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REVIEW

Understanding perinatal mortality

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Abstract

The term perinatal death is used to describe antepartum and intrapartum stillbirths, and early neonatal deaths. Although the overall rate of perinatal mortality is falling, a slower rate of reduction has been observed in stillbirth compared to neonatal death. Antenatal stillbirth contributes to a greater proportion of cases in high income countries and associated risk factors include maternal age, smoking, obesity and small for gestational age fetus. At term, intrapartum stillbirth and neonatal death are collectively referred to as delivery related perinatal death, and the incidence in nulliparous and multiparous women is approximately 1 in 1000 and 1 in 2000 births, respectively. Associated factors include advanced maternal age, small for gestational age, fetal macrosomia, breech labour and previous caesarean delivery. The impact of obstetric interventions in labour on delivery related perinatal death, including rising rates of caesarean delivery, is complex and unclear.

Key words: Perinatal mortality, antepartum stillbirth, intrapartum stillbirth, early neonatal death, term births

Definition of Perinatal Death

The World Health Organization (WHO) defines a perinatal death as ‘A death occurring at 22 completed weeks of gestation and over, during childbirth and up to seven completed days of life’. This includes stillbirth (intrauterine fetal death) and early neonatal death (infant death occurring in the first 7 days of life). However, WHO also recommends a different definition for international comparison ($\geq 1000\text{g}$ birthweight or ≥ 28 completed weeks of gestation). This “international” definition exists for two main reasons: firstly because national registries use different gestational age thresholds to define stillbirth; and secondly due to the under-reporting of stillbirths below 28 weeks in selected regions. It is recognised that the “international” definition for comparisons underestimate the real burden of perinatal mortality as a considerable proportion of fetal deaths occur before 28 weeks of gestation (35-50% in high income countries). In the United Kingdom, 24 completed weeks is used as the lower gestational limit to define a perinatal death (Table 1). Gestations at the limit of viability can pose difficult problems for classification of events with respect to the incidence of late miscarriage or early neonatal death. A CMACE report has indicated that 7.3% of early neonatal deaths in London were born at less than 22 weeks, whereas this figure is 18.8% in the West Midlands. This highlights the lack of consistency in defining type of death across the country. Global comparisons are challenging as there are inter-country, and indeed intra-country variations in definitions, data collection, neonatal care at the gestational age of viability, timing of death, and even legal requirements to report death. International comparisons can be further complicated by changes of definitions over time.

A Global perspective

An estimated 98% of all perinatal deaths occur in countries of low income and the perinatal mortality rate is roughly five times greater than that of wealthier countries. This figure emphasises low income countries should be the focus of improvement programmes to reduce the burden of perinatal mortality globally. Although the overall rate of perinatal mortality is falling, a slower rate of reduction has been observed in stillbirth compared to neonatal death. This enhanced reduction in neonatal death is likely to be related to the Millennium Development Goal 4, which aims to reduce the under-five mortality rate.

Between 1990 and 2015 the under-five mortality rate declined by more than half, highlighting that targeting specific health outcomes can promote change. Stillbirth was not a specific target of the Millennium Development Goals, but recently the WHO launched the Every Newborn Action Plan (2014) which enhances and supports coordinated, comprehensive planning and implementation of newborn-specific actions with the specific goal of ending preventable stillbirth and neonatal death. Reduction in perinatal deaths requires financial, cultural and political will to implement universal access to good quality care in pregnancy, childbirth and the neonatal period. However, the strategy should vary according to local epidemiology. In low income countries intrapartum death is a major component of perinatal mortality, reaching over 50% of stillbirth in specific areas (Table 2). Training health care providers to ensure appropriate management of deliveries and providing pregnant women with access to health care facilities are recognised measures that reduce intrapartum stillbirth. The remaining 2% of global perinatal deaths, which occur in countries of high income, are associated with different risk factors and causes, therefore different interventions are required to further improve outcomes (Table 3). In high income countries, intrapartum stillbirths account at most for 15% of all stillbirths (0.5-1.2 per 1000 births). A variation in the overall stillbirth rates is also observed between high income countries. If all countries had a low rate (2.0 per 1000 birth), approximately 20,000 late gestation stillbirths would be avoided. It is not clear the reason for those differences observed in high income countries, neither the best way to tackle antenatal stillbirth. In the UK, the stillbirth rate has fallen in the last decade from 5.7/1,000 livebirths in 2004 to 4.7/1,000 livebirth in 2014 (Figure 1). Some of the strategies being suggested to further improve this rate involve smoking cessation, increasing maternal awareness of reduced fetal movements and improved screening and follow up of small for gestational age fetus (SGA). The focus of the rest of this review is on the incidence and causes of perinatal mortality in high income countries.

Classification

There are over 30 classification systems of perinatal mortality. Many of these classification systems were designed for different reasons with different definitions and levels of complexity. In the UK in the 1950s, a classification system was developed to group

perinatal death according to the obstetric cause. The aim of this system was to identify the factor which initiated the chain of events leading to death, hence the system was hierarchical. For example, it was assumed that a lethal fetal malformation would take precedence over any other cause of death. With time it became clear from national surveys of perinatal deaths that there was a need to further develop classification of cases to incorporate changes in obstetric practices such as the significantly improved prognosis of very low birth weight babies. Classification systems incorporating the use of specific diagnoses such as those listed in the International Classification of Disease (ICD) have also been used. However, many specific diagnoses relating to perinatal death are missing from even the most recent ICD classification.

Each of the different systems has its merits, however, a systematic approach to the classification of perinatal death is required to improve the understanding and prevention of perinatal death. In addition, it is recognised that the contribution from each cause of death will be different for antenatal, intrapartum and neonatal death. Moreover, approximately 50% of stillbirth (antenatal and intrapartum deaths) were unexplained according to different cause-related classification systems. A more recent classification system takes into account the relevant condition at death (ReCoDe) and reduces the number of deaths previously classified as unexplained to 15% (Figure 2). The major difference of this system is to acknowledge conditions associated with death instead of reporting only causative disorders. Although causal relationship is not proven, the prevalence of associated conditions helps to inform where interventions are more likely to impact on the rate of stillbirth. It is of note that fetal growth restriction, not accounted for in previous classifications, is present in approximately 40% of stillbirths. Irrespective of the classification, the cause of death should ideally be decided by a medically qualified assessor with access to all the relevant data, including clinical records and the results of postmortem investigations.

Antepartum Stillbirth

Approximately two thirds of all perinatal deaths are stillbirths occurring in the antenatal period and there has been considerable research focused on risk prediction of this event.

Tackling antenatal stillbirth is especially important to reduce stillbirