
Black/ Black Irish	2 (1.6)	2.1%

Notes: *Ethnicity unknown for 3 individuals. **From latest Census data available

Table 2.2 provides further context for ethnicity. The ethnic category of the individuals who experienced SB in this study, covering the years 2018-2021 for CUMH, and the available national statistics for the Irish female population aged between 15 and 49 years old from the 2022 Census were compared. Some small variances can be seen, For example, those with Irish Traveller ethnicities appear overrepresented in this study's cohort of individuals who experienced SB (3.1% vs 0.7%) compared with the general population. However, this is based on small sample sizes. Small numbers can result in more variability in percentages and may not accurately reflect the true rates.[40]

Table 2.3: Employment status of those experiencing stillbirth in this study cohort compared to female population

Employment status*	**Stillbirth in CUMH (2018-2020); N=126 n(%)**	**15-44 year of age national female population, 2022[39]****
Employed	105 (82.7)	60.4%
Unemployed	7 (5.5)	8.0%
Home Duties	11 (8.7)	8.6%
Student	2 (1.6)	22.1%
Other	1 (0.8)	0.8%

Notes: *Employment status unknown for 1 individual. **From latest Census data available

Table 2.3 provides a comparison between the employment status of the individual's experiencing SB in this study to the available national data which includes the general female population aged between 15 and 44 years of age in Ireland, as captured by the 2016 Census. The vast majority of those who experienced SB were documented to be in employment, 82.7%. In comparison, the general population data indicates that 60.4% were in employment, based on the 2022 Census data from the general female population aged between 15 and 44 years old.[39]

There was a total of 30 different reasons that were determined to be the infant's main cause of death in the SB cohort in this study. Due to the substantial number of individual reasons, with many occurring only once, the data were grouped into eight defined categories, as per the NPEC definitions.[41] This categorisation was applied for all causes of death except placental abruption, which is grouped into the category of "antepartum or intrapartum haemorrhage" as per the NPEC categorisations. However, as this was the only cause in this category, it is represented as a standalone cause of death for the purpose of this study (Table 2.4, Figure 2.1).

Congenital anomaly was seen in this cohort to be primary reason in determining the cause of death with n=45 of 127, 35.4% SB in this category. Congenital anomaly refers to any genetic or structural defect from conception or embryogenesis,[41] for example chromosomal anomalies such as Trisomy 18, Edwards Syndrome. The next most prevalent cause of death was placental conditions, which accounted for n=41 of 127 (32.3%). Placental conditions included those such as fetal or maternal vascular malperfusion. A total of 9 SB (7.1%) had a cause of death that was deemed to be

undetermined or unexplained. Mechanical issues (n=9, 7.1%) causing the death included cord prolapse, nuchal cord or other cord entanglement or knots, shoulder dystocia and uterine rupture. Fetal conditions (n=8, 6.3%) included problems such as twin-to-twin transfusion syndrome and feto-maternal haemorrhage.

Table 2.4: Main cause of death for stillbirths in this study cohort

Cause of death	**Frequency, N=127 n(%)**
Congenital anomaly	45 (35.4)
Placental condition	41 (32.3)
Mechanical	9 (7.1)
Specific fetal condition	8 (6.3)
Placental abruption	6 (4.7)
Infection	6 (4.7)
Maternal disorder	3 (2.4)
Unexplained	9 (7.1)

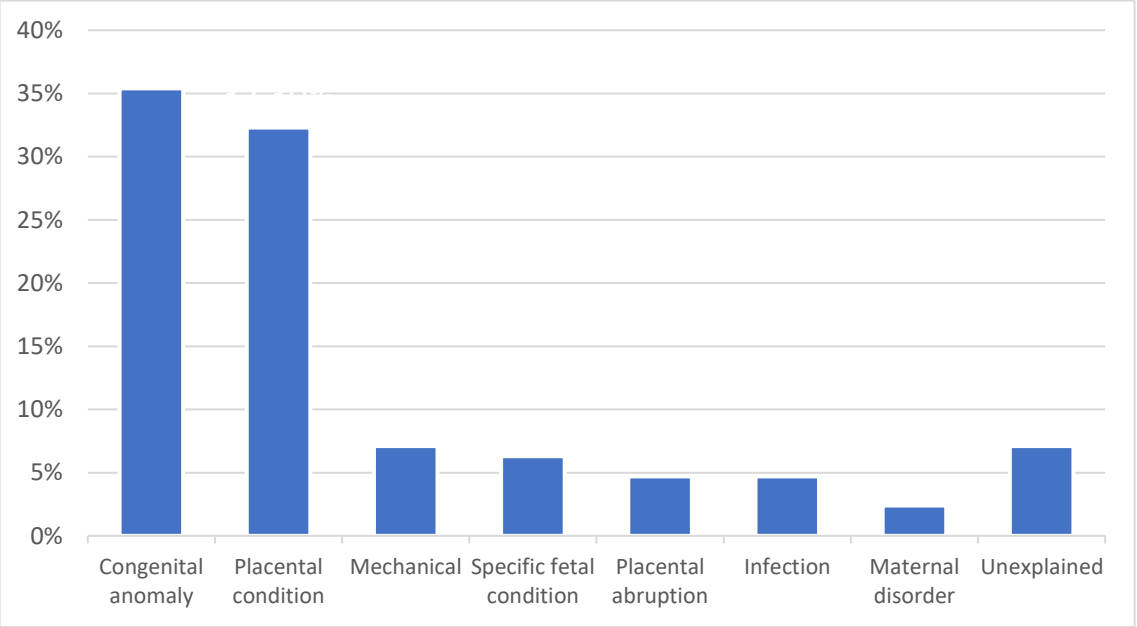

Figure 2.1: Main cause of death for stillbirths in this study cohort

2.3.2 Characteristics of cases and controls

A total of 127 SB (32.3%) and 266 controls (67.7%) were selected according to the inclusion criteria outlined in the methods section. This achieved the approximate ratio of 2:1 sought for this study.

Infant details were examined for the cohort, examining birthweight and gestation for SB cases and controls, as demonstrated in Table 2.5, Figure 2.2 and Figure 2.3

Table 2.5: Birthweight and gestation at delivery for stillbirths and controls

		Control n(%)	**Stillbirth n(%)**	**Total N(%)**
Birthweight	<500g	0 (0)	18 (14.2)	18 (4.6)
	500-999g	0 (0)	31 (24.4)	31 (7.9)
	1000-1499g	4 (1.5)	16 (12.6)	20 (5.1)
	1500-1999g	2 (0.8)	14 (11)	16 (4.1)
	2000-2499g	9 (3.4)	11 (8.7)	20 (5.1)
	2500-2999g	26 (9.8)	13 (10.2)	39 (9.9)
	3000-3499g	91 (34.3)	14 (11)	105 (26.8)
	3500-3999g	100 (37.7)	5 (3.9)	105 (26.8)
	4000g+	33 (12.5)	5 (3.9)	38 (9.7)
	Total	265* (100)	127 (100)	392 (100)
Gestation	<24 weeks	0 (0)	7 (5.5)	7 (1.8)
	24-27 weeks	0 (0)	30 (23.6)	30 (7.7)
	28-31 weeks	5 (1.9)	22 (17.3)	27 (6.9)
	32-36 weeks	17 (6.4)	32 (25.2)	49 (12.5)
	37-41 weeks	242 (91.7)	36 (28.3)	278 (71.1)
	Total	264* (100)	127 (100)	391 (100)

Notes: *Birthweight unknown for 1 control, gestation unknown for 2 controls.

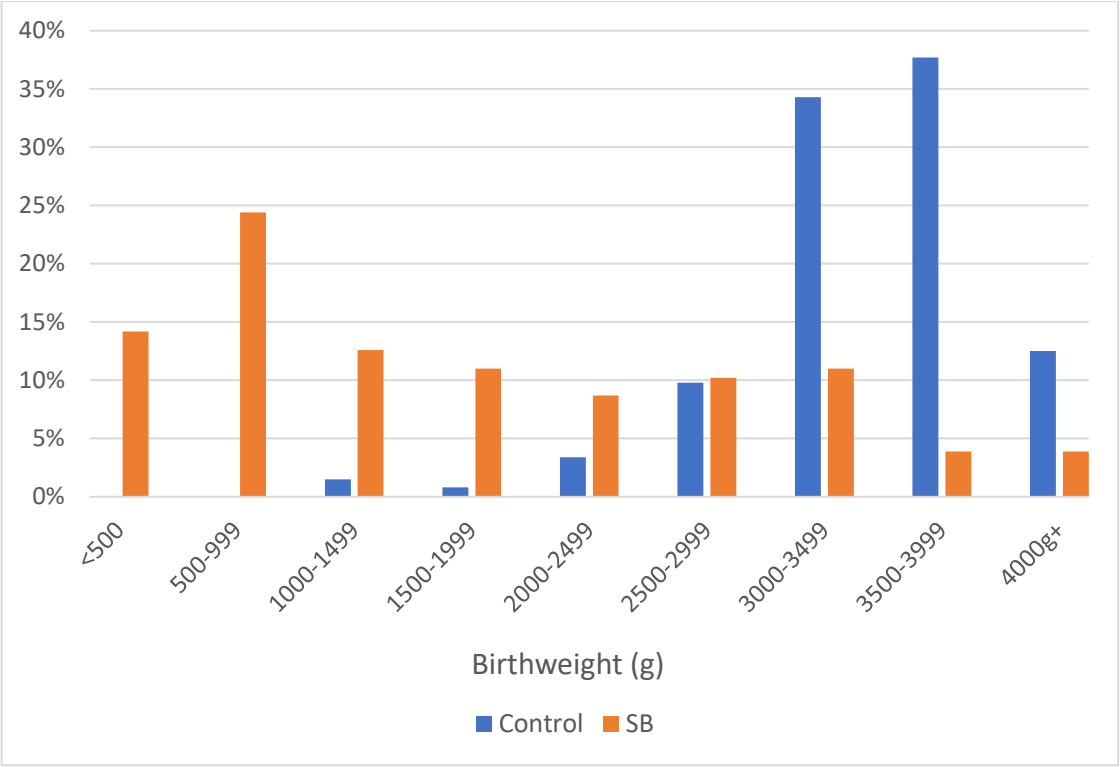

Figure 2.2: Birthweight of stillbirths (SB) and controls, in grams (g)

As demonstrated in Figure 2.2, the birthweight of the SB cohort was varied throughout the birthweight categories with an increase noted in the 500-999g (24.4%) birthweight category and a smaller minority of infant's reaching a birthweight over 3500g (7.9%). Which is in vast contrast to the control group that were primarily 3000g or more (84.5%, missing for 1 control), with no control birthweight below 1000g.

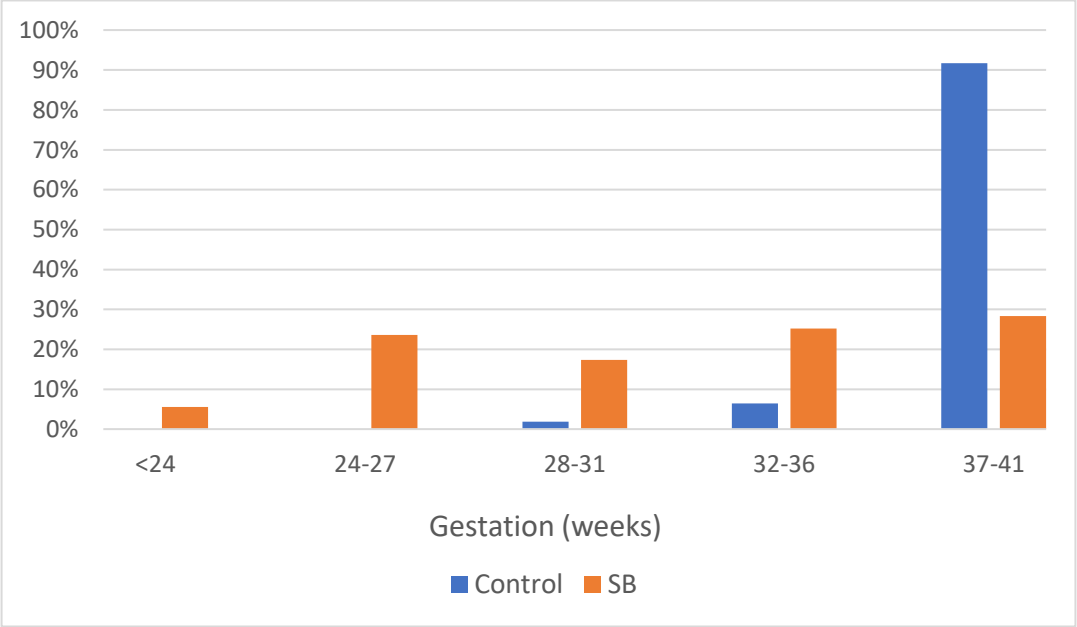

Figure 2.3: Gestation of stillbirths (SB) and controls at delivery, in weeks of gestation

Figure 2.3 shows the variation of the cohort across the gestational periods, with a small minority of SB cases in the <24 weeks category of gestation (5.5%). This is reflective of the Irish SB definition discussed in the methods section, which includes having a gestational age of 24 weeks or more and/or a birthweight of over 500g.[28] The vast majority of the control group (91.7%, missing for 2 controls) were classified as a term gestation (37-41 weeks gestation), with no control births less than 28 weeks gestation.

2.3.3 Association of deprivation with SB

Table 2.6: Deprivation levels for stillbirths and controls

Level	**Control n(%), N=266**	**Stillbirth n(%), N=127**	**Total N(%), N=393**
Very affluent	7 (2.6)	3 (2.4)	10 (2.5)
Affluent	41 (15.4)	11 (8.7)	52 (13.2)
Marginally above average	125 (47)	59 (46.5)	184 (46.8)
Marginally below average	61 (22.9)	41 (32.3)	102 (26)
Disadvantaged	26 (9.8)	11 (8.7)	37 (9.4)
Very disadvantaged	6 (2.3)	2 (1.6)	8 (2)

SB and controls are examined in Table 2.6 across the deprivation categories as defined by the Pobal Deprivation Index. Pearson chi-squared tests were used to identify a p-value of 0.288, indicating that there is not a statistically significant difference between deprivation levels for the case and control groups. This suggests that there is not an association between risk of SB and level of deprivation.

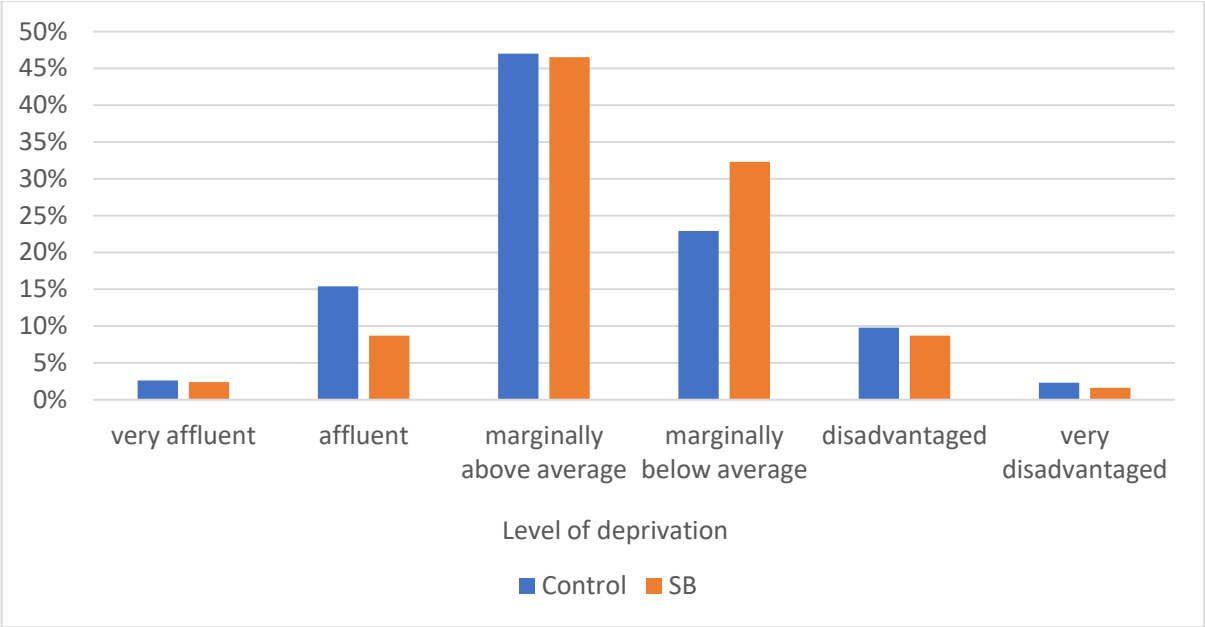

Figure 2.4: Percentage of stillbirths (SB) and controls across each level of deprivation

As shown in Figure 2.4, although there is no statistically significant difference overall. There is some variance throughout the categories with a slightly higher percentage of controls in the “affluent” category (15.4% controls vs 8.7% cases) and a slightly higher percentage of cases in the “marginally below average” category (22.9% controls vs 32.3% cases).

Although the Pobal Deprivation Index utilised eight categories of deprivation[31], the cohort being examined in this study were distributed within six of these eight categories. There were no individuals in this sample living within the “extremely affluent” or “extremely deprived” areas of the country. While the data encompassed cases and controls from a tertiary maternity unit that serves a wider population than that of the Cork county alone, it is worth noting that there are no areas of “extreme affluence” in county Cork and only one area of “extreme disadvantage”, as per the Pobal deprivation map 2016.[30]

As noted in Table 2.6, small numbers were categorised into the lesser extreme levels of “very affluent”, n= 10 (2.5%) and “very disadvantaged”, n=8 (2%). A large portion of the study population were distributed into the “marginally above average” category at 184 (46.8%), with a further 102 (26%) in the “marginally below average" category. This demonstrates that the vast majority of the study population, n=286 of 393 (72.8%), lies within in the marginal or middle categories.

Considering the underrepresentation of the more extreme levels of deprivation using the Pobal categories, the data was instead classified into quintiles, using the unique score identified for each small area. This was done in order to further examine the association in a more appropriate representation of the national profile of this cohort. Table 2.7 illustrates the SB across the five levels of deprivation, with 1 being the most affluent and 5 being the most disadvantaged.

Table 2.7: Deprivation levels of stillbirths and controls, using quintiles

Level	**Control n(%), N=266**	**Stillbirth n(%), N=127**	**Total N(%), N=393**
1 – affluent	57 (21.4)	21 (16.5)	78 (19.8)
2 – above average	51 (19.2)	28 (22)	79 (20.1)
3 – average	59 (22.2)	20 (15.7)	79 (20.1)
4 – below average	49 (18.4)	30 (23.6)	79 (20.1)
5 – deprived	50 (18.8)	28 (22)	78 (19.8)

Pearson's chi-squared test identified a p-value of 0.311 when assessing the risk of SB over the five deprivation levels, which shows that using quintiles does not alter the statistical significance.

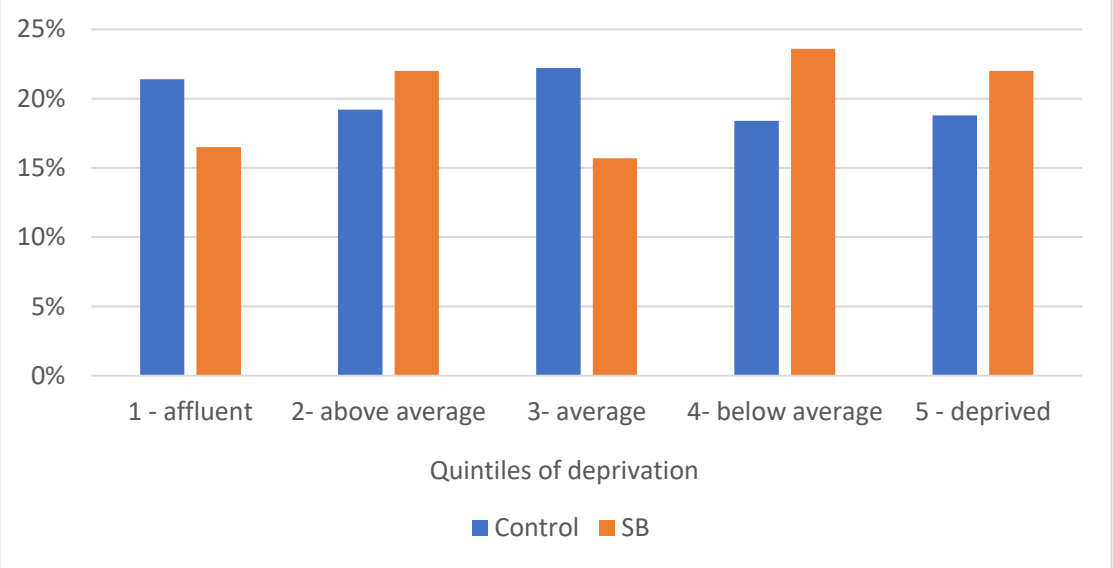

Figure 2.5: Percentage of stillbirths (SB) and controls across each level of deprivation, using quintiles

Figure 2.5 continues to demonstrate that there is some variance throughout the levels of deprivation for cases and controls when analysing the deprivation over five

categories. Although there is still no statistical significance overall, there's a slightly higher representation of SB in the more deprived groups 4 and 5, while there is a slightly higher representation of controls in the affluent group 1 and middle group 3. For group 2, the "above average" group, a marginally higher percentage of SB is noted. For the remainder of the analysis in this study, quintiles will be used as the measure of deprivation to more accurately reflect the range of deprivation experienced by this study cohort specifically.

2.3.4 Association with deprivation and cause of death

Anomaly cases were identified and analysis for deprivation was repeated, after removing the SB cases with congenital anomaly identified as the main cause of death. After removing the cases of SB diagnosed with congenital anomaly from the analysis, 82 SB cases remained with the 266 controls, indicating a larger ratio of approximately 3:1.

Table 2.8: Deprivation levels for stillbirths and controls, after adjustment for congenital anomaly, using quintiles

Level	**Control n(%), N=266**	**Stillbirth n(%), N=82**	**Total N(%), N=348**
1 – affluent	57 (21.4)	15 (18.3)	72 (20.7)
2 – above average	51 (19.2)	14 (17.1)	65 (18.7)
3 – average	59 (22.2)	13 (15.9)	72 (20.7)
4 – below average	49 (18.4)	19 (23.2)	68 (19.5)
5 – deprived	50 (18.8)	21 (25.6)	71 (20.4)

When the analysis was repeated to adjust for congenital anomaly (i.e. excluding cases of congenital anomaly), there was no difference in the risk of SB noted with a Pearson chi-squared p-value of .433.

This analysis was repeated to examine association of deprivation with specific causes of death. Cause of death was analysed in three groups: congenital anomaly cases, the next most prevalent cause of death, which was placental conditions, and the remaining causes were grouped into an "other" category.

Table 2.9: Association between cause of death and deprivation

Level	Control n(%), N=266	Anomaly n(%), N=45	Placental n(%), N=41	Other n(%), N=41
1 – affluent	57 (21.4)	6 (13.3)	7 (17.1)	8 (19.5)
2 – above average	51 (19.2)	14 (31.1)	9 (22)	5 (12.2)
3 – average	59 (22.2)	7 (15.6)	3 (7.3)	10 (24.4)
4 – below average	49 (18.4)	11 (24.4)	13 (31.7)	6 (14.6)
5 – deprived	50 (18.8)	7 (15.6)	9 (22)	12 (29.3)
Pearson chi-square p-value	-	0.230	0.106	0.509

As seen in Table 2.9, when examining the specific causes of death, no significant association with deprivation was noted.

A slight increase in the percentage of placental cause of death for the more deprived quintiles 4 and 5 was present (53.7% compared to 37.2% of controls, Table 2.9). Although based on small numbers, this was examined further in a chi-squared test look at quintile 1 to 3 and quintiles 4 and 5 separately with cases whose cause of death was due to a placental condition compared with controls. Pearson's chi-squared p-value was 0.045, demonstrating that this was statistically significant.

2.3.5 Potential confounding factors on the association between deprivation and SB

Age, BMI and booking visit gestation were all identified as potential confounding factors from a review of the literature as highlighted in the introduction. Hence, these were analysed individually using individual sample t-tests.

Table 2.10: Comparison of potential confounding factors between stillbirths and controls, using individual samples t-test

Factor*	Control	Stillbirth		
	M (SD)	M (SD)	t(df)	p-value
Age	32.5 (5.3)	33.4 (5)	-1.64 (256.3)	0.102
BMI	26.3 (5.1)	27.9 (6.3)	-2.64 (381)	0.009
Booking visit gestation	13.6 (3.5)	14 (4.9)	-1.03 (379)	0.303

Notes: M=Mean. SD = Standard Deviation. t= t statistic. df= degree of freedom.

*Age unknown for 1 case. BMI unknown for 9 cases, 1 control. Booking visit gestation unknown for 4 cases, 8 controls. Parity unknown for 1 case.

As can be seen in Table 2.10, the p-value associated with BMI is 0.009, showing evidence of a difference in BMI between cases and controls.
The other variables of maternal age and booking visit gestation did not show statistically significant differences, as their p-values are above the threshold of 0.05. Parity was not examined in this table due to the categorical nature of the variable.
Using the categories as described in the methods section, Chi-squared tests were then completed on the confounding factors of age, BMI, booking visit gestation and parity, as demonstrated in Table 2.11.

Table 2.11: Association between potential confounding factors for stillbirths and controls

Factor	**Category**	**Control n(%)**	**Stillbirth n(%)**	**Total N(%)**	**Pearson chi-squared p-value**
Age	<25 years	20 (7.5)	8 (6.3)	28 (7.1)	
	25-29 years	42 (15.8)	16 (12.7)	58 (14.8)	
	30-34 years	103 (38.7)	43 (34.1)	146 (37.2)	
	35-39 years	79 (29.7)	51 (40.5)	130 (33.2)	
	>40 years	22 (8.3)	8 (6.3)	30 (7.7)	0.330
BMI	lean	127 (47.7)	48 (40.7)	175 (45.6)	
	overweight	92 (34.6)	34 (28.8)	126 (32.8)	
	obese	47 (17.7)	36 (30.5)	83 (21.6)	0.019
Booking visit gestation	8-14 weeks	213 (82.6)	100 (81.3)	313 (82.2)	
	15-19 weeks	33 (12.8)	9 (7.3)	42 (11)	
	20 + weeks	12 (4.7)	14 (11.4)	26 (6.8)	0.020
Parity	Nulliparous	105 (39.5)	51 (40.5)	156 (39.8)	
	Multiparous	161 (60.5)	75 (59.5)	236 (60.2)	0.850

As can be seen in Table 2.11, BMI and booking visit gestation were identified as being significantly associated with risk of SB, with a p-value of 0.019 and 0.020, respectively. While maternal age and parity did not show any significance across the groups. This varies slightly to the results of Table 2.10 where booking visit gestation was not seen as statistically significant. This suggests a possible effect of the categorisation of gestation at booking visit appointment, as opposed to the individual gestations, as examined by t-tests in Table 2.10.
Binary logistic regression was then undertaken on deprivation, using deprivation quintiles, and the confounding factors of age, BMI, booking visit gestation and parity (Table 2.12).

Table 2.12: Crude association of deprivation and potential confounding factors with stillbirth

Factor	Category	Odds ratio (OR)	Lower 95% CI	Upper 95% CI	p-value
BMI	Lean	1.00 (ref)			
	Overweight	0.98	0.58	1.64	0.932
	Obese	2.03	1.17	3.5	0.011
Age	<25 years	0.96	0.39	2.34	0.925
	25-29 years	0.91	0.46	1.8	0.791
	30-34 years	1.00 (ref)			
	35-39 years	1.55	0.94	2.55	0.088
	>40years	0.87	0.36	2.11	0.760
Booking visit gestation	8-14 weeks	1.00 (ref)			
	15-19 weeks	0.58	0.27	1.26	0.169
	20+ weeks	2.49	1.11	5.57	0.027
Parity	Nulliparous	1.00 (ref)			
	Multiparous	0.96	0.62	1.48	0.850
Deprivation	1 – affluent	1.00 (ref)			
	2 – above average	1.49	0.76	2.94	0.250
	3 – average	0.92	0.45	1.88	0.819
	4 – below average	1.66	0.85	3.27	0.141
	5 – deprived	1.52	0.77	3.01	0.228

Table 2.12 demonstrates the crude rates of deprivation and the confounding factors of age, BMI, booking visit gestation and parity for cases and controls. The odds ratio (OR) of SB for those who were overweight was .978 (95% CI 0.584-1.636, p-value .932), while individuals with obesity were shown to be twice as likely to experience SB as those in the lean category, with an OR 2.03 (95% CI 1.173-3.501, p-value 0.011). Age continued to show no statistical significance in relation to SB risk, although a small increase in risk was noted for those aged between 35-39 years at time of booking with an OR 1.55 (95% CI 0.937-2.551, p-value 0.088). Individuals who had their initial booking visit over 20 weeks gestation were seen to have over double the risk of SB than those attending their booking appointment between 8 and 14 weeks of gestation with an OR 2.485 (95% CI 1.109 – 5.568, p-value 0.027). No significant difference was noted in whether the individual was nulliparous or multiparous. Deprivation, when examined through logistic regression, also continued to demonstrate no statistically significant differentiation in risk throughout the five levels. While level 4 and 5 had an OR 1.66 and OR 1.52, respectively, the p-value did not indicate significance. Level 4

demonstrated a 95% confidence interval of 0.845-3.267, p-value 0.141 and level 5 a 95% CI of 0.769-3.005, p-value 0.228.

Table 2.13 demonstrates the multivariate model, considering deprivation quintile, age, BMI and booking visit gestation. As parity thus far has shown no effect on risk, the multivariate model was carried out including and excluding parity. When parity was included, the omnibus tests of model coefficients was 0.42 and the Hosmer and Lemeshow test was 0.72. When parity was excluded, the omnibus test of model coefficients was 0.34 and the Hosmer and Lemeshow test was 0.920. Therefore, it was decided to exclude parity from the multivariate model.

Table 2.13: Adjusted association of deprivation and potential confounding factors with stillbirth

Factor	**Category**	**Odds ratio (OR)**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
BMI	Lean	1.00 (ref)			
	Overweight	0.92	0.54	1.56	0.751
	Obese	1.91	1.07	3.4	0.028
Age	<25 years	0.77	0.28	2.07	0.598
	25-29 years	0.75	0.36	1.59	0.457
	30-34 years	1.00 (ref)			
	35-39 years	1.72	1.01	2.92	0.047
	>40years	0.78	0.3	1.99	0.602
Booking visit gestation	8-14 weeks	1.00 (ref)			
	15-19 weeks	0.6	0.27	1.34	0.215
	20+ weeks	2.37	0.97	5.77	0.058
Deprivation	1 – affluent	1.00 (ref)			
	2 – above average	1.27	0.62	2.6	0.523
	3 – average	0.88	0.42	1.84	0.729
	4 – below average	1.86	0.91	3.79	0.090
	5 – deprived	1.18	0.56	2.52	0.661

As demonstrated in Table 2.13, individuals in the age group 35-39 years are shown to have an OR 1.7 (95% CI 1-2.9, p-value 0.047), indicating a statistically significant risk in this age category. BMI continues to demonstrate that those in the obese category are at higher risk of experiencing SB with a OR 1.9 (95% CI 1.1-3.4, p-value 0.028). While a booking visit gestation of over 20 weeks demonstrates an OR 2.4; in the multivariate model this does not indicate statistical significance with a 95% CI 0.97-5.77, p-value 0.058. With regards deprivation, quintile 4 can be seen to show a weak association

with risk of SB, though not of statistical significance with an OR 1.86 (95% CI 0.91-3.8, p-value 0.09).

2.4 Discussion

In this case-control study at a tertiary maternity unit in the ROI, a generalised association between level of deprivation and risk of SB was not evidenced. While this finding may differ from the international literature on the topic, as evidenced in the scoping review in Chapter 1 of this thesis, it is important to recognise the contextual factors influencing perinatal outcomes in Ireland. The absence of a clear association underscores the complexity of SB aetiology and highlights the need for ongoing investigation. This study may serve as a starting point, highlighting the need for extending research efforts nationally to obtain a more thorough understanding of the relationship between deprivation and SB and further perinatal outcomes in the Irish context. Collecting this data as part of wider national audits and research will allow for stronger and more representative datasets. More in-depth investigation into the nuances and factors relating to SB that might be influenced by deprivation would create opportunity for the development of targeted intervention and improved perinatal care.[42,43]

Although there is much literature that evidences area-level deprivation indices as being accurate in capturing the multidimensional nature of deprivation, other research has suggested that the sensitivity of the composite measurements is low.[44,45] This may be a particular consideration for areas that do not exhibit the extreme categories of deprivation levels (i.e. “extremely affluent” or “extremely deprived”), such as that seen in the CUMH data in this study. Within this cohort, no participants met the “extreme” levels of the Pobal Deprivation Index[30] and the vast majority lay within the marginal categories (72.8% of the study cohort). Repeating the study using larger cohorts from areas that represent more diversity may be useful to examine if the significance of the association is affected.

While adjusting to quintiles did not affect the statistical significance of the effect of deprivation on risk of SB, the variances between SB and controls were altered slightly with the more deprived levels 4 and 5 showing a higher proportion of cases than controls. This may be more suggestive of the trend in international literature which associates higher levels of deprivation with higher risks of experiencing SB, as identified in the scoping review in Chapter 1 of this thesis. Conversely, levels 1 (affluent) and level 3 (average) encompassed a higher percentage of the control group, averaging a slightly

more above average affluent demographic for the control group. Again, this mirrors more closely the large body of evidence suggesting the association between deprivation and SB. However, the findings are not strong enough to draw firm conclusions from. A weak association is potentially indicated, which was highlighted further when examining the different causes of death in the SB cases across the deprivation quintiles. A subtle yet important trend was noted in the increased percentage of SB attributed to placental causes within the more deprived quintiles of 4 and 5. This allowed for more in depth examination which identified the statistically significant association (p-value 0.045) between placental cause of death in SB and above average deprivation, which is an important finding, demonstrating the influence of deprivation on placental efficiency in this study cohort. There is some evidence in the available literature that supports this observation, with two studies identifying a significant association between placental related SB and deprivation OR 1.89 (95% CI 1.23-2.98, p-value 0.005)[46] and OR 2.17 (95% ci 1.80 – 2.63, p-value <0.001).[47] Although the significance did not remain in one study once adjusted for certain maternal risk factors.[46] Another retrospective population based study also found higher rates of SB in more deprived groups, and discussed the potential influence of deprivation on placental sufficiency.[48] However, the study authors speculated that smoking could be a significant contributory factor in this outcome.[48] Smoking is noted in the literature as affecting placental efficiency, with other risk factors such as alcohol consumption, obesity and advanced maternal age (>35years) also negatively impacting on placental function.[49-51] This evidence might suggest what is influencing the higher placental related SB in the case group of this study. The relationship between placental related SB and deprivation is a notable finding that could provide an opportunity for targeted clinical intervention, with a possibility of implementing enhanced screening protocols to address this specific issue.[46,52,53]

The concept of deprivation has been proven to be complex, with many factors potentially influencing an individual's unique experience of disadvantage and health outcome, as evidenced in the scoping review in Chapter 1 of this thesis and in the published literature.[9]

Also noted in this study were other contributing factors, such as BMI and booking visit gestation, that were seen to increase the risk of experiencing SB. BMI consistently

showed a statistically significant association with SB throughout the analysis, while booking visit gestation varied slightly in the strength of the effect, with significance noted in the chi-squared test (p-value = 0.020) and the crude risk (p-value of 0.027) for a booking visit after 20 weeks gestation. Categorising booking visit gestation may have been a factor in altering the significance of the risk on SB. The categorisation for this variable might be important in measuring the risk associated with attending the first antenatal appointment at a later gestation. Possibly indicating that a day-to-day difference in attendance is not significant while a shift in the category, e.g. from attending at 20 weeks gestation compared to attending at 15 weeks gestation, might make a difference to the relative risk. Crude analysis of booking visit gestation compared to the multivariate model also appeared to alter the significance of the association with SB risk. This potentially indicates that the timing of the first antenatal visit is influenced by the other factors examined in the multivariate model, such as deprivation, BMI and maternal age. Interestingly, there is literature to suggest that placental dysfunction related SB can be mitigated by specific early screening in those identified as more at risk, ideally at a gestation of 11-13 weeks,[46] which would be a crucial initiative to support both tailored screening and encouraging access to antenatal care earlier in the pregnancy. As another study notes, umbilical cord dopplers are only performed for at risk pregnancies, but socioeconomic status is not currently considered in this "at risk" category.[52] Due to the finding of placental causes being more prevalent in more deprived groups, this could be a consideration for clinical practice.

Further research notes that initiatives encouraging access to care should also include respectful and tailored care, continuity of care, cultural sensitivity, active community engagement, awareness programmes and family planning education.[54-59] For the purpose of this study, booking visit gestation was used as an indicator to how individuals access care during pregnancy. Further exploration into other elements of access to care would be important in developing interventions to promote engagement with services for those identified as having higher levels of deprivation, such as frequency of attendance.[60] Other factors such as discrimination, personal and structural accessibility, and the comprehensibility and understanding of their treatment and care were noted as barriers to service access.[59,61]

The robust association between BMI and SB, consistently observed in this study, is also a noteworthy finding strongly supported by existing literature.[62-65] Individuals who have a BMI in the obese category (>30kg/m2) were identified in this study as having a two-fold risk of experiencing SB, reflecting what has been found in previous research.[66] Again, this is a factor that has the potential to benefit from preconception care and intervention.[62] There is a complex interplay of the factors associated with deprivation and SB risk, for example, individuals with obesity and social deprivation have been shown as more likely to access care later in their pregnancy.[67] Assessing for confounding risk factors is crucial when examining deprivation, to identify effect and influence of these factors on outcomes, but also to identify possible avenues for intervention.[68] The evidence highlights that targeting modifiable or behavioural risk factors can lower SB risk.[69,70] The results of this study demonstrate that although the area-level deprivation itself may not influence the overall likelihood of SB for this cohort, as per above, there are modifiable risk factors possibly more prevalent in these areas that could be targeted specifically.[71]

Contrary to previous evidence that would indicate nulliparity as risk factor for SB,[64,70,72] parity did not evidence an association with this outcome in our case-control study. Further research on this issue in Ireland would be useful in better understanding the possible contribution of parity towards risk of SB.

The slight increase in risk of SB in the group with maternal age 35-39 year (aOR 1.7; 95% CI 1-2.9, p-value 0.047) and higher proportion of cases in this group (40% vs 29.5% controls) could be indicative of an increase in SB risk with advancing maternal age. This is reflective of the available literature that identifies a consistent increased risk of SB with advanced maternal age over 35.[73,74] However, the literature indicates that the risk continues to increase as maternal age increases,[73,75] which was not found in this study, with individuals over 40 in this sample not showing an increased SB risk. Although the increased risk of SB and maternal age increases was not a finding of this study, the number of those aged 40 or more during their pregnancy in this cohort, were small (n=30 of 392, 7.7%) and hence, possibly did not identify the association that is seen in other literature.

More research is needed to identify what contributing socioeconomic factors might influence perinatal health outcomes in the Irish context. For example, the association

of ethnicity is not fully explored in this study due to the availability of data. The strong combined influence of ethnicity and deprivation on SB risk has been evidenced in the literature,[76,77] such as that highlighted in recent MBRRACE-UK Reports.[78] The reports show that while deprivation is leading to inequality in SB risk, this is exacerbated further by the individual's ethnicity, with perinatal mortality rates are higher in those of Black or Asian ethnicities across every level of deprivation.[79] While ethnicity was available for the case group of individuals experiencing SB in this study, it could not be obtained for the control group and thus, was compared to available national statistics. However, the numbers of those who were not of white Irish ethnicity in this study sample were small, which weakened any findings relating to ethnicity, again, indicating the need for studies with wider samples to examine the effect.

Globally there is an imperative to examine factors influencing SB and adverse perinatal outcome.[80-83] It is essential for Ireland to actively contribute to and engage in this global discourse, aligning its efforts with international initiatives aimed at improving maternal and child health and reducing inequalities, such as those highlighted in the United Nations' "Sustainable Development Goals (SDGs)"[82] and the "Global Strategy for Women's, Children's, and Adolescents' Health".[83] These global strategies provide a framework for the implementation of health-related SDGs and present valuable opportunities for the ROI to align its efforts with broader international initiatives. It could be argued that the health inequalities divide is potentially limited in the ROI during perinatal period due to the free maternity care that is available through the Health Service Executive's (HSE) Maternity and Infant Care Scheme,[84] which may allow for increased accessibility across socioeconomic groups.[85,86] However, some studies note that poor pregnancy outcomes are still seen in higher rates amongst individuals from more disadvantaged areas despite universal healthcare systems being available.[21,87] While access to health care is important, it may not be sufficient to improve health outcomes of those more socioeconomically deprived.[88] Overall improvements in deprivation were seen in the release of the 2022 Pobal Deprivation Index for Ireland[89], however, not all areas had proportionate improvements compared to the 2016 findings. Thus, inequality and deprivation persist in some areas in Ireland, again highlighting the need to explore this topic in a wider national cohort.

Ultimately, additional data is required on the effect of deprivation on perinatal outcomes in the Irish context. As seen in MBRRACE-UK reports, involving sociodemographic indicators in audit data collection might be an opportunity to identify and yield actionable outcomes.[78,79,90] Integration of socioeconomic data into clinical audit could support a more comprehensive and equitable approach to healthcare delivery. The Lancet SB series also highlights urgent audit on perinatal death to understand causes and guide prevention measures.[81]

2.4.1 Strengths and limitations

Strengths and limitations of this case-control study contribute to a comprehensive understanding of the observed associations. The study addresses a unique and pertinent issue, responding to a gap in the literature regarding the impact of deprivation on SB within the Irish population as identified in the scoping review in Chapter 1 of this thesis. The utilisation of a random and statistically significant 2:1 control-to-case ratio, along with a randomised approach to the selection of the control group, minimises bias risks.[91,92] While this method was considered most effective for this study, there are alternative approaches to selecting a control group that may offer additional advantages, depending on the study's aims and design such as a matched cohort or stratified sampling, among others. For instance, a matched cohort design involves pairing each case with one or more controls that are similar in key characteristics, such as maternal age, gestation at birth, or other confounding variables.[93] This approach can reduce the impact of confounding variables and improve the internal validity of the study by ensuring that the groups being compared are more comparable on these specific factors. However, while matched cohorts can enhance precision in comparisons, they do have limitations. One challenge is the potential for selection bias if an adequate matching criterion is not identified or if the available control subjects do not sufficiently reflect the general population. [93] This may result in a loss of generalisability due to overly stringent criteria. In contrast, the randomised approach used in this study was deemed most appropriate because it ensures that the control group is not subject to selection bias. Randomisation allows for a more accurate representation of the general pregnant population without requiring complex matching or stratification processes.[94] This approach also ensures that the study's

results are not unduly influenced by any specific confounding variables, as the random process distributes potential biases evenly across both the case and control groups. [95] Considering this, the random approach was deemed to be most appropriate for this study to most effectively represent the general pregnant population.[92, 94] The study benefits from clearly defined measurements and a robust triangulation of data between two datasets, with one undergoing a thorough consolidation process with a government agency, the NPRS. Adjustment for available confounding factors, consideration of a recent time period, and an in-depth analysis collectively contribute to the strength of this study.

However, some limitations warrant consideration. The focus on a single outcome, SB, may limit the broader insights that more extensive perinatal outcome data could offer for guiding clinical care and policy. The homogeneity of the study cohort might influence the generalisability of outcomes.[96] The study's single time period examined may not capture dynamic changes. Despite efforts, obtaining the data on all confounding factors was not entirely feasible, influencing the study's ability to adjust for all known maternal risk factors. Incomplete reporting of ethnicity hindered the analysis of its potential confounding effects or its role as a risk factor. This limitation extends to other factors also, such as smoking status, which was not uniformly reported and thus, could not be considered in the analysis. This represents an important limitation of the study as smoking is a significant confounder associated with SB risk.[97]

2.5 Conclusion

In this case-control study at an Irish tertiary maternity unit, no clear association was found between deprivation and SB risk, deviating from the international literature. The absence of a clear link underscores the complexity of SB aetiology, highlighting the need for further national research to understand the relationship between deprivation and adverse perinatal outcome in the Irish context.

While adjusting to quintiles did not change the overall significance, a subtle shift in the variances, particularly in SB due to placental causes, was observed. This revealed a higher percentage of SB attributed to placental causes in the more deprived quintiles. The study highlights additional factors like BMI and booking visit gestation influencing SB risk and maternal age showing more nuanced associations. The results of this study indicate the need for more extensive, diverse population studies on this topic, and integrating socioeconomic indicators into clinical audit. This would allow for the development of focused initiatives to improve maternal and infant outcomes and enhance healthcare equity.

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Thesis Considerations

This thesis, comprised of a scoping review and a case-control study, delves into the intricate relationship between area-level deprivation and SB. The concept of deprivation was demonstrated as complex and multidimensional, mirroring that of the World Health Organisation's Social Determinants of Health (SDH), which are identified as some of the most important influences on health.[1] The scoping review, encompassing upper-middle and high-income countries, consistently revealed a positive correlation between higher levels of deprivation and increased SB risk, evidenced in 22 of the 29 studies included for review (75.9%). The conclusions emphasised the significance of understanding deprivation as a social determinant of perinatal health, advocating for the assessment of deprivation when evaluating SB risk. The subsequent case-control study at an Irish tertiary maternity unit demonstrated no statistically significant correlation between level of deprivation and risk of experiencing SB (p-value 0.288). Hence, deviating from the majority of available international literature, underscoring the complex nature of SB aetiology. The study, adjusting to quintiles, identified a subtle shift in variances, particularly in SB due to placental causes. SB due to placental conditions were seen to be significantly higher in more deprived quintiles (p-value 0.045). This finding is important and could have powerful clinical relevance when assessing a woman's risk factors during her pregnancy. There is a clear opportunity for further research around influence of deprivation on specific cause of death and to further examine why placental causes of death are more prevalent in more deprived areas. Monitoring placental function, with specific screening programs and more frequent monitoring for those more at risk, has the potential for early detection and intervention.[2]

Additional factors like BMI, maternal age and booking visit gestation were identified as impacting SB risk. Obesity >30kg/m2 (aOR 1.9, 95% CI 1.1-3.4, p-value 0.028), advancing maternal age of 35-39 years old (aOR 1.7 (95% CI 1-2.9, p-value 0.047) and late booking visit gestation after 20 weeks gestation (Pearson chi-squared p-value 0.020) demonstrated increased risk. The literature identifies that these risk factors have the potential to be modified through awareness, lifestyle modification and efficient antenatal care.[3,4] This finding demonstrates how both individual level factors (BMI, age and accessing care) and sociodemographic factors contribute to an

individual's risk of experiencing SB. Although, it's worth considering how individual factors are shaped by the broader sociodemographic context. For example, those living in more deprived areas experiencing barriers to accessing their care[5] and thus, having later booking visits. A key point is that area-level deprivation does not operate in isolation but interacts with personal circumstances, which may create compounded vulnerabilities. The intricacies of how sociodemographic and individual factors intersect would benefit from further research. Potentially identifying whether targeting one more than the other can reduce disparities in adverse perinatal outcomes.

While there are many factors that could have influenced the results of the case-control study which did not show a clear association between area deprivation and risk of SB, another consideration is the quality of the service available to pregnant people. The inequality in risk of experiencing SB that was highlighted in the international literature examined in the scoping review in Chapter 1 was not evidenced for the deprived communities of this CUMH cohort. However, in the ROI, there are ongoing national initiatives may be influencing equal and accessible maternity care services in Ireland such as Sláintecare,[6] aiming to transform health care and provide universal access, and also the Maternity Strategy,[7] focusing on the improvement of maternity services in Ireland. A consideration for future research in this area might involve studying more closely the impact of equity of access on the association of SB and adverse perinatal outcomes in the context of deprivation in upper-middle and high-income countries. It would be important to note if the countries represented in the scoping review in Chapter 1 have similar universal access to maternity care. However, simply ensuring that care is available is not enough. This research, in line with previous studies, highlights that even in countries where healthcare is free and seemingly accessible, delays in engaging with services persist. Factors such as lack of awareness, mistrust of healthcare services, and logistical challenges can contribute to delayed bookings for example.[5] One Irish study[8] examining lived experiences of maternity care highlighted several positive aspects of care, including a respectful approach from staff, continuity of care, cost-free services, and convenient appointments. These aspects of care are all potential barriers to individuals accessing the services, especially in more deprived groups.[5] Therefore, tailored approaches that promote healthcare engagement through education, community outreach, and culturally sensitive support systems are essential

to encourage earlier and more consistent care access. By addressing not just the availability but also the utilisation of healthcare services, especially in deprived communities, disparities in perinatal outcomes may be reduced. Further research should explore the effectiveness of these tailored interventions and whether targeting specific sociodemographic factors (e.g., education and healthcare awareness) could alleviate some of the compounded risks associated with both individual and area-level deprivation.

The importance of a systematic and multidisciplinary approach to the reduction of health inequality has been highlighted in the literature.[9] The importance of a multi-agency collaboration has been emphasised to reduce inequalities in pregnancy outcomes by addressing the broader social determinants of health, including that of area deprivation.[10] However, it is also noted that interventions must address the needs of target population.[9] Implementing these models for intervention requires careful adaptation to the specific needs and context of each community to ensure relevance and effectiveness. One recommendation is the involvement of peers in the delivery of such intervention.[9] Facilitating access to care and encouragement of the use of services has also been identified in the literature as areas for targeted intervention.[9,11] Other evidence promotes the application of individualised maternity care, including tailored antenatal risk assessments paired with specific preconception care, also demonstrating the need for collaboration with local public health initiatives.[12,13] This community-responsive approach should be considered in addressing any potential disparities in perinatal outcomes associated with deprivation.

It is also worth noting that not all possible confounding factors could be examined in this study, highlighting the need for more extensive, diverse population studies. Ethnicity, for example, could not be examined in this case-control study. A sociodemographic indicator which notably, is also not encompassed routinely within international deprivation indices, as examined in the scoping review. This absence makes it challenging to fully understand how ethnic background might contribute to socioeconomic deprivation and risk of SB. Given that the literature has identified ethnicity to be an important factor in perinatal health disparities,[10,14,15] it is essential to further explore the relationship between deprivation, sociodemographic indicators and

perinatal health outcomes. Thus, better informing healthcare strategies that assess risks associated with adverse perinatal outcome.

Also evidenced in the scoping review in Chapter 1, is the variance of SB definitions internationally. The extent of the impact of this lack of standardisation cannot be overstated. Primarily, the effect on the families with lived experiences, but also impacting the research around SB and how the rates are compared internationally.[16-18] With no standardisation, the globally reported rates of SB are difficult to compare or draw meaningful conclusions from. Hence, it is imperative for Ireland to also review the nation's definition of SB, to align with international recommendations. Revising the definition of SB could prompt updates to clinical guidelines and healthcare protocols.[15] This would ensure that families receive consistent care and support in line with international best practices, including bereavement care. Moreover, adopting a globally accepted definition can help improve Ireland's internal public health monitoring, guiding more precise healthcare strategies and interventions.[16-18]

While this thesis highlights many important findings, it also identifies areas that would benefit from future research. To better understand the impact of deprivation on perinatal outcome, the case-control study outlined in Chapter 2 could be repeated on a wider, and thus potentially more diverse, national population. Further access to potential confounding factors, such as smoking and ethnicity, would also strengthen the findings. The significance of placental cause of death being higher in more deprived areas noted in this study is an important finding that has the potential to create targeted care plans for those more at risk, this association and the factors contributing certainly warrant deeper review.

Given these insights, it is essential that national health, maternal, and perinatal audits systematically integrate deprivation measures to ensure a comprehensive understanding of the impact of socioeconomic disparities on health outcomes. Incorporating this into routine audits would provide a clearer understanding of the role that deprivation plays in adverse maternal and perinatal outcomes. Consistent reporting of deprivation data in audit would benefit in identifying the areas that are most in need of support, ensuring effective distribution of resources and services. Audit would also allow for the monitoring of trends and effectiveness of

interventions.[19] This in turn, would allow for more targeted healthcare strategies. Thus, supporting a more equitable and efficient maternity service.

The synthesis of the findings from this thesis suggests a nuanced approach to understanding and addressing deprivation's role in adverse perinatal outcomes, encouraging focused initiatives, integrating socioeconomic indicators into clinical audits and research, and ultimately striving for enhanced maternal and infant outcomes with improved healthcare equality.

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Appendices

Appendix A: Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

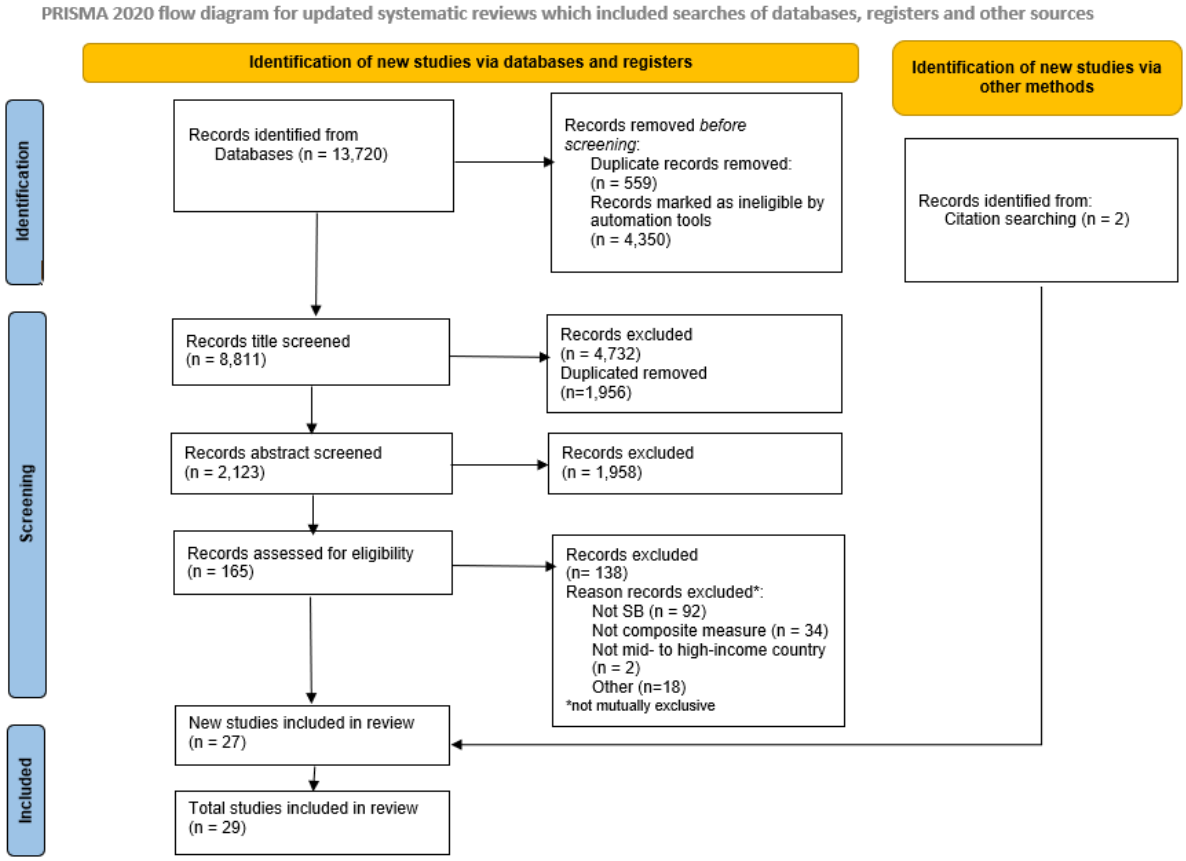
SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	4, 10-11
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	vii-viii
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	10-11
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	11
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	N/A
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	12
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	12-13, Appendix C
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix C
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	13-14
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	14
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	14
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	N/A
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	14

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	15, Figure 1.1, Appendix B
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	16-18/Table 1.1
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	N/A
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	21-25/Table 1.2
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	19-20, 26, 29
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	30-34
Limitations	20	Discuss the limitations of the scoping review process.	34-35
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	36
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	N/A

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.
* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.
† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).
‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.
§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.

