Pan-Lancashire Neonatal Mortality Review

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December 2013

Introduction

Over recent years there have been steady decreases in neonatal mortality rates for England and Wales from around 6.7 neonatal deaths per 1000 live births in 1981, to 2.9 deaths per 1000 live births in 2011. Improvements in maternal healthcare have greatly contributed to this reduction. Despite this there is evidence that many deaths taking place in early infancy are linked to modifiable or lifestyle factors such as smoking, alcohol and obesity. Consanguinity also has an important role to play in excess infant mortality locally and rates tend to be higher in some south Asian communities.

The Child Death Overview Panel for Lancashire collates and reviews agency level data for every child death under the age of 18 years. The resulting dataset and individual case notes contain a valuable source of information that can be used to support the efforts of public health policy and practice to reduce neonatal mortality. The aim of this study is to provide an analysis of the data collected by CDOP for neonatal deaths that took place between 2008-11. A review of the literature was undertaken to identify key modifiable risk factors for early infant death. Associations between risk factors and reported neonatal deaths were then explored with recommendations for action.

Aim

The aim of this was study was to provide an analysis of modifiable risk factors associated with neonatal mortality in Lancashire using routine data collected by Child Death Overview Panel 2008-11. Modifiable risk factors were broadly defined as those factors that may be changed through lifestyle choices.

Methods

Case Definition

Cases were identified through the CDOP database using the following definition:

Infant deaths were included as cases in the study if they met all of the following criteria:

- Death of an infant<28 days that occurred between April 1st 2008-March 31st 2011
- A gestational age 24 weeks+
- Infants with a gestational age of >24 weeks
- Normal residence-Lancashire, Blackpool, Blackburn with Darwen
- Death reported to and reviewed by the Child Death Overview Panel (CDOP).

NB The analysis does not include infants born at less than 24 weeks gestation as these are not considered viable pregnancies.

Exclusion criteria

The following cases were not included in the study. It was agreed that these groups would be analysed separately.

- Stillbirths, births <24 wks and late Termination Of Pregnancies

Development of a database

In line with guidelines set out by *Working Together to Safeguard Children* the Child Death Overview Panel collates and reviews agency level data for every child death under the age of 18 years. Information is submitted to the CDOP administrator using the document A/B-Agency Report Form. This data is collated and stored as an individual case file. As part of the review process CDOP maintains a database containing a minimum dataset of all child deaths.

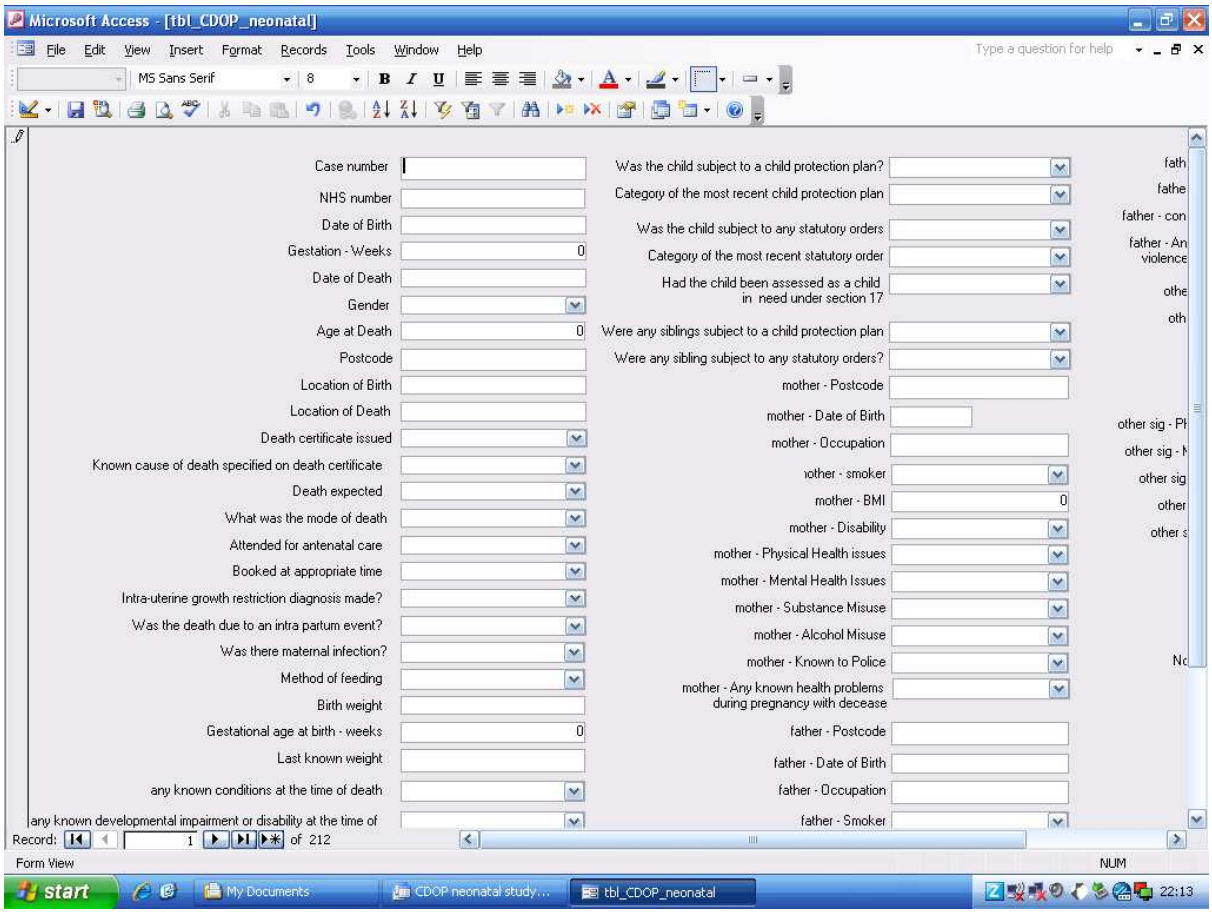
It was recognised that the existing database was fairly limited on the information that could be used for the purposes of this study. Although individual case records contained a wealth of information around maternal health and obstetric notes this level of information is not included in the CDOP database. For example, case records include information derived from clinical notes on maternal lifestyle factors such as body mass index (BMI), smoking status and alcohol use. In order to capture this detailed information it was necessary to construct a bespoke database.

A small public health intelligence task group met to determine the relevant data fields to be included in the database. A dataset was constructed using data fields derived from the Form A/B-Agency Report Form. The benefits of this approach were that this information is collected routinely and would therefore be fairly complete. Additional data fields were informed by a literature review that identified modifiable risk factors (and other areas of interest) associated with perinatal- neonatal deaths. These risk factors included:

- Maternal age
- Maternal Health-obesity, chronic diseases, infection, substance misuse
- Multiple deliveries
- Living in deprived area
- Gestational age/weight (small or large for gestational age)
- Gender of infant (male preponderance)

A full list of the data fields included in the collection tool is included in appendix 1. The database was constructed by a public health intelligence specialist using a Microsoft Access platform. A form view was created to facilitate entering information on to the database from each of the individual case records. See fig 1 for a screenshot of the database.

Figure 1



Information Governance

The Caldicott Guardian for NHS Central Lancashire was contacted about the research and to check if formal ethical approval was required. It was also required to liaise with Lancashire County Council to adhere to information principles adopted there. In order to carry out the research I was required by the Safeguarding manager to sign a confidentiality agreement with the council. All data collection that required accessing individual case records was carried out at the Safeguarding offices. All data extracted from the case records was recorded on the database constructed specifically for the study. The dataset for each individual was pseudo

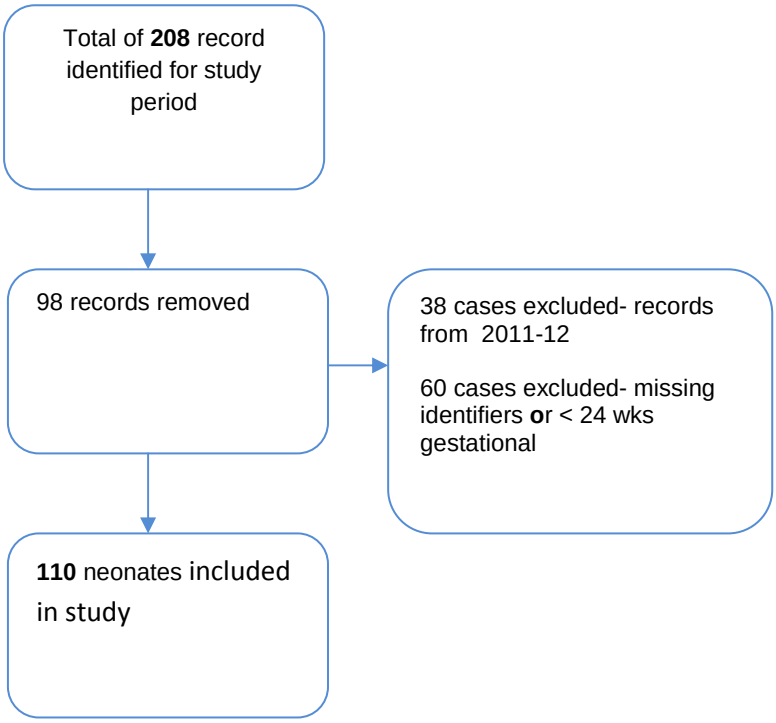
anonymised by stripping out personal identifiable information and allocating a unique number so it could be linked to the case record if necessary. All data was stored in password protected files on an encrypted portable laptop.

Results

A total of 208 records were extracted from the CDOP database. A total of 98/208 cases were excluded. 38 cases were removed from further analysis as they were records from the financial year 2011-12 and a further 60 cases were also excluded either because they had missing identifiers or were for cases that were born at less than 24 weeks gestational age. It is intended that these infants born at less than 24 weeks are analysed in a separate study. The reason for this is so that the case definition used for neonates in this study is comparable with definitions used in other studies.

After exclusion criteria had been applied the total number of cases included in the study group was 110 neonates for the period April 1st 2008 to March 31st 2011 inclusive. See fig. 2

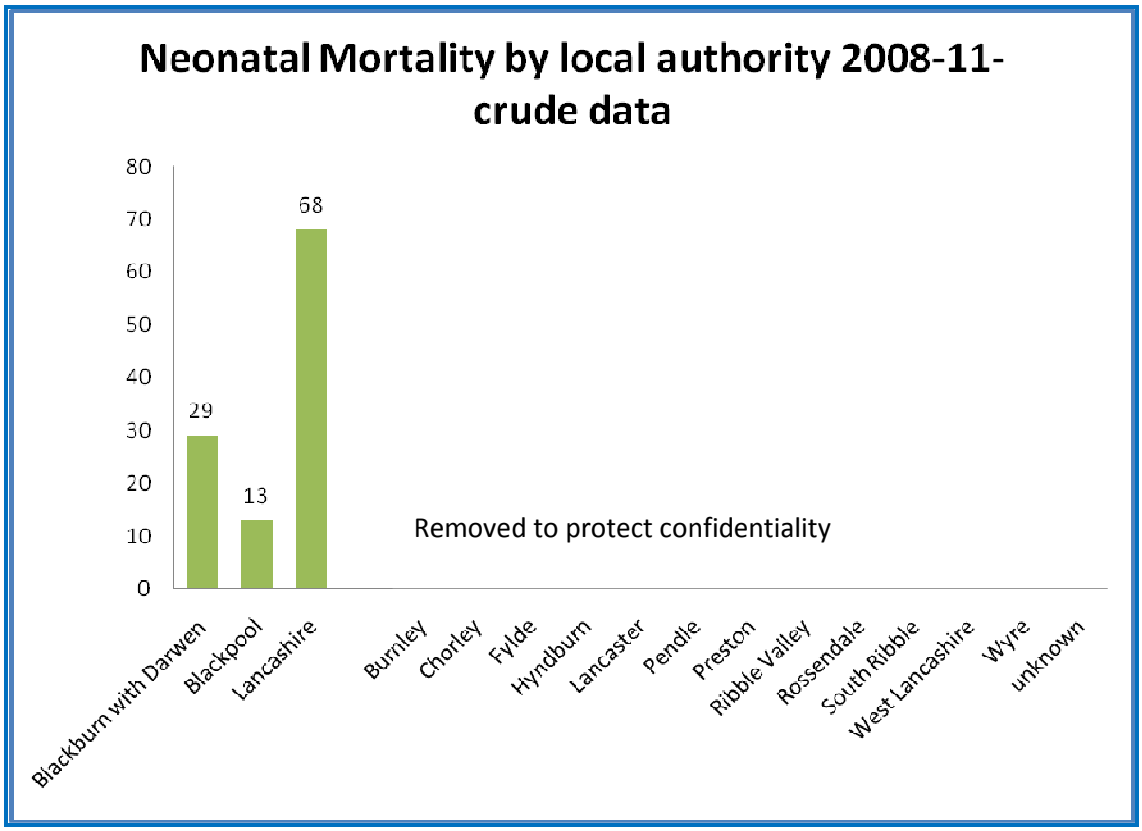
Figure 2 Flow chart of inclusion and exclusion process



Neonatal Mortality-by local authority

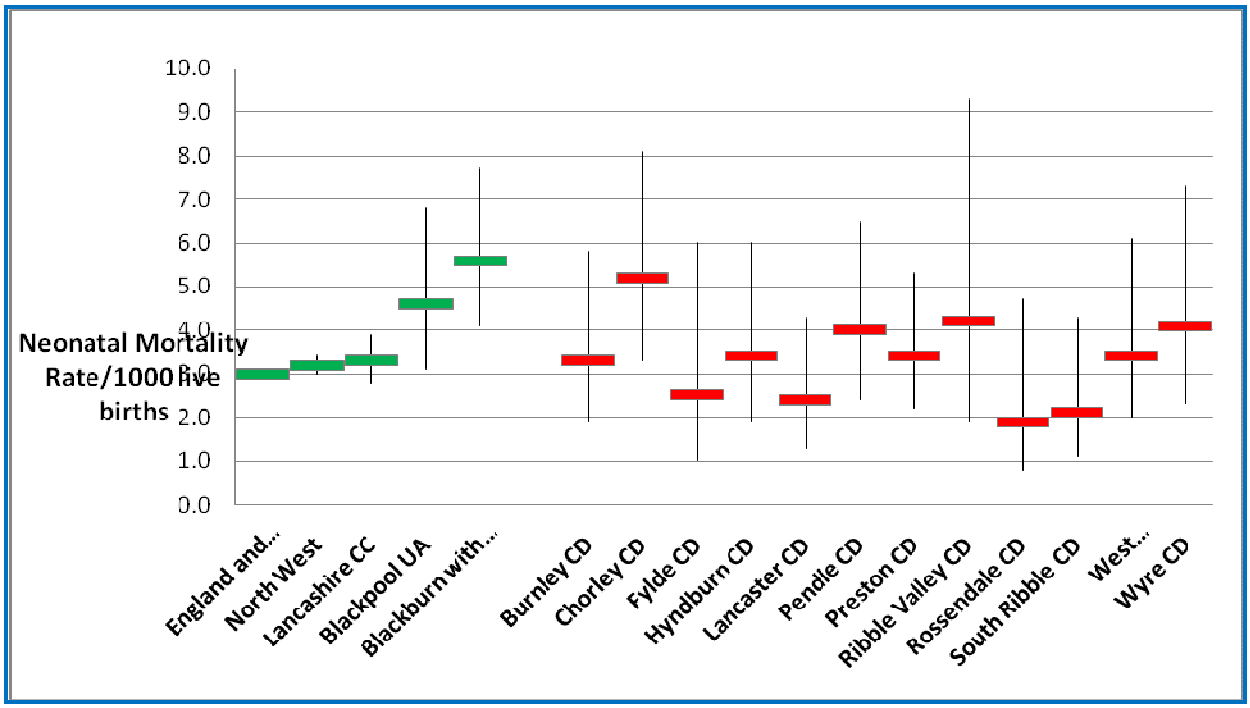
Figure 3 displays the number of neonatal deaths reviewed by CDOP for each local authority area between 2008-2011. Lancashire county had the highest number of neonatal deaths (n=68) over the 3 year study period. However this is crude data and does not account for the size of the population for the area.

Figure 3



Neonatal mortality can more accurately be compared using neonatal mortality rates. Fig 4 displays neonatal mortality rates extracted from ONS with national, regional and local comparisons(pooled 2009/11.) Mortality rates and corresponding confidence intervals are given in Table 1.

Figure 4



For England & Wales and the North West region neonatal mortality rates were 3.0 per 1000 and 3.2 per 1000 live births respectively in 2009/11 (pooled data). Rates for Lancashire are slightly higher at 3.3 per 1000 live births (2.8-3.3). However these differences are not statistically significant (95% CI's overlap with England and Wales and the North West). Blackpool has a neonatal mortality rate of 4.6 per 100 live births (3.1-4.6). However differences between Blackpool and regional and national comparisons are not statistically significant. Blackburn with Darwen has the highest neonatal mortality rates with 5.6 per 1000 live births (CI 4.1-5.6). Blackburn does appear to have an excess of neonatal mortality with a rate of 5.6/1000 compared with NW and Lancashire. (95% CI's do not overlap). See table 1.

Table 1 Neonatal mortality rates (pooled 2009-11)

	Rate per 1,000 live births	RateLL	RateUL
England and Wales	3.0	3.0	3.1
North West	3.2	3.0	3.4
Lancashire CC	3.3	2.8	3.9
Blackpool UA	4.6	3.1	6.8
Blackburn with Darwen UA	5.6	4.1	7.7
Burnley CD	3.3	1.9	5.8
Chorley CD	5.2	3.3	8.1
Fylde CD	2.5	1.0	6.0
Hyndburn CD	3.4	1.9	6.0
Lancaster CD	2.4	1.3	4.3
Pendle CD	4.0	2.4	6.5
Preston CD	3.4	2.2	5.3
Ribble Valley CD	4.2	1.9	9.3
Rossendale CD	1.9	0.8	4.7
South Ribble CD	2.1	1.1	4.3
West Lancashire CD	3.4	2.0	6.1
Wyre CD	4.1	2.3	7.3

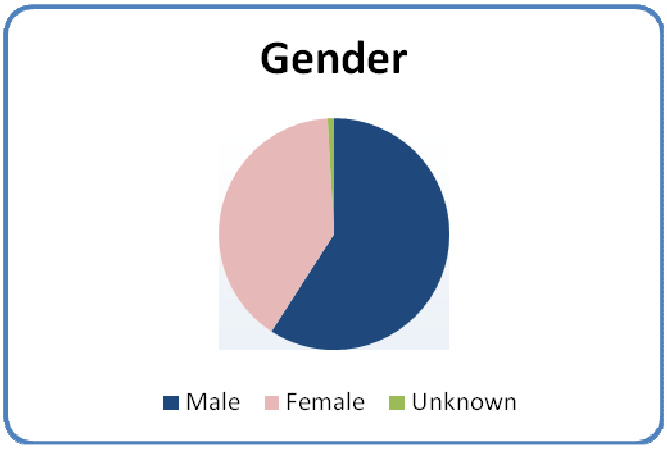
CHARACTERISTICS OF CASES

In total there were 110 cases over the time period 1st April 2008 to March 31st 2011 included in the study. The following section sets out the characteristics of cases.

Cases-by gender

For neonatal deaths recorded by CDOP there was a higher proportion of males to females (see fig 5) 65/110 cases (59%) of cases were male; 44/110 cases were female; 1 case was unrecorded. It is well known that mortality rates are higher for males in early neonatal period than females. One study by Binet (2012)[i] examined outcomes and survival of extremely premature babies by gender. Mortality was highest for neonates born at 24-26 weeks and this was significantly higher for males.

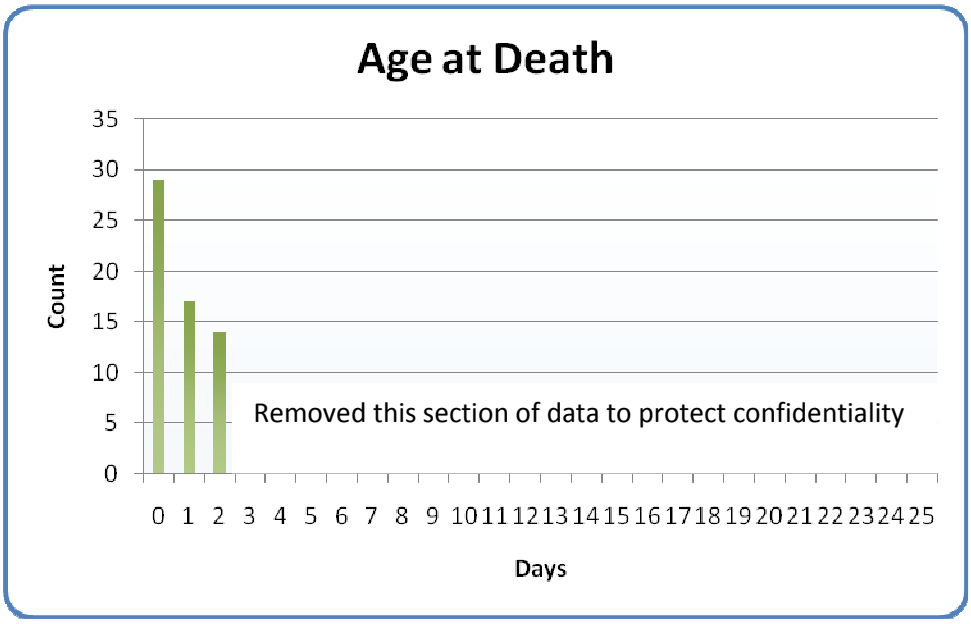
Figure 5



Cases-by age at death

In the study period the majority of neonatal deaths 81/110 occurred in the seven days of life (73.6%). The remaining 29 cases died between 8-28 days- after birth see figure 6. This is in line with a report produced by WHO (2012) that reported around three quarters of all newborn deaths occur in the first week of life.[ii]

Figure 6. Neonatal mortality-age at death



Cases- by gestational age

Pre-term births refer to those births that take place before 37 weeks gestation. A large proportion of cases in the study were pre-term babies: 69/110 of cases (63%). The majority of live births nationally (88.6%) take place at term (37-41 weeks). The category 'pre-term' can be further sub-divided:

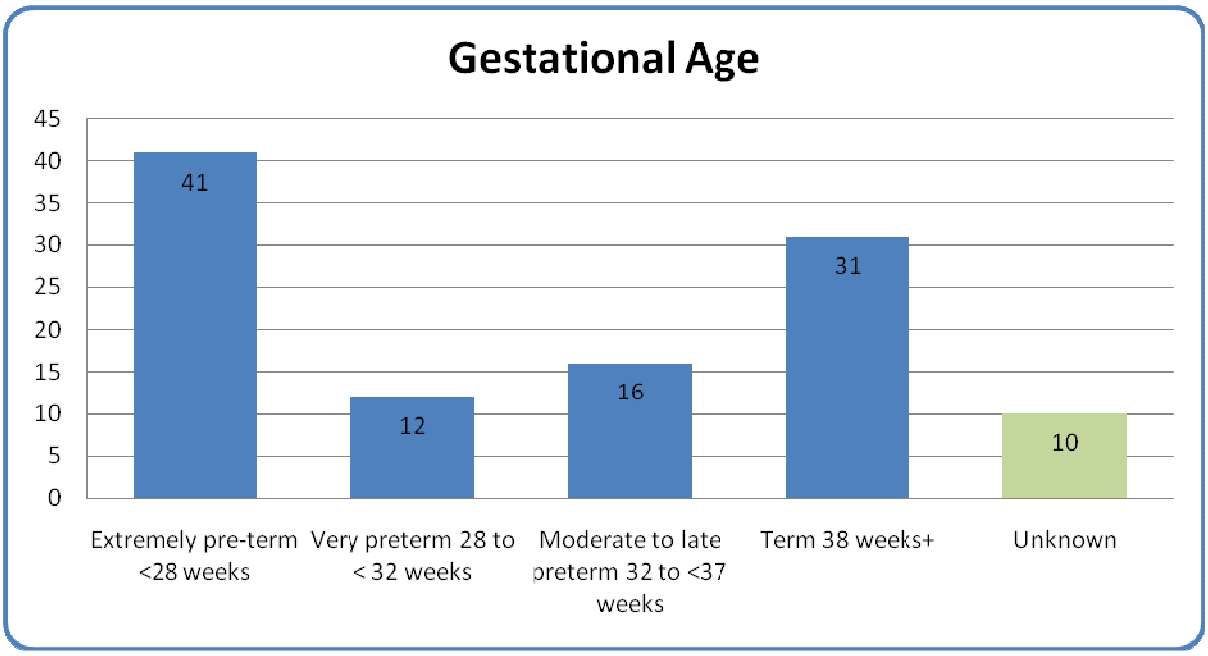
- Extremely pre-term < 28 weeks
- Very pre-term 28 to < 32 weeks
- Moderate to late pre-term 32 to < 37 weeks

Figure 7 displays the number of neonatal deaths by gestational age category. The majority of neonatal deaths were in *extremely pre-term* infants between 24 and 28 weeks gestation n=41 (37.3%). 12 cases (10.9%) were *very preterm* between 28 to

< 32 weeks and a further 16 cases (14.5%) were *moderate to late* pre-term 32 to <37 weeks.

Term births are those infants born at a gestational age of 38 weeks and over with *post term* births defined as those infants at 42 weeks or over. The second highest of proportion of cases was in term babies (38 weeks +).

Figure 7-cases by gestational age stratum



Prematurity or pre-term delivery is a well known major risk factor linked to infant death. In one large cohort study by Khashu et al (2009) the risk of dying in the first week of life was seven times higher for pre-term infants compared with term infants and this was stastically signifant (RR 7.0 CI 3.8-8.9).

Recommendation: to carry out further analysis and explore evidence base around pre-term births including late preterm.

Cases-by Cause of Death

Following review by the CDOP a category for cause of death is assigned to each case. These are a numerical value 1-10. Figure 8 displays the cause of death for:

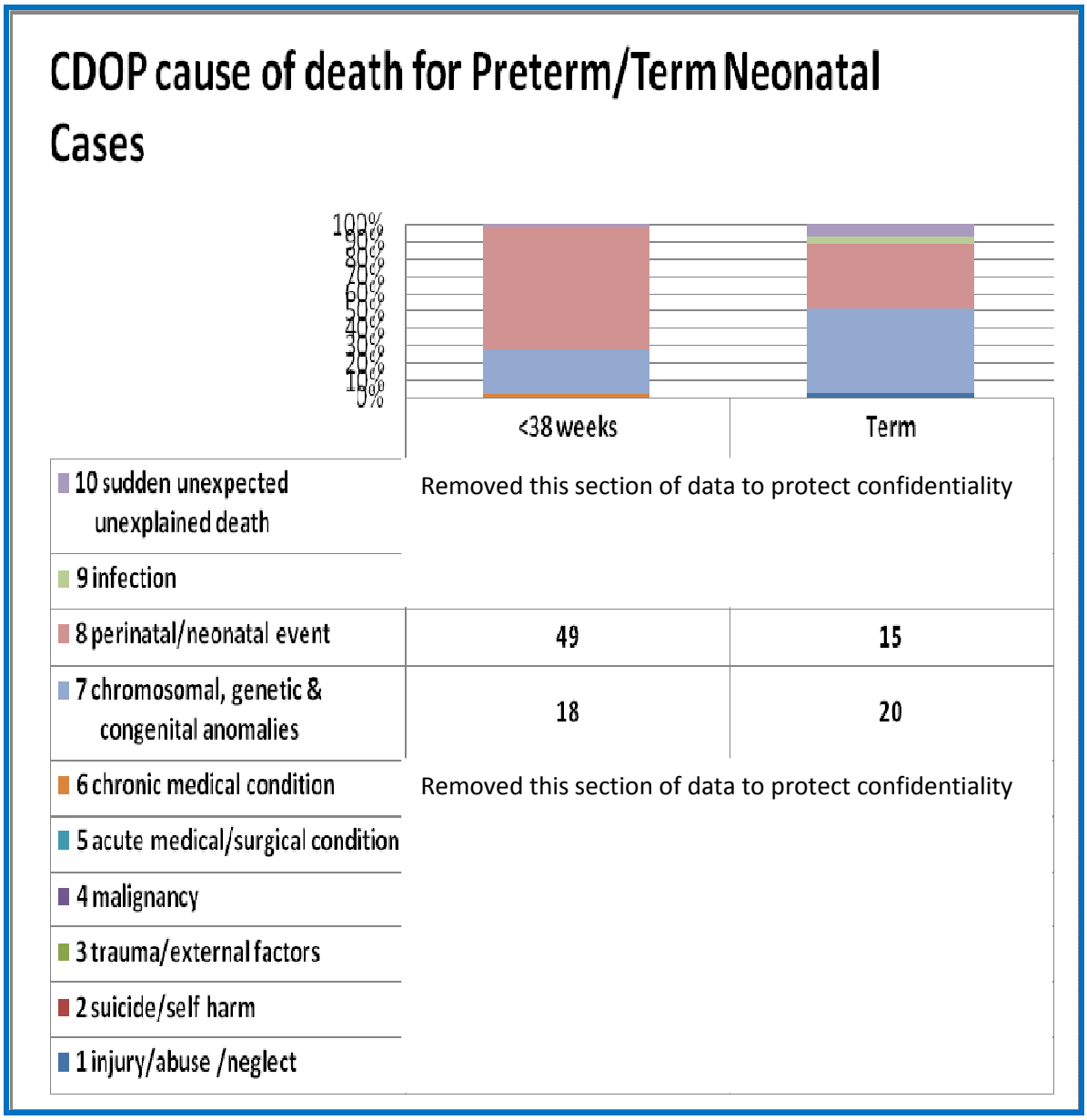
(1) preterm babies (infants born at 38 weeks gestation or less) and

(2) term babies (infants born at 40 weeks or more)

For **pre-term** infants the largest proportion of deaths was for category 8-perinatal/neonatal events-49/69 case (71%); followed by category 7 chromosomal/genetic/congenital anomalies-18/69 (26.1%). For **term** infants the largest proportion was for category 7 Chromosomal/genetic/congenital followed by category 8-perinatal/neonatal events 15/41 (36.5%).

The differences in proportions may be due to larger numbers being in the preterm group compared with the term group. The definitions for the categories use are also very wide and it may be useful to have more detail e.g. ICD coding for each case.

Figure 8



Recommendation: review definitions used by CDOP for cause of death and look at other ways of providing more detail.

Cases-by birthweight

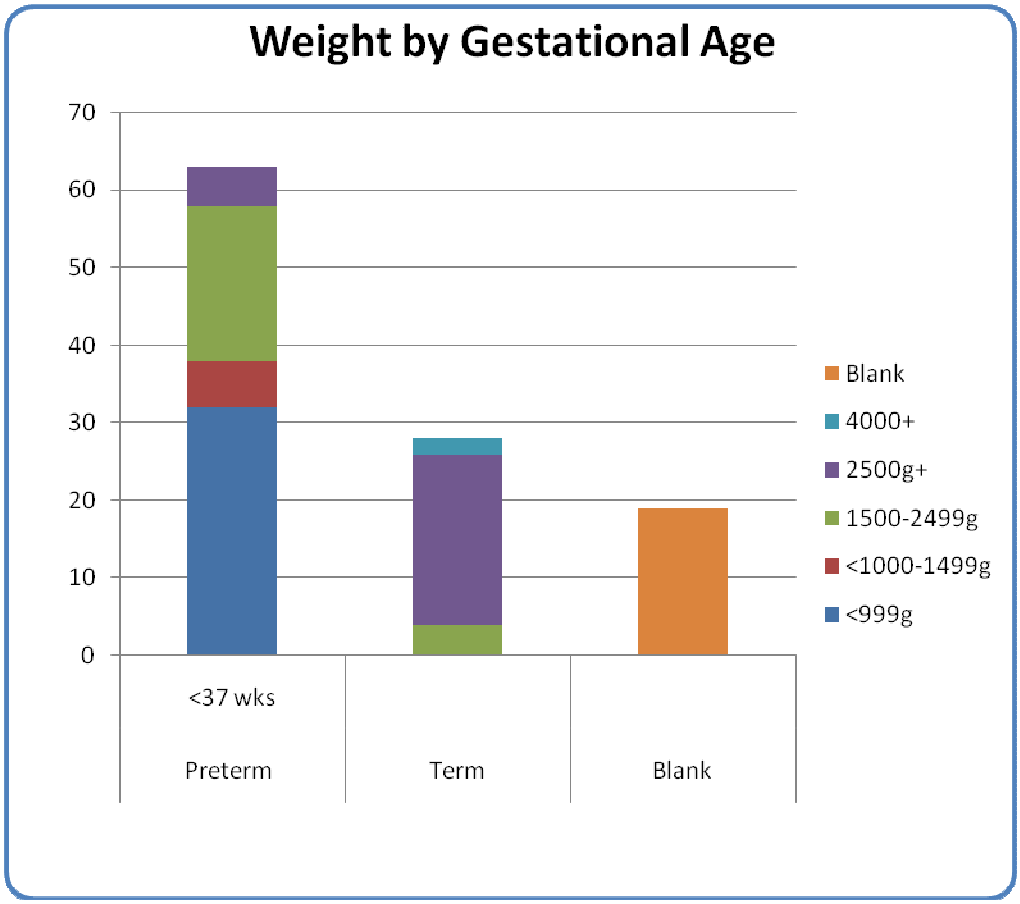
There is a strong association between gestational age and birth weight. Low birth weight is defined as an infant born with a birthweight 2500g or less regardless of the gestational age. In this study data on weight and gestational age was available for

91/110 cases. Overall the birthweight of 62/91 cases (68%) was considered to be low birth weight.

In *pre-term* infants 58/63 cases (92%) were low birth weight. Around half of those cases 32/63 (50.8%) had birth weights <999g.

In *term* infants with a gestational age of 38 weeks and over 4/28 cases (14%) were low birth weight. Fig 9 shows proportions of cases by weight and gestational age.

Figure 9



Cases-by Size for Gestational Age

Size for gestional age (SGA) is a measure of foetal development and is a composite measure combining gestional age and birth weight. Measurements for newborns can be plotted against standardised growth curves set out by the World Health Organisation. Categories for newborn infants weight for gestational age are set out below:

- **Large for gestational age**: Weight is above the 90th percentile at gestational age
- **Macrosomia**: Weight is above a defined limit at any gestational age
- **Appropriate for gestational age**: Normal birth weight
- **Small for gestational age**: Weight is below the 10th percentile at gestational age
- **Low birth weight**: Weight is below a defined limit at any gestational age

25/110 cases recorded by CDOP were small for gestational age ie <10th percentile. A number of studies have indicated that SGA infants are at increased risk of mortality and pre-term infants are at particular risk. Grisaru-Granovsky (2012)[iii] found that SGA infants of 24-31 weeks gestation had over a twofold risk of mortality OR 2.37 (CI 1.94-2.90) compared with a reference population of infants with normal birth weights.

However the aetiology of SGA may be constitutional rather than pathological. In one study by approximately 50-70% of fetuses with a birth weight below the tenth centile for gestational age were reported as constitutionally small[iv] Furthermore there may also be differential birth weights between ethnic groups. Infants born to South Asian women do tend to have lower birth weights. This presents important life course challenges as low birth weights are linked with adult cardiovascular disease and diabetes. Some of the factors cited for lower birth weight in south Asian communties are genetic factors, sub-optimal maternal nutrition, low pre-pregnancy weight and low socio economic status.[v]

Studies have shown that infants who are LGA or macrosomic are at increased risk of early mortality. In a cohort study by Zhang (2008)[vi] 5 983 409 infants with birth

weights 4500-4999g had significantly higher risks of early neonatal mortality OR 1.8 (1.3 to 2.4) compared with reference category 3500-4499 g. In the CDOP study 5/110 cases were large for gestational age(> 90th percentile). In an article by Vasudevan (2011) adverse consequences of maternal obesity included increased risk of foetal macrosomia.[vii]

CDOP do not routinely collect data on 'weight for gestational age' however this could be incorporated into future datasets as this is an important metric for childhealth with lifecourse implications.

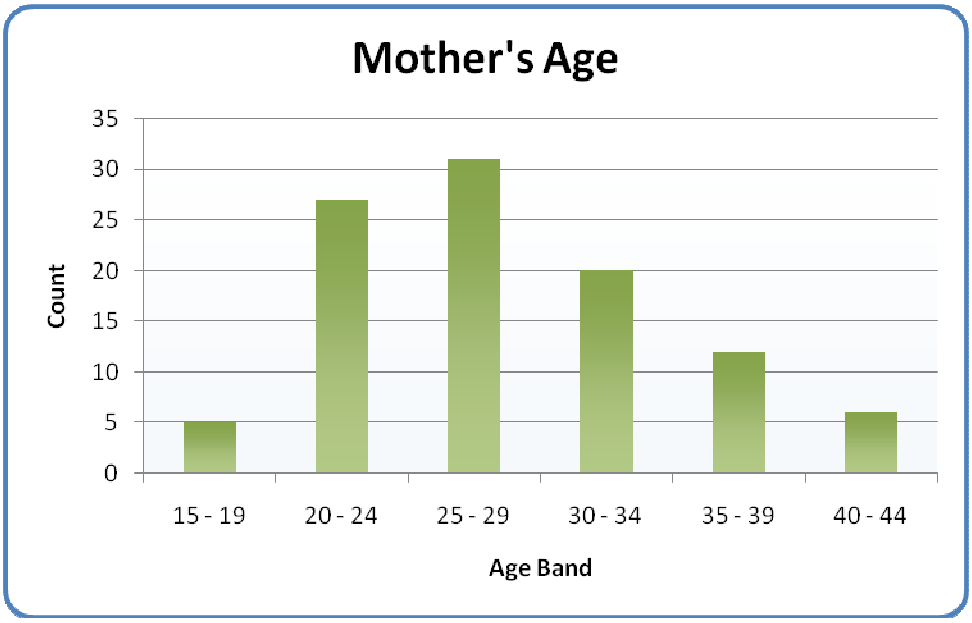
Recommendation: Look at the feasbility of reporting the weight for gestational age for infant mortality cases.

CHARACTERISTICS OF MOTHERS

Maternal Age

Figure 10 displays the frequency of the maternal age for the neonatal deaths across the study period. The largest numbers of cases were born to women aged 25-29 years. ONS data for 2011 indicates that babies born in England and were most likely to have a mother aged 25–34, with over half (56%) of mothers in this age group.[viii]

Figure 10



Maternal age is an important risk factor for perinatal and neonatal mortality. In a systematic review by Carolan & Frankowska (2011) older maternal ages 35-39 years and over 40 years were at increased risk of neonatal mortality.[ix] Furthermore in a cohort study by Lisonkova (2010) older mothers were found to be at increased risk of pre-term birth and small for gestational age infants (adjusted Odds Ratio 1.5 (CI 1.4 to 1.7) for women aged 35 to 39 years; and aOR 1.6 (95% CI 1.3 to 2.0) for women aged 40 years.[x]

Socio-economic Status

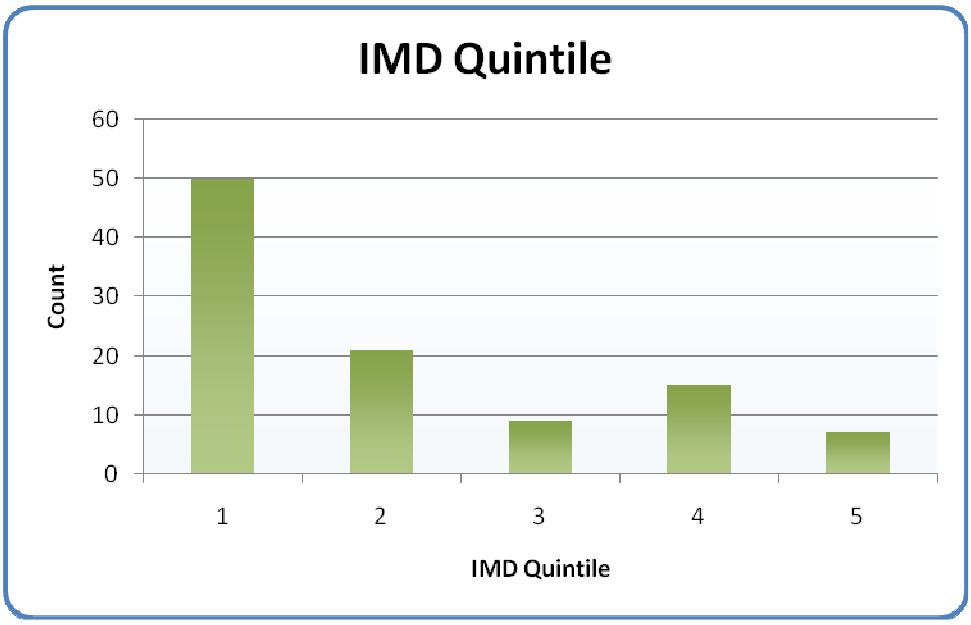
The Index of Multiple Deprivation is a composite measure of deprivation for small areas known as lower super output areas. Lower Super Output Areas are homogenous small areas of relatively even size (around 1,500 people) of which there are 32,482 in England**.** Deprivation is scored across 6 domains: Income Deprivation, Employment Deprivation, Health Deprivation and Disability, Education Skills and training Deprivation, Barriers to Housing and Services, Crime, and Living Environment Deprivation[xi]. LSOAs can be grouped and divided up into deprivation quintiles with 1 being the most deprived and 5 the least deprived.

The postcode of residence for each neonatal death in the CDOP study was linked to the corresponding IMD quintile. Figure 11 displays the frequency of cases by IMD quintile. Neonatal mortality demonstrates a social gradient with the majority of cases being from the poorest neighbourhoods. 50 cases (45.5%) were from the poorest neighbourhoods.

The majority of cases were from poorer areas with highest proportions for Blackburn with Darwen 19/50 (38%) followed by Blackpool 7/50 (14%) then Preston. Blackpool and Blackburn are local authorities with high proportions of the most deprived lower super output areas in the country.

It should be noted that lower socio-economic groups also tend have a higher fertility rate so a disproportionate number of infants are born to those groups compared with more affluent neighbourhoods. However the relationships between deprivation, and adverse pregnancy outcomes are well documented in the literature. In a retrospective cohort study examining outcomes of over 200 000 pregancies in Liverpool by Taylor-Robinson (2010) risk for neonatal death in the most deprived areas was 5 times that of the least deprived areas (RR 5.9 (1.4,10.3).[xii]

Figure 11

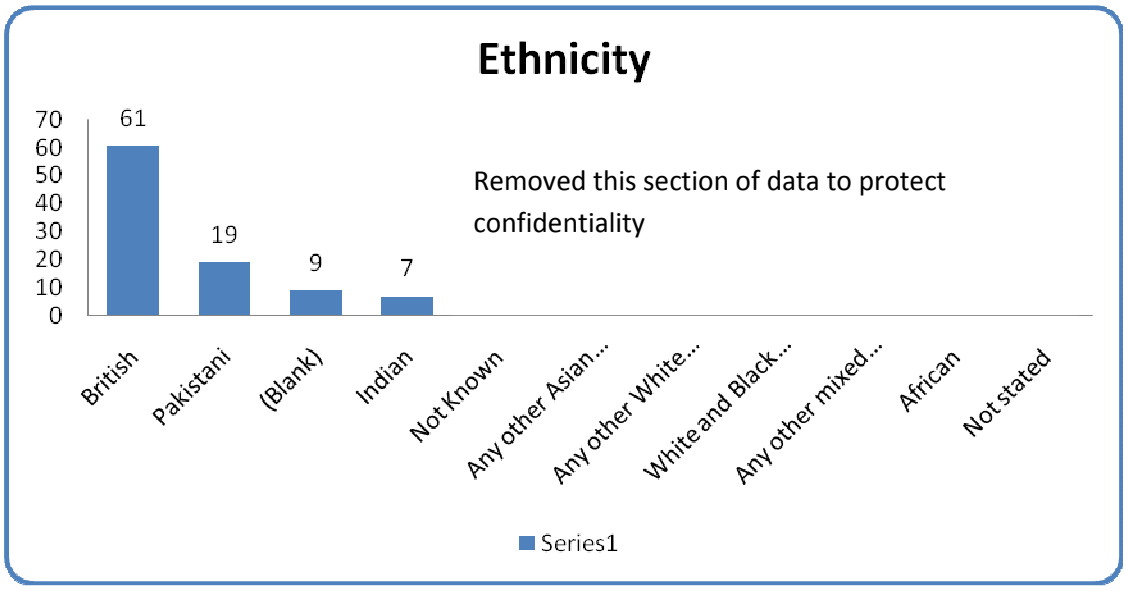


Recommendation: Look at ways of calculating neonatal mortality rates adjusted for maternal age and deprivation

Ethnicity

Figure 12 shows the frequency of cases by ethnicity. The largest number of neonatal deaths were classified as British n=61 (55.5%) followed by Pakistani (17.3%).

Figure 12



Consanguinity

Consanguineous marriages relates to partnerships between close blood relatives. In the UK consanguinity is found throughout various social groups but most predominantly in those groups who identify themselves as Pakistani. Consanguinity is known to increase the risk of inherited disorders caused by recessive genes with risks of increased rates of child mortality and lifelong disability. [xiii]

At the start of the CDOP study anecdotal reports suggested that consanguinity may be a feature associated with neonatal mortality amongst ethnic minority groups. In the hand held pregnancy notes pregnant women are asked to provide information on whether the baby's father is a blood relative. In cases of neonatal death this information is routinely collected by the CDOP AB form.

Table 2 displays the number of cases that involved a consanguineous partnership recorded by CDOP over the study period. 21 cases were recorded.

However it should be noted that there were a significant number of missing data items (n=48, 43.6%) for this item.

Table 2

Consanguineous union?	Number of cases	%
Yes	21	19.1
No	39	35.5
Unknown	Removed this section of data to protect confidentiality	
Blank record	48	43.6

Figure 12 displays the breakdown of the cases by ethnic grouping. 16/21 cases were Pakistani.

Figure 12 Consanguinity-by ethnic grouping

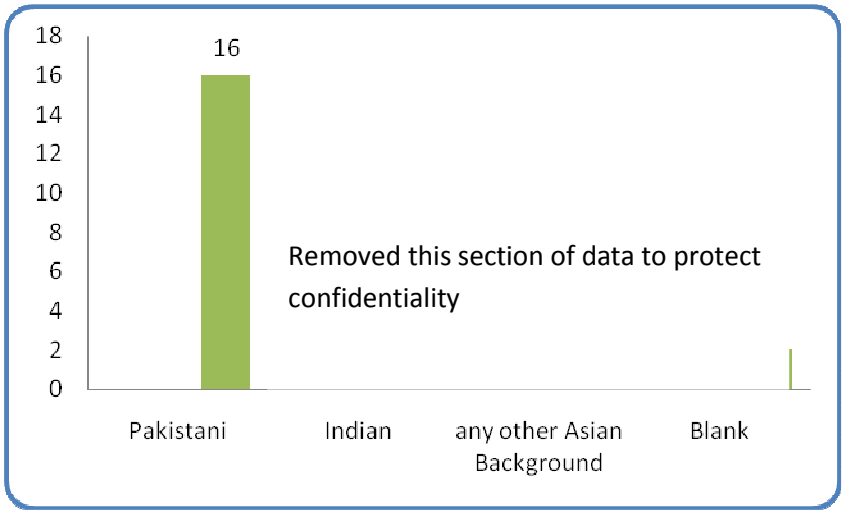


Figure 13 displays the area of residence for the cases. The highest proportions were for Blackburn with Darwen 12/21 an area with a large Pakistani community. There is currently further study being undertaken by the public health team at Blackburn with Darwen Council to examine community and professional perspectives across these issues.

Figure 13 consanguinity –by area of residence

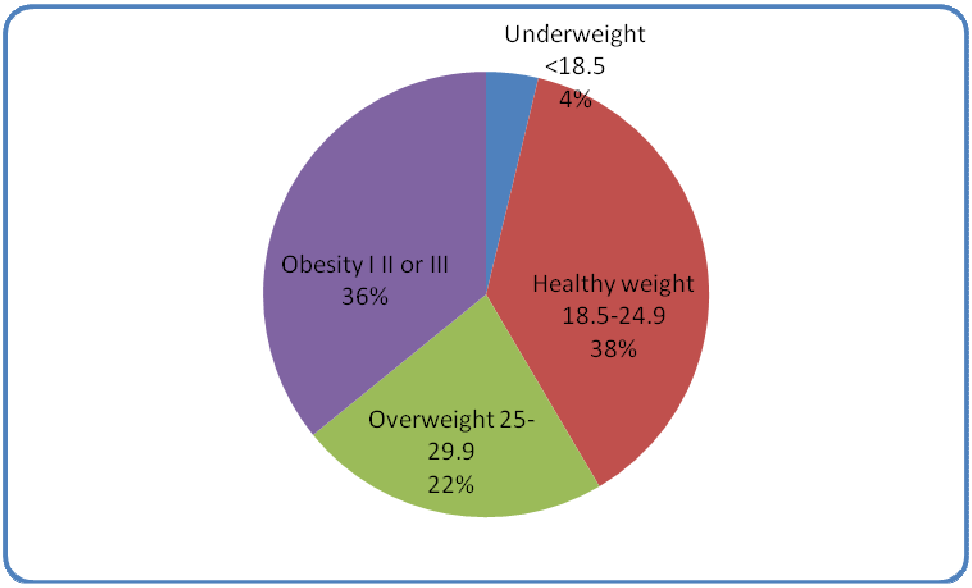
Removed this section of data to protect confidentiality

Recommendation: Explore the apparent excess of mortality associated with consanguinity in Blackburn with Darwen as part of the larger scale public health genetics programme of work.

Maternal weight

Figure 14 displays the proportions for cases by maternal body mass index BMI. The largest proportion of cases had a mother classed as 'healthy weight' (38%). However when the overweight and obese groups are combined this is overwhelmingly the majority group (58%). It should be noted however that 57/110 of cases (52%) had missing data.

Figure 14



There are a multitude of studies that have identified associations between high BMI and adverse pregnancy outcomes. For example in a retrospective cohort study of 40932 pregnancies Tennant et al (2011)[xiv] found that women with a BMI of 30 or higher had a twofold increased risk for neonatal death and risk was highest in the early neonatal phases (less than 7 days following birth). This increased risk remained significant even when statistical adjustments were made for maternal age, ethnicity, smoking and birth weight.

Recommendation:

Review local weight management pathways and initiatives

Examine the factors that may contribute to low recording of maternal weight.

Maternal substance misuse at booking

Figure 15 displays maternal substance misuse at the time of booking. 5/110 were classed as 'alcohol misusing'; 5/110 were classed as substance misusing and 26/110 were smokers. However there were a large number of unreported and blank data fields. Substance misuse is an important concern for public health and therefore the completeness and quality of this data should be addressed by stakeholders.

Figure 15

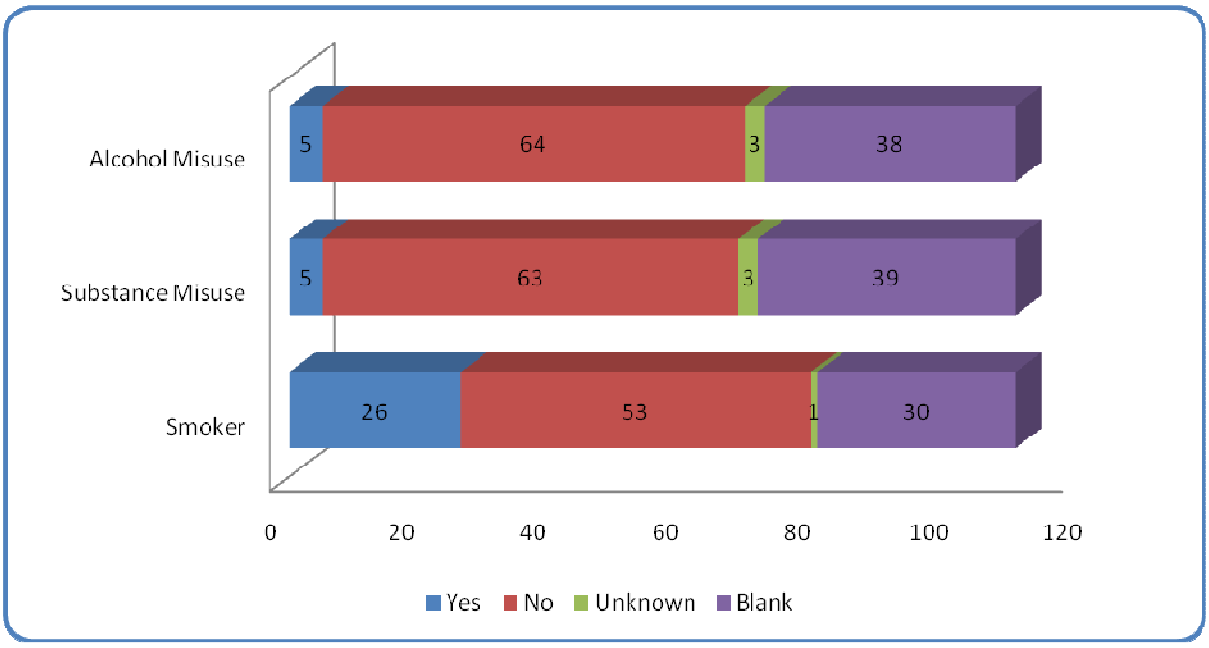
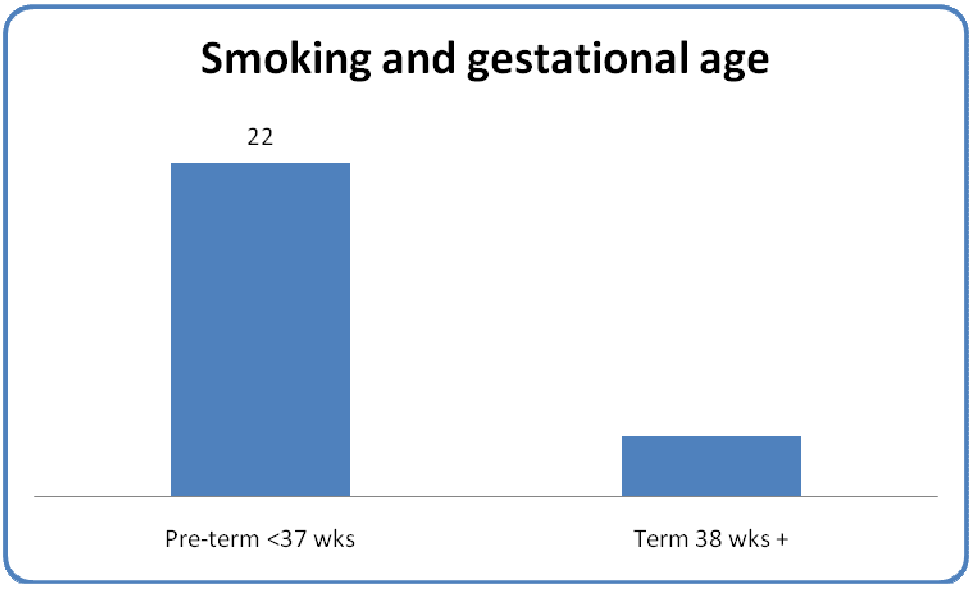


Figure x illustrates the gestational age of cases born to smoker mothers. 22/26 were born *pre term* at less than 37 weeks and 4/26 cases were *term.* Smoking is a well known risk factor for a range of adverse pregnancy outcomes including prematurity. In a Swedish study Kallen et al (2001)[xv] examined the outcomes of 1 413 811 pregnancies. The study found an increased risk for intrauterine growth restriction, small head circumference and pre-term birth. There was also a dose response relationship between smoking and increasing risk across all adverse outcomes.

Recommendation:

Examine factors that may contribute to low recording of substance misuse issues.

Figure 16



Further issues

Other potentially modifiable risk factors associated with neonatal mortality that could not be analysed in this study due to a lack of routinely collected data by CDOP are:

Diabetes- a number of studies have demonstrated evidence that both type 1 and type 2 diabetes and poor glycaemic control are linked with a range of adverse pregnancy outcomes, This includes increased risks of macrosomia (extremely large for gestational age infants) which in turn is linked to an increased risk of neonatal mortality.

Inter-pregnancy interval- an interval of less than 6 months between pregnancy have been identified as an independent risk factor for extremely preterm birth aOR 2.2, (CI 1.3 to 3.6)

Previous neonatal deaths

In one study women with a previous history of death of a neonate are at a five fold increased risk of subsequent neonatal death of infant aOR 5.73 (3.46–9.50)

CDOP and Data Issues

The Data Quality Management Model[xvi] is a framework used to understand different data challenges (fig 17). The model has four dimensions: application, collection, warehousing and analysis. These dimensions are discussed below in relation to information management used in relation to CDOP data.

Application: *the purpose of the data collection*.

Each CDOP has a responsibility to collect data on all child deaths under the age of 18 years. This data is used by the CDOP to fully understand the events leading up to a childs death and inform recommendations around lessons learned and future service improvments.

Collection: *the processes by which data elements are accumulated*

Agency level data for each child death is collected using the document A/B-Agency Report Form. All data must be returned within a specified timeframe.