Appendix B: PRISMA 2020 flow diagram



Appendix C: Full electronic search strategy terms for database Pubmed

Database: Pubmed **Date: 07/05/2023**		
	Search Terms	**Results**
Concept 1 Problem		
	TI/AB Depriv*	
	TI/AB Poverty	
	TI/AB Inequal*	
1	**Search with OR**	177,205
Concept 2 Setting		
	TI/AB Area-level	
	TI/AB Area	
	TI/AB Neighbourhood*	
	TI/AB Index*	
	TI/AB Geograph*	
	TI/AB Measure	
	TI/AB Location	
	TI/AB Score*	
	TI/AB Calculation	
	TI/AB Formula*	
	TI/AB Social	
	TI/AB Sociodemographic*	
	TI/AB Socioeconomic*	
2	**Search with OR**	5,083,059
Concept 3 Population		
	TI/AB Fetal	
	TI/AB Perinatal	
	TI/AB Pregnanc*	
	TI/AB Intrauterine	
	TI/AB Neonat*	
	TI/AB Intrapartum	
	TI/AB Infant	
3	**Search with OR**	1,170,367
Concept 4 Impact and Outcome		
	MESH Stillbirth	
	MESH Fetal death	
	MESH Perinatal mortality	
	MESH Miscarriage	
	TI/AB Loss	
	TI/AB Death	
	TI/AB Demise	
	TI/AB Mortalit*	
4	**Search with OR**	2,731,496
5	**1 AND 2 AND 3 AND 4**	**1,902**

Appendix D: Deprivation indices included in this review

Deprivation index	Specific measures used
Index of Multiple Deprivation (IMD)	Income, employment, education, health, crime, barriers to housing and services and living environment.
Welsh Index of Multiple Deprivation (WIMD)	Income, employment, health, education, access to services, housing, community safety, physical environment.
Bavarian Index of Multiple Deprivation (BIMD)	Income, employment, education, municipal/district revenue, social capital, environment, security.
Multiple Deprivation Index (MDI) Chile	Crime, education, surrounding green areas, housing, demographics, and Mapuche population.
New Zealand Deprivation Index (NZDep)	In single parent families and aged under 60, on means tested benefit and aged 18-59, below threshold for equivalised household income, without access to a car and aged 18 or over, without qualifications and aged 18-59, unemployed and aged 18-59, separated or divorced and aged 18-59, not in owned home, below threshold for equivalised occupancy, separated or divorced and aged 60 or over.
Dutch index of deprivation	Housing, employment, education, integration and safety.
Social deprivation index (SDI) Brazil	Proportion of permanent private homes that are: a) without water supply connected to the main network, b) with no garbage removal service, c) without a bathroom for the exclusive use of people living there, d) without sewage collection through the main general network for either sewage or pluvial discharge, e) with no nominal monthly income, and f) in which the person responsible for the home was illiterate.
Social Deficiency Index (ICS) Brazil	Proportion of women heads of household, without complete elementary school, and with children under 15 years of age; dependency ratio; distortion rate of secondary education due to total administrative dependency (state, municipal, federal or private); proportion of the population with bathroom and running water; proportion of unemployed persons aged 18 years old or older; and proportion of the extremely poor and mean household income of those vulnerable to poverty.
Socioeconomic status indicator (SESI) Argentina	Percentage of the population who lived in an urban area, had no access to running water or sewer system, had gas connection, met any indicator of unmet basic needs (UBNs), completed only primary education, owned a house, and were employed.
Townsend deprivation score (TDS)	Unemployment, non-car ownership, non-home ownership, and household overcrowding.
Jarman score	Percentage of: elderly living alone, children under 5, unskilled workers, overcrowded households, changed address in last year,

	ethnic minorities, unemployed, households containing lone parents.
Carstairs socioeconomic deprivation score	Car ownership, male unemployment, overcrowding and low social class.
Carstairs-Morris scores	An extension of the Carstairs score, additional variable of low educational attainment and material deprivation.
'Townsend/Carstairs like' index	The proportion of the labour force unemployed; proportion of households with no car access; proportion of households not owner occupied, and the proportion of employed men and women in Social Class 4 or 5.
Index of Relative Socio-Economic Disadvantage for Western Australia	Income between $1 and $25,999 per year, families with children under 15 years of age who live with jobless parents, occupied private dwellings with no internet connection, people aged 15 years and over whose highest level of education is Year 11 or lower, people (in the labour force) who are unemployed, employed people classified as Labourers, occupied private dwellings paying rent less than $215 per week (excluding $0 per week), one parent families with dependent offspring only, people under the age of 70 who have a long-term health condition or disability and need assistance with core activities, people aged 15 years and over who are separated or divorced, employed people classified as Machinery Operators and Drivers, employed people classified as low skill Community and Personal Service workers, occupied private dwellings with no cars, occupied private dwellings requiring one or more extra bedrooms, people aged 15 years and over who have no educational attainment, and people who do not speak English well.
Deprived neighborhoods determined by Dutch government	40 deprived neighbourhoods identified based on: Physical deprivation, propensity to move, level of education, average disposable income per household, employment rates, physical nuisance based on 4 indicators, social nuisance based on 5 indicators, dwelling dissatisfaction, environment dissatisfactions, rates of notified crime and rates of insecurity.
Department of Environment Index (DoE) UK	Social, economic, housing.
National Operations Department report Sweden	Characterized by low socioeconomic resources with high rates of unemployment, foreign-born individuals, overcrowding, a high grade of segregation, criminality and norm-breaking behaviours.

Appendix E: Ethical approval from University College Cork Clinical Research Ethics Committee, including amendments

COISTE EITICE UM THAIGHDE CLINICIÚIL

Clinical Research Ethics Committee of the Cork Teaching Hospitals

Tel: +353-21-4901901
Email: crec@ucc.ie

University College Cork
Lancaster Hall
6 Little Hanover Street
Cork
Ireland

CREC Review Reference Number: ECM 4 (q) 13/12/2022

Date: 7th December 2022

Professor Richard Greene
Consultant Obstetrician
5th Floor
Cork University Maternity Hospital
Wilton
Cork

Study Title: Socioeconomic deprivation as a risk factor for stillbirth: a case-control study

Approval is granted to carry out the above study at:

Cork University Maternity Hospital.

The following documents have been approved:

Document	Approved	Version	Date
Application Form	Yes		Signed 22nd November 2022
CV for Chief Investigator	Yes		
Proof of Insurance	Yes (CIS)		
Data Protection Officer Email	Yes		21st November 2022
Data Collection Sheet	Yes	1.3	17th November 2022
Study Protocol	Yes	1.3	17th November 2022

We note that the co-investigator(s) involved in this project will be:

Name	Appointment Details
Mrs Jessica Keane	Clinical Research Officer
Dr Paul Corcoran	Senior Lecturer & Statistician
Dr Irene O'Farrell	Post-doctoral Senior Researcher
Dr Sara Leitao	Post-doctoral Senior Researcher
Professor Keelin O'Donoghue	Consultant Obstetrician
Ms Laura Robinson	2nd Year Medical Student.

The date of this letter is the date of authorization of this low-risk study.

Please keep a copy of this signed approval letter in your study master file for audit purposes. The study must be carried out in accordance with General Data Protection Regulation and Health Research Regulation 2018/2021.

You should note that ethical approval will lapse if you do not adhere to the following conditions:

1. Submission of an Annual Progress Report/Annual Renewal Survey (due annually from the date of this approval letter). **We would encourage you to keep note of this date as the CREC will not issue a reminder.**
2. Report unexpected adverse events, serious adverse events or any event that may affect ethical acceptability of the study
3. Submit any change to study documentation (minor or major) to CREC for review and approval. Amendments must be submitted on an amendment application form and revised study documents must clearly highlight the changes and contain a new version number and date. Amendments cannot be implemented without written approval from CREC.
4. Notify CREC of discontinuation of the study

5. Submit an End of Trial Declaration Form and Final Study Report/Study Synopsis when the study has been completed.

Yours sincerely

Professor David Kerins
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

COISTE EITICE UM THAIGHDE CLINICIÚIL

Clinical Research Ethics Committee of the Cork Teaching Hospitals

Tel: +353-21-4901901
Email: crec@ucc.ie

University College Cork
Lancaster Hall
6 Little Hanover Street
Cork
Ireland

CREC Review Reference Number: ECM 4 (q) 13/12/2022
& ECM 3 (uu) 09/05/2023

Date: 12th April 2023

Professor Richard Greene
Consultant Obstetrician
5th Floor
Cork University Maternity Hospital
Wilton
Cork

Study Title: Socioeconomic deprivation as a risk factor for stillbirth: a case-control study

Dear Professor Greene

The following documents have been approved:

- Amendment application form signed 5th April 2023
- Data Collection Sheet Version 1.5 dated 27th March 2023
- Study Protocol Version 1.5 dated 27th March 2023.

Full approval has been granted to implement this amendment.

Yours sincerely

Professor David Kerins
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

Appendix F: Data collection sheet V1.5

1 - List of variables to be obtained via CUMH maternity records:

Demographics:

Age

Marital status

Employment status

Ethnicity

BMI

Smoking status

Alcohol use

Drug use

Medical history:

Previous or ongoing conditions requiring treatment

Previous pregnancy:

Number of previous pregnancies

Number of previous live births

Number of previous perinatal losses

Previous pregnancy problems

Antepartum care:

Booking visit gestation

Number of antepartum visits

Birth:

Gestation at delivery

Onset of labour

Mode of birth

Birthweight

2 - List of variables to be obtained via NPEC Perinatal Mortality Audit:

Demographics:

Age

Marital status

Employment status

Ethnicity

BMI

Smoking status

Alcohol use

Drug use

Medical history:

Previous or ongoing conditions requiring treatment

Previous pregnancy:

Number of previous pregnancies

Number of previous live births

Number of previous perinatal losses

Previous pregnancy problems

Antepartum care:

Booking visit gestation

Birth:

Gestation at delivery

Onset of labour

Mode of birth

Birthweight

Stillbirths:

Main cause of death

Gestation at diagnosis of death

Antecedent factors

3 - List of variables to be obtained via iPMS (Integrated Patient Management System):

Address, or postcode where available, to calculate small area code

Appendix G: Local Information Governance Group (LIGG) and Data Protection Officer approval

NH Niamh Henderson (PA to Director of Midwifery, CUMH) <Niamh.Henderson@hse.ie>
To: Jessica Keane

LIGG Report Template.docx
306 KB

[EXTERNAL] This email was sent from outside of UCC.