Warehousing: *Processes and systems used to store data*

Report forms are collated and stored as individual case files to be reviewed by the CDOP panel. In addition a database containing a minimum dataset of all child deaths and uses the financial year as the reporting cycle. For the purposes of this study a bespoke database had to be constructed. Each case file was accessed and the information was used to populate the database. This proved to be very onerous and time consuming. CDOP collects very comprehensive dataset for each child death record. However without further investment in a database or data warehouse there is little scope for public health research

Analysis: *The process of translating data into usable, meaningful information*

Figure 17 The Data Quality Management Model

Characteristics of Data Quality

Data Accessibility:

There are legal and mandatory requirements for agencies to collect all the information required by the AB form. Data is collected, retrieved and stored confidentially in line with information governance regulations**.**

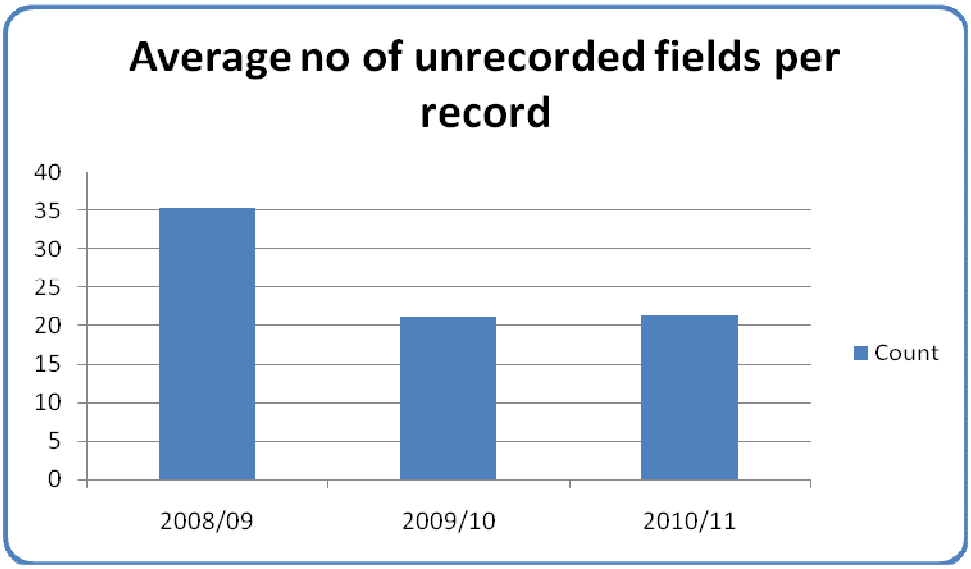
Data Accuracy:

It is difficult to assess the extent to which CDOP data are free of identifiable errors. Quality checks would be useful as part of the overall assurance process.

Data Comprehensiveness:

Processes for the recording of child death data by CDOP is improving over time. Figure 18 shows the number of missing data items per record

Figure 18



However there are still significant gaps for important fields including BMI, substance misuse and consanguinity. Reporting agencies should be reminded of the importance of completing all data fields for public health research and statistical analysis**.** Where there are gaps it may be worth exploring if these are sensitive areas that practitioners find difficult to discuss and therefore record.

Data Consistency:

The AB forms is based upon the pregnancy and birth notes and are therefore reliable and consistent across reporting organisations.

Data Currency:

Data collected by the CDOP remains current and does not become incorrect or redundant at different times.

Data Definition:

Definitions used in the collection and collation of data are universal across health care agencies. This is useful for comparing datasets. However, reporting years across different organisations. For example ONS mortality data is collected by calendar year whereas CDOP collects data by financial year.

Data Granularity: The level of detail of healthcare data provided is variable. For example for substance misuse responders are asked to indicate whether a mother uses substances by stating yes, no or unknown with additional space for details. However this data cannot be collated in a meaningful way for analysis. Considerations should be given to how information relating to lifestyle choices are reported to support further analysis.

Data Precision: CDOP data is fairly precise with data collection based on universal reporting methods

Data Relevancy: A wealth of information is collected for each infant death to support the CDOP process. However this information only be accessed on a case by case basis as the data is stored in individual files. Resourcing of a database is essential to support future research and development purposes.

Data Timeliness: CDOP data is up to date as far as possible. However the availability of data can be significantly delayed due to legal restrictions such as police or coroner investigations.

Recommendations: There is significant under-reporting across a number of data fields. Reporting agencies should be reminded of the importance of completing all data fields for public health research and statistical analysis**.**

CDOP may consider a data validation exercise to provide assurances that all infant deaths are reviewed. This would involve data matching with another routine mortality data source such as death registration records.

Most importantly CDOP should consider investing in a comprehensive database that can be used to analyse trends and generate hypotheses for further study.

Literature Search Strategy: Modifiable Risk Factors and Neonatal Mortality

Aim: To identify relevant literature relating to maternal modifiable lifestyle factors associated with an increased risk of neonatal deaths.

Focused Question:

What is known from the existing literature about modifiable risk factors during pregnancy that may result in higher risk of neonatal deaths?

Search methods for the identification of studies

The following concepts and keywords were identified from the focused question and used for the search strategy.

What is known from the existing literature about modifiable risk factors during pregnancy that may result in higher risk of neonatal mortality?

Concept	Keywords	Search Terms
Pregnancy	**Pregnancy** **Maternity** **Antenatal**	**Pregnan* OR** **Matern* OR** **Antenatal**
Risk Factor	**Risk factor(s)** **Risk(s)** **Feature(s)**	**Risk* OR** **Factor* OR** **Feature***
Neonatal	**Neonatal** **Perinatal**	**Neonat*** **Perinatal**
Mortality	**Death** **Mortality**	**death OR mortality OR outcome**

Boolean Operators

Boolean operators 'AND' / 'OR' and truncated word endings denoted by * were used to define and facilitate the search strategies.

Medical Subject Headings (**MeSH**)

MeSH is a controlled vocabulary for indexing journals and can be used as a thesaurus for searching the MEDLINE database. MeSH terms were also defined for the literature search using the online search engine:

"Infant Mortality/etiology"[Mesh]

Inclusion Criteria

In order to capture the most recent research only literature published from 2000 to 2013 published in the English language was included in the review. Types of studies included in the search were: systematic reviews, meta-analyses, cohort studies and case-control studies. As this was a preliminary literature review to inform the neonatal study relevant articles were also included. Studies and articles were included if the focus was modifiable risk factors associated with perinatal or neonatal deaths. Modifiable risk factors were broadly defined as those factors that may be changed through lifestyle choices.

Exclusion Criteria

Literature focusing solely on stillbirths was excluded. Studies from developing countries and those that focused on non-modifiable risks were also excluded.

Electronic searches

The following bibliographic databases were used for the search. These databases are included in the NHS Evidence search engine.

- **MEDLINE-**1950 to Present
- **CINAHL-**1981 to Present
- **EMBASE**-1980 to Present
- **BNI**-1985 to present British Nursing Index

Other sources for searching relevant literature included:

- **NICE**
- **The Lancet**
- **BMJ**
- **Google Scholar**
- **SANDS**
- **The Cochrane Library**
- **Bandolier**

Search Strategies

The following sets out search strategies for the electronic database used in the literature search.

MEDLINE

1.	MEDLINE	(risk * OR factor*).ti,ab [Limit to: English Language and Humans and Publication Year 2000-current]; 1152214 results
2.	MEDLINE	(neonat* OR perinatal).ti,ab[Limit to: English Language and Humans and Publication Year 2000-current]; 63271 results
3.	MEDLINE	exp. INFANT MORTALITY/etiology ; 72562
4.	MEDLINE	(death OR mortality OR outcome).ti,ab[Limit to: English Language and Humans and Publication Year 2000-current]; 592179 results
5.	MEDLINE	(UK OR Eng OR Brit* OR Scot* OR Wales OR Ireland OR Eire)ti.ab [Limit to: English Language and Humans and Publication Year 2000-current];209454 results
6.	MEDLINE	1 AND 2 AND 3 AND 4 [Limit to: English Language and Humans and Publication Year 2000-current]; 623 results

CINAHL and EMBASE

1.	CINAHL EMBASE	(risk* OR factor*).ti,ab [Limit to Publication Year 2000-2013]; 263786 results
2.	CINAHL EMBASE	(neonat* OR perinatal).ti,ab [Limit to Publication Year 2000-2013]; 20202 results
3.	CINAHL EMBASE	(death OR mortality OR outcome).ti,ab[Limit to Publication Year 2000-2013];
4.	CINAHL EMBASE	1 AND 2 AND 3 [Limit to Publication Year 2000-2013];2579 results

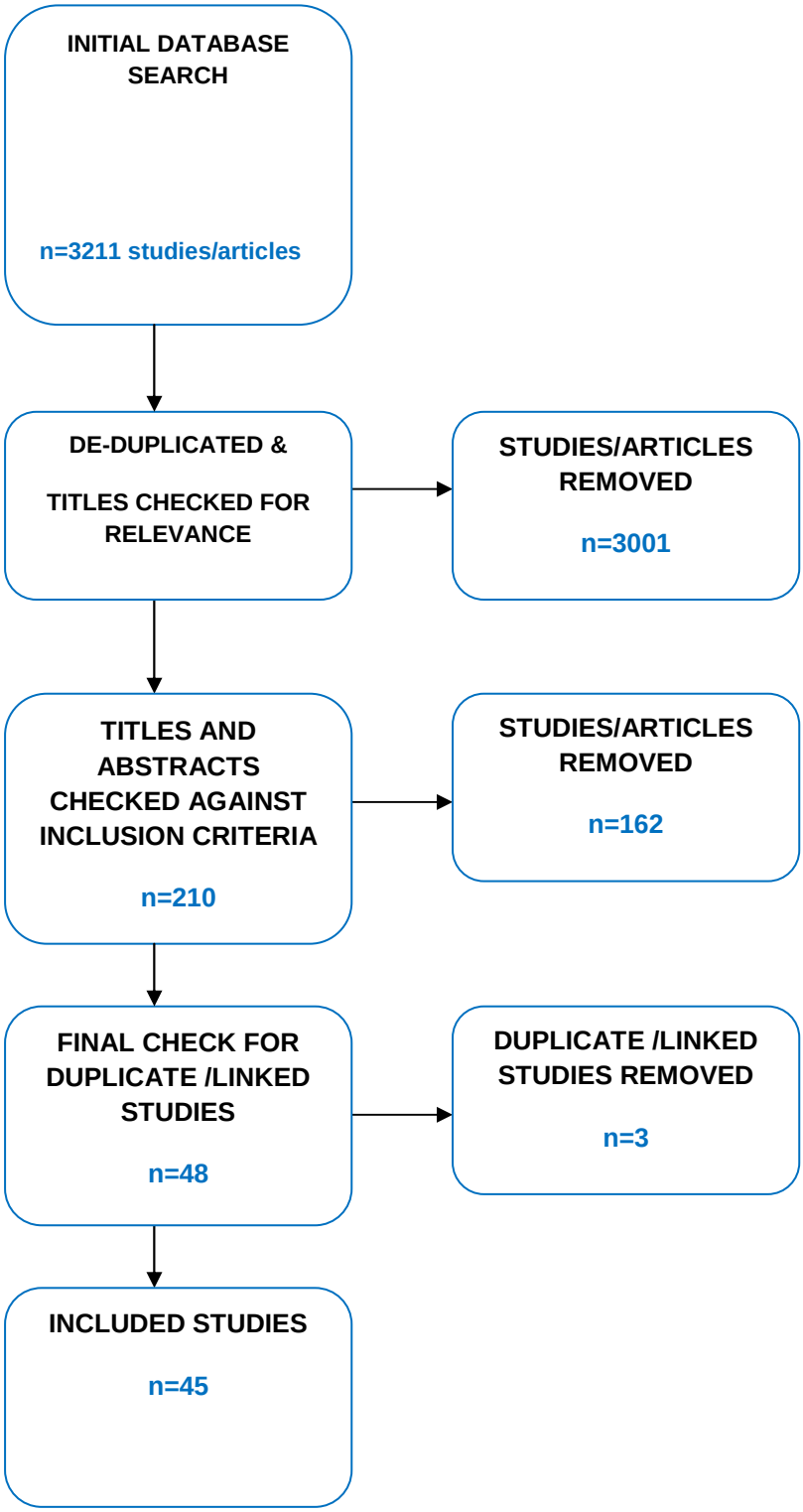
BNI

1.	BNI	(pregnan* OR matern*).ti,ab;8255 results
2.	BNI	(risk* AND factor* OR feature).ti,ab;3974 results
3.	BNI	exp. PERINATAL AND NEONATAL MORTALITY/;717 results
4.	BNI	1 AND 2 AND 3 AND 4; 9 results.

Results of the search strategies

3211 records were retrieved from the initial database search. The first sift of the search results involved checking the titles for relevance and removing any titles that obviously did not meet the inclusion criteria. Checking the study titles and de-duplication of the records resulted in 3001 titles being removed. The abstracts of the remaining 210 records were analysed against the inclusion criteria and 162 irrelevant records were eliminated. 48 full studies were downloaded and the content checked against the inclusion criteria. A further 3 studies were excluded and reasons for exclusion are listed in appendix 2. This resulted in 45 studies being included in the final review. See **figure 1** for an overview of the search results.

Figure 1 Inclusion and Exclusion of Studies for Review



Summarising the data

Key data from each included study or article was extracted and recorded. Data items included:

- Theme
- Study (author, year and country)
- Study design
- Aim
- Outcome
- Sample size
- Results
- Conclusions
- Level of Evidence

Hierarchy of Evidence

The different types of research evidence included in the review were graded using the system adopted by NICE (2009). This sets out a *hierarchy of evidence* with different levels corresponding to the different grades of evidence. For example a score of 1++ is the highest possible level ascribed to meta-analyses of randomised controlled trials (RCTs) whereas level 4 evidence is ascribed to lower categories of evidence such as expert opinion. Articles and other miscellaneous information were not included in the grading of evidence. The framework used by NICE is set out in Table 1.

Reporting the results

Individual studies were then grouped by key risk factors. This was an iterative process so that once key themes were identified more extensive literature searches could be undertaken for discrete research areas. The studies included in the literature scoping search were summarised and tabulated in table 2.

Levels of evidence for intervention studies NICE (2009)[1]

Level of evidence	**Type of evidence**
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1–	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*
2++	High-quality systematic reviews of case–control or cohort studies. High-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2–	Case–control or cohort studies with a high risk of confounding bias, or chance and a significant risk that the relationship is not causal*
3	Non-analytic studies (for example, case reports, case series)
4	Expert opinion, formal consensus

[1] National Institute for Health and Clinical Excellence (January 2009) The guidelines manual. London: National Institute for Health and Clinical Excellence. Available from: www.nice.org.uk

Table 2 Literature Search Results					Glossary: **aOR Adjusted odds ratio** **RR Relative Risk** **CI – 95 % confidence interval**		
Topic	Author/Year	Type	Aim	Outcomes	Sample	Results/Findings	Grade of evidence
Socio economic	Haggarty et al 2009 Aberdeen, Scotland	Prospective Cohort	To evaluate nutrient intake and status in pregnancy in relation to a measure of multiple deprivation in a Scottish population. Particular attention was given to the B vitamins.	Pre-term Birth Neonatal Treatment Birth weight	n=1461 singleton pregnancies	Deprivation significant risk factor for pre-term birth (OR 1.14, CI 1.03-1.25) and neonatal treatment (OR 1.07, CI 1.01-1.14) Risk factors for low birth weight: diet low in Vitamin C (0.79, 0.64-0.97) Riboflavin (OR 0.77, CI 0.63-0.93) Pantothenic acid (OR 0.79, 0.65-0.97) even after adjustment for deprivation, smoking, marital status and parity)	2-

Socio economic status	Joseph 2007 Canada	Cohort	To determine if perinatal outcomes vary by income	Gestational diabetes Gestational age at birth Weight for gestational age Mortality	n=92 914	Lower income groups had statistically significant higher rates of gestational diabetes RR 1.44 (CI 1.21-1.73) Pre-term birth RR 1.20 (CI 1.06-1.35) SGA RR 1.81 (CI 1.66-1.97) No significant differences found for perinatal death.	2++
Socio economic status	Taylor-Robinson 2010 Liverpool ,England	Retrospective cohort	To explore risk factors for pre-term birth and socio economic status	Pre-term birth	n=50 486	Most deprived compared to least deprived quintiles: Pre-term delivery aOR 1.60 (CI 1.28-2.0). Increase of risk after adjustment for smoking and maternal weight.	2+

Socio economic status	Guildlea 2001 Wales	Cohort	To investigate the relation between social deprivation and causes of stillbirth and infant mortality.		211 072 live births, 1147 stillbirths, and 1223 infant deaths.	Late neonatal deaths RR 5.9 (1.4,10.3) for most deprived compared with least deprived areas	2+
Maternal weight	Khashan 2009 Manchester, England	Cohort Study	Effect of BMI in early pregnancy on adverse outcomes	Pre-term birth Neonatal Death Stillbirth Macrosomia SGA/LGA	n= 99 403 babies	Risk of preterm birth was reduced in overweight (RR = 0.89 CI: 0.83, 0.95) and obese women (RR = 0.90, CI: 0.84, 0.97) Risk of preterm birth increased in underweight women (RR = 1.33, CI: 1.16, 1.53). Risks for fetal macrosomia and operative delivery increased with BMI: morbidly obese women (RR of macrosomia = 4.78 CI:	2++

						3.86, 5.92	
Maternal weight	Kristensen 2005 Denmark	Cohort Study	Association between pre-pregnancy BMI and risk of stillbirth/neonatal death	Stillbirth Neonatal Death	n=24,505 singleton pregnancies	Obesity (BMI 30+) was associated with risk of neonatal death (OR 2.6 CI 1.2-5.8). No risk found for underweight or overweight women. Adjustment for factors including: smoking, alcohol maternal age did not alter results)	2+
Maternal weight	Langford 2011 Missouri	Cohort Study	Association between gestational weight gain and adverse maternal/infant outcomes	Pre-eclampsia CS Macrosomia Low birth weight	n=34 143 singleton full term deliveries	Women who gained most weight (25lb +) at increased risk for macrosomia (2.1 CI 1.9-2.3) decreased risk for LBW (0.6 CI 0.5-0.6)	2+
Maternal weight	Smith 2007 Scotland	Retrospective Cohort Study	Association between maternal BMI and risk of preterm delivery	preterm delivery neonatal death	n=187 290	For women with BMI 35+ statistically significant increased risk for: Overall pre-term delivery AOR 1.34 (CI 1.15-1.56)	2++

				delivery of an ELBW infant delivery of an ELBW infant surviving to 1 year of age Preeclampsia.		Neonatal death AOR 2.77 (1.54-4.99) ELBW infant 3.31 (2.13-5.14) NB 40%-45% risk of severe neuro-developmental delays in childhood	
Maternal weight	Stuebe 2012	Cohort	Association of pregravid BMI glucose intolerance and pregnancy outcomes	Gestational hypertension Large for gestational age infants Neonatal fat mass	n=1250	Untreated mild gestational glucose intolerance associated with: Gestational hypertension Large for gestational age infants Neonatal fat mass	2-

Maternal weight	Tennant 2011 Northern England	Retrospective cohort	Association between early BMI in pregnancy and risk of fetal/infant deaths	Fetal death Perinatal death Infant death	n=40 932 singleton pregnancies	For women with BMI 30+ statistically significant increased risk for: Early neonatal death 2.57 (CI 1.13-5.86) Neonatal death 2.07 (1.03-4.13) OR remained significant when adjusted for maternal age, ethnicity, smoking and also birth weight and gestational age.	2++
Maternal weight	Pathi 2006	Article	-	-	-	The incidence of morbid obesity in pregnancy in a maternity unit was 7.5% during the study period and this was associated with statistically significant increased maternal and perinatal morbidity.	-

Maternal weight	Vasudevan 2011	Article	Adverse consequences of maternal obesity	-	-	Obesity in pregnancy associated with risk of :perinatal death, severe birth defects, fetal macrosomia birth injuries and perinatal asphyxia .	-
Maternal weight	Yu 2006	Article	Risks associated with obesity	-	-	Maternal obesity linked to perinatal mortality (1.4/1000 vs. 5.7 per 1000 in obese group) macrosomia (>90th percentile: 9 vs. 17.5% in obese group)	-
Ethnicity	Balchin 2007	Prospective study	Stillbirth		n=197 061	S Asian women had higher rates of perinatal mortality across all	2-

	London, England		Perinatal mortality			gestational ages OR 1.6 CI 1.4-1.9) compared with white and black pregnant women	
Maternal age	Carolan & Frankowska 2011	Review	To examine current knowledge in respect of foetal welfare for childbearing women aged 35-39 years	Perinatal/neonatal outcome including stillbirth	> 4 million women	9 cohort/cross-sectional studies included. 8 studies examined link between maternal age (35-39/40 years) and still birth. All met quality assessment using CASP. • 7/8 studies found maternal age to be risk factor for neonatal death	2++
Maternal age	Lisonkova 2011	retrospective cohort study	comparison of perinatal • Mortality • preterm birth • small for gestational age (SGA) • Apgar score between twins of 25	-	-	Twins of older women were more likely to be born preterm (<37 weeks), but not very or extremely preterm (<33 weeks). Twins were not at increased risk of perinatal death,	2-

			to 34 and >35-year-old women				
Maternal age	Lisonkova 2010	retrospective cohort study	To examine the effect of parity on the association between older maternal age and adverse birth outcomes	stillbirth neonatal death preterm birth small for gestational age, neonatal intensive care unit admission	69 023 women were aged 20 to 29 25 058 were aged 35 to 39 and 4816 were aged 40 and over	NICU admission: Older women at increased risk of NICU admission compared with younger controls. aOR 1.2 (CI 1.0 to 1.3) in women aged 35 to 39 years 1.4 (95% CI 1.1 to 17) in women aged >40 years Risk of preterm birth and SGA differed by age aOR 1.5 (CI 1.4 to 1.7) for women aged 35 to 39	2++

						years aOR 1.6 (95% CI 1.3 to 2.0) for women aged 40 years In multiparas the aOR for preterm birth was 1.1 (% CI 1.1 to 1.2) in women aged 35 to 39 and 1.3 (CI 1.1to 1.5) in women ≥40 years. The aOR for SGA in primiparas was 1.2 (CI 1.1 to 1.4) for women aged 35 to 39 and 1.4 (CI1.1 to 1.7) for women aged ≥40 years. The risk of neonatal death was not significantly different between groups.	