Dear Jessica,

I can confirm your proposal 'Socioeconomic deprivation as a risk factor for stillbirth: a case-control study' has been noted by the LIGG and approved by the EMC. We would like to wish you every success in the completion of your study and look forward to receiving your final results.

The final report (template attached) can be forwarded via email to niamh.henderson@hse.ie This report will be sent to the LIGG.

Many Thanks,

Niamh Henderson
PA to Katie Bourke, Director of Midwifery
4 East Room 19 | Cork University Maternity Hospital
Tel: (021) 4920699 | + 353 (0)87 4374029 | **E-Mail :** niamh.henderson@hse.ie

IRELAND SOUTH WOMEN & INFANTS DIRECTORATE | UCC University College Cork, Ireland Coláiste na hOllscoile Corcaigh

From: Katie Murphy (PA to General Manager CUMH) <katie.murphy6@hse.ie> **On Behalf Of** Miriam Lyons (CUMH General Manager Head of Operations)
Sent: Monday 21 November 2022 11:02
To: Joye McKernan <joye.mckernan@ucc.ie>
Cc: miriam.lyons <Miriam.Lyons@hse.ie>
Subject: FW: Study for review: Socioeconomic deprivation as a risk factor for stillbirth: a case-control study

[EXTERNAL] This email was sent from outside of UCC.

Hi Joye,

I can confirm that Miriam Lyons as DPO has reviewed and approved the following application: **Socioeconomic deprivation as a risk factor for stillbirth: a case-control study**

Kind Regards,

Katie Murphy

PA to Miriam Lyons General Manager | Head of Operations

4 East, Cork University Maternity Hospital
☎ 021-4920502 / 087-4303850

IRELAND SOUTH WOMEN & INFANTS DIRECTORATE | UCC University College Cork, Ireland Coláiste na hOllscoile Corcaigh

From: Joye McKernan <joye.mckernan@ucc.ie>
Sent: Thursday 17 November 2022 19:00
To: Katie Murphy (PA to General Manager CUMH) <katie.murphy6@hse.ie>

Appendix H: Data request form submitted to the National Perinatal Epidemiology Centre (NPEC)

NATIONAL PERINATAL EPIDEMIOLOGY CENTRE

Data Request Form

Section 1: Requester Information	
Name	**Jessica Keane**
Job Title	**Research Support Officer, MSc student**
Employer/Place of Work	**NPEC**
Telephone	**0861360039**
E-mail	**Jkeane@ucc.ie**
Names of other persons having access to data	
Prof. Richard Greene	
Dr. Paul Corcoran	
Dr. Sara Leitao	
Prof. Keelin O'Donoghue	
Ms. Laura Robinson	

Section 2: Data Requested
Please specify data items required: CUMH Stillbirth cases -
Demographics (Age, marital status, employment status, ethnicity, BMI, smoking status, alcohol and drug use)
Medical history (Previous or ongoing conditions requiring treatment)
Previous pregnancy details (Number of prev. pregnancies/ live births/ perinatal losses or any previous pregnancy problems)
Booking gestation
Birth details (gestation, onset, mode of birth, birthweight)
Stillbirth main cause of death, gestation at diagnosis, antecedent factors

CUMH Severe Maternal Morbidity cases-	
Admission to ICU	
Years for which data is required	2018-2021
Maternal age range	All
Geographical area of residence (County, HSE region, electoral division)	All

Section 3: The Proposed Research

Description of the proposed study (including title, objectives, methods)

Socioeconomic deprivation as a risk factor for stillbirth: a case-control study

This study aims use a deprivation index to measure a woman's level of deprivation based on her residence and analyse whether there is an association between socioeconomic deprivation and risk of stillbirth, assessing for relevant confounding factors.

An observational design will be utilised for this research project. A case-control study will be conducted, matching cases of stillbirth with a control cohort of live births. A ratio of 2 controls: 1 case will be identified.

This case control study will use retrospective data over 5 years, from January 1st 2018 to December 31st 2021. The study will be conducted in Cork University Maternity Hospital (CUMH) using clinical records for chart review and secondary data analysis. The project is being done in the context of a Research Masters degree, whereby the student will be working under direct supervision of the PI, a consultant obstetrician in the CUMH.

This data request is being made to the National Perinatal Epidemiology Centre (NPEC) for data pertaining to stillbirth cases submitted by the CUMH for the annual Perinatal Mortality Audit for the 5-year reporting period. The data points relating to maternal, obstetric and infant factors, as outlined above, will be gathered and compiled onto the study excel database. The request also includes data from the NPEC's Severe Maternal Morbidity Audit pertaining to maternal admission to ICU for the control cohort to match this variable to the cases. The MSc student has the capacity to interact with

the co-ordinators of the audits on the CUMH site to help identify cases and link details in this regard.

Request to access the maternity clinical records via the electronic health record called the Maternal and Newborn Clinical Management System (MN-CMS) will also be submitted. A list of MRNs for the stillbirth cases will be provided by the NPEC Perinatal Mortality Audit co-ordinator for the CUMH, who is a co-investigator of this project, in order to access the relevant maternity clinical records. Once the required data has been collected, this list will be securely destroyed.

The CUMH maternity records will be accessed, via the MN-CMS, to gather further information for the stillbirth cases that is not collected as part of the NPEC audit, including number of antepartum visits. The data in the CUMH maternity clinical records for the stillbirth cases will then be crosschecked with the data submitted for the NPEC Perinatal Mortality Audit to ensure no cases are missed and to allow for the triangulation of data using NPEC's standardised and validated dataset.

The CUMH maternity clinical records will also be accessed for selection of the live births for the control group. The list of births on the MN-CMS will be accessed to identify two live births as per the inclusion criteria. A randomised approach may be used to identify the control cohort such as randomly selecting two times the number of stillbirth cases from the study period (after removing the stillbirth cases from the birth list) or a systematic approach may be utilised, such as selecting the 3rd birth before and after the stillbirth. Where this birth does not meet the inclusion criteria, the next live birth from this will be selected.

Data will also be collected from iPMS (Integrated Patient Management System). This system will be accessed for the woman's address, or postcode where available, in order to calculate the small area code that will used to measure level of deprivation for the whole cohort.

The data points will be collected from the sources outlined and compiled onto the main study database. The same data will be collected for the cases and controls, except in some instances where there will be non-applicable points such as cause of death.

Data will be extracted from the maternity clinical records by the MSc student under direct supervision of the PI using a HSE computer. Only the MSc student and PI will have access to the identifiable data in order to extract the relevant data points. All data will then be fully anonymised and compiled on the main study database. No identifiable data (e.g. date of birth, address) will be available on the main

study database. The woman's address will be used to identify a small area of residence and a code representing this small area will be recorded in the main study database, not the address. The fully anonymised dataset will be kept on an encrypted UCC server with restricted access to the research team only. UCC staff co-investigators of this project will only gain access to the anonymised dataset for analysis purposes. Data compiled onto the main study excel file will then be analysed using SPSS (Statistical Package for the Social Sciences) software. General Data Protection Regulation (GDPR) protocols will be adhered to throughout the project with confidentiality maintained.

Type of analysis to be performed on data
Odds ratios will be calculated using logistic regression including multivariable models that will adjust for relevant confounding factors.

Proposed linkages with other databases – please specify the databases
MN-CMS, Maternal and Newborn Clinical Management System (electronic health records) iPMS (Integrated Patient Management System)

Previous research in this area by you/your institution
The institution, NPEC, have established audits on perinatal mortality. No previous research has been done in relation to level of deprivation and its effect on stillbirth rates by me or my institution to my knowledge.

Proposed journals/reports for publication:
Literature review and case-control study, aim to submit to Obstetric/Maternity related journals.

Proposed end date of project	December 2023

Declaration by Requester

I have read and understand the conditions under which this data is being provided by the

National Perinatal Epidemiology Centre.

I undertake:

a) to use the data only for the purposes specified in the request;
b) not to transmit or provide the data to anyone not mentioned in the data request. I will ensure that all approved collaborators understand that they may not share the dataset or any part of it;
c) not to use the data, or allow it to be used, in any way which is in breach of the EU General Data Protection Regulation ("GDPR") and the Irish Data Protection Acts, 1988 to 2018 (the "DPA") – known collectively in this policy as "the Data Protection Acts".
d) not to attempt to identify any individual from the data;
e) to delete or destroy the data at a specified time, and to inform the NPEC that this has been done;
f) to acknowledge the NPEC as the source of the data , e.g. "based on data provided by the National Perinatal Epidemiology Centre, Ireland", or similar agreed acknowledgement in any publication;
g) to acknowledge NPEC contributors and stakeholders as follows: "We thank the patients and staff of the maternity units in Ireland who have contributed data to the National Perinatal Epidemiology Centre. We are grateful to the individual units for their participation in the NPEC national clinical audits and the data co-ordinators at unit level who facilitate data submission. We thank the NPEC, the NPEC Governance Committee and the NPEC Perinatal Mortality Group / Severe Maternal Morbidity Group (as appropriate) which facilitate this work. {Additional Contributors to be added where necessary}";
h) not to present in the results of analyses or other reports, or in releases of information concerning such reports, any information that might identify a patient;
i) to seek ethical approval where applicable.

Print Name: Jessica Keane

Signature:  Date: 21/02/2023