Maternal Substance Misuse	Pollack et al 2000	Case Control	To analyse the effects of maternal smoking on birth outcomes among singletons and twins	Birth weight/gestation Mortality Placental abruption	National Centre for Health Statistics Perinatal Mortality Data Set for 1995 n=3899589 including 96785 infants identified as twins.	Maternal smoking (> 10 cigarettes/day) associated with a significantly increased risk of low birth weight (RR 2.21, CI 2.10- 2.33), very low birth weight RR 1.61 (1.39-1.86),and gestation of less than 33 weeks for both singletons and twins and with an increased risk of gestation of less than 38 weeks RR 1.39 (1.25-1.55), infant mortality, and placental abruption for singletons	2-
Maternal Substance Misuse	Aliyu 2010	Case Control	To assess if an association exists between prenatal alcohol consumption and preterm birth		n = 1 221 677 singleton preterm births,	Prenatal alcohol use associated with spontaneous preterm birth aOR 1.34 (CI 1.28-1.41)	2-

Maternal Substance Misuse	Kallen 2001 Sweden	Cohort	to investigate the impact of maternal smoking and adverse outcomes	IUGR small head circumference Pre-term birth Mortality	n=1 413 811	For any of adverse outcomes associated with smoking (<10 cigarettes/day) OR 1.39 (1.37-1.41); (>10 cigarettes/day) OR 1.65 (1.62-1.68	2+
Maternal Substance Misuse	Raatikainen 2007	Case Control	To assess maternal outcomes for current smokers, women who reduced smoking rate during pregnancy, non-smokers	Prevalence SGA Preterm birth Perinatal mortality		Smoking prevalence reduced by week 20 of pregnancy from 25.7% to 12.7%.Smokers tended to be young, primiparous or unmarried and used alcohol. Women who reduced smoking were also likely to have quit using alcohol. Continuing to smoke was associated with elevated risks of small-for-gestational-age babies (SGA) (OR 2.11), preterm birth (OR 1.15) and perinatal death (OR 1.15). NB no 95% CI's given.	3

Diabetes	Das 2011	Survey	To compare the neonatal outcomes and birth injuries of macrosomic infants born to diabetic mothers (IDM) and non-diabetic mothers (non-IDM).	Morbidities	n=305	Infants of diabetics s are at increased risk for macrosomia and other morbidities including hypoglycaemia, respiratory distress syndrome and birth injury	3
Diabetes	Handisurya 2011	cohort	to assess differences in infant morbidity and mortality for women with Type 1 and Type 2 Diabetes	Congenital anomalies Mortality Adverse outcomes	n=200	Glycaemic control and increased BMI during first trimester was strongest predictor of adverse outcome. Women with Type 2 diabetes tended to have higher BMI.	3

Diabetes	Inkster 2009	Community Cohort Study	Assessment of adverse pregnancy outcomes for women with pre-existing diabetes	Miscarriage Stillbirth Neonatal	n=211 pregnancies	Women with poor glycemic control pre-conceptually and at booking increased risk in adverse fetal outcome compared with mothers having fair control, odds ratio (OR) 2.59 (CI 1.11–6.03)	3
Diabetes	Howarth 2007	cohort	Assessment of risks associated with Type 1 diabetes and vascular disease	morbidities	n=138 type 1 diabetic pregnancies	women with Type 1 diabetes and vascular disease increased risk for IUGR (OR 6.0 CI 1.54-23.33) and decreased risk for macrosomia (OR 0.46 CI 0.224-0.928)	2-
Diabetes	Luo 2011	retrospective cohort	Assessment of differential neonatal outcomes diabetic and non-diabetic pregnancies	Macrosomia Congenital anomalies Neonatal mortality	n=14 298 367 singletons n= 422 068 twins	Diabetes associated with increased risk for congenital anomalies, pre-term birth and macrosomia.	2+

Diabetes	Murphy 2007	Article	Discusses improving outcomes for pregnant women with Type 1 and Type 2 diabetes	-	-	Poor pregnancy outcomes for women with Type 1 and Type 2. Increasing prevalence of Type 2 especially in BME groups and women from deprived communities. These women are less likely to attend diabetic clinics and take folate supplements.	-
Diabetes	Murphy 2011 East Anglia	Prospective Cohort Study	Comparison of pregnancy outcomes for women with Type 1 and Type 2 diabetes		n=408 Type1 n=274 Type 2	Women with Type 2 diabetes were older, heavier, and more socially disadvantage (all $p<0.001$). However outcomes for glycaemic control, macrosomia, pre-term infants and neonatal admissions were better for mothers with Type 2 compared with Type 1 diabetes.	3

Diabetes	Nielsen 2006 Denmark	Cohort	To assess the association between measures of HbA1C in first trimester and adverse pregnancy outcomes in Type 1 diabetics	stillbirth neonatal mortality Major congenital anomalies	n=573	Dose response relationship found between levels of HbA1C and adverse pregnancy outcomes	3
Diabetes	Shand 2008 Australia	Cross sectional study	To assess population rates and adverse outcomes for pre-gestational and gestational diabetes	morbidity Mortality	n=370 703 1248 pre-GDM and 17 128 GDM	Higher risk for adverse outcomes for morbidity and mortality for pre-GDM OR 3.2 (CI 2.6-3.9), GDM OR 1.2 (CI 1.1-1.4) when compared with non diabetic women	3
Diabetes	Yang 2006 Nova Scotia, Canada	Population-based cohort study	To estimate whether the incidences of adverse foetal and neonatal outcomes in infants of mothers with pre-existing types 1 and 2 diabetes 1) differ from	Mortality Major Congenital Anomaly Gestational age	n=516 infants of diabetic mothers n=150,589 infants of non-diabetic mothers from	Infants of diabetic mothers had significantly higher rates of perinatal mortality RR 3.01, (CI 1.55–5.84), major congenital anomaly RR 2.97 (CI 2.25–3.90),	2+

			infants of non-diabetic mothers		singleton pregnancies	large for gestational age birth RR 3.59, (CI 3.26 –3.95) when compared with outcomes for infants of non-diabetic mothers.	
Maternal Substance Misuse	Leonardi-Bee 2011	Systematic review & meta-analysis	To assess adverse outcomes for non-smoking pregnant women exposed to second-hand smoke	Spontaneous abortions Stillbirth congenital malformation perinatal/neonatal death	19 studies	no statistically significant effect of second-hand smoke exposure on the risk of spontaneous abortion (OR: 1.17 [95% CI: 0.88 – 1.54]; 6 studies). second-hand smoke exposure significantly increased the risk of stillbirth (OR: 1.23 [95% CI: 1.09 – 1.38]; 4 studies) and congenital malformation (OR: 1.13 [95% CI: 1.01–1.26]; 7 studies),	1+

						Second-hand smoke exposure had no significant effect on perinatal or neonatal death	
Interpregnancy Interval	Smith 2003 Scotland	Retrospective Cohort	To determine whether a short interval between pregnancies is an independent risk factor for adverse obstetric outcome	Intrauterine growth restriction extremely preterm birth (24-32 weeks) moderately preterm birth (33-36 weeks) perinatal death.	n=89 143 women having second births in 1992-8 who conceived within five years of their first birth.	short interpregnancy intervals (< 6 months) was an independent risk factor for extremely preterm birth aOR 2.2, (CI 1.3 to 3.6) moderately preterm birth (aOR 1.6 (CI 1.3 to 2.0) Neonatal death unrelated to congenital abnormality aOR 3.6 (CI 1.2 to 10.7).	2+

Interpregnancy interval	de Weger 2011 the Netherlands	Retrospective Cohort	Evaluation of short inter-pregnancy intervals and perinatal outcomes for maternal age	Preterm delivery Low birth weight SGA	n=263 142 Dutch women with second deliveries between 200-2007	Short inter-pregnancy intervals positively associated pre-term delivery and low birth weight	2+
Previous neonatal deaths	Salihu 2011 Missouri USA	Retrospective cohort study	to assess whether young maternal age is associated with recurrence of recurrent perinatal death	Perinatal mortality	n=766,710	Women with previous history of death of a neonate are at increased risk of subsequent neonatal death of infant aOR 5.73 (3.46–9.50) No significant difference found between age groups and outcomes for subsequent pregnancies	2+

Weight for gestational age	Boyle 2013	Article	-	Review of available literature	-	Article discusses large proportion of infants born at late pre-term stage that are at increased risk of morbidity and mortality.	-
Weight for gestational age	De Reu 2011	Case note review	To identify causes associated with perinatal mortality	Perinatal mortality	1885 preterm children	166/1885 died perinatally (8.81%). Small-for-gestational-age 47.6% and previous episodes of perinatal mortality (21.1%) were identified as important risk factors	3
Gestational age	Khashu 2009	Cohort study	To compare the mortality and morbidity of late pre –term infants to those born at term	Mortality Morbidity Factors	preterm n=6381 term=88 867	Mortality risk was greater for pre-terms infants compared with term infants: Death at < 7days RR 7.0 (CI 3.8-12.7) Death at < 28 days RR 5.6 (3.5-8.9)	2-

Weight for gestational age	de Reu 2010 Netherlands	Cohort study	To analyse avoidable perinatal mortality in SGA infants	Perinatal mortality	n=22 189 newborns > 24 weeks	20 927 singletons 2396 were SGA (< 10th percentile). 59/2396 perinatal deaths identified. Failure in correct and timely diagnosis of SGA important factor	2+
Gestational Age	Grisaru-Granovsky 2012	population-based observational study	To evaluate growth restriction and outcomes for morbidity/mortality in pre-term VLBW and SGA infants	Morbidity Mortality	-	Infants of 24-31 weeks gestation < 10th percentile at increased risk or mortality OR 2.37 (CI 1.94-2.90) compared with reference 25th -50th percentile.	3
Weight for gestational age	Xiangming Qiu 2012	Cohort	To compare the effect of small for gestational age (SGA) on mortality, major morbidity and resource utilization among singleton very preterm infants (<33 weeks gestation) admitted to neonatal intensive care units (NICUs)	Morbidity Mortality	n=11,909	SGA infants (*n* = 1249) increased risk of: mortality aOR 2.46(CI 1.93-3.14) necrotizing enterocolitis aOR 1.57 (CI 1.22-2.03) bronchopulmonary dysplasia aOR 1.78 (CI 1.48-2.13 severe retinopathy of	2+

						prematurity aOR 2.34; CI 1.71-3.19)	
Weight for gestational age	Pulver 2009 Utah USA	Retrospective cohort	To compare neonatal and infant mortality rates of weight for gestational age (WGA) and late preterm, early term, and term newborns To determine the relative risk of neonatal and infant death for each WGA category; To examine causes of neonatal and infant death	birth weight gestational age mortality	n=343 322 live newborns > 34 weeks between 1999 and 2005	Neonatal mortality rates highest for SGA pre-term infants Late-preterm SGA boys RR 47.6 (28.3–80.2) Late-preterm SGA girls RR 52.3 (30.9–88.5)	2+

Weight for gestational age	Bacak 2005	Population based case control	To examine characteristics associated with neonatal mortality amongst extremely low birth weight infants < 1000g	Maternal age Mortality	n=835	Infants born with severe congenital anomalies and at youngest gestational ages at greatest risk. Maternal age identified as risk	3
Weight for gestational age	Zhang 2008 US	cohort	To assess birth weight and morbidity and mortality risk	Perinatal death Neonatal morbidity Caesarean delivery	n=5 983 409 singletons weighing 2500g +	infants with birth weights 4500-4999g had significantly higher risks of early neonatal mortality OR 1.8 (1.3 to 2.4) infants with birth weights 5000g + OR 6.4 (3.9 to 10.4) compared with reference category 3500-4499 g	2
Pre-term vs term	Young 2007 Utah	cohort	to determine the relative risk for mortality for late-preterm newborns (34–36 weeks) compared with those born at term.	Early neonatal mortality Neonatal mortality Infant mortality	283 975 births of infants with an EGA _34 to _42 weeks	Compared with those born at 40 weeks, mortality rates were significantly higher for all 3 of the periods for newborns who were born at 34, 35, 36, and37 weeks.	3

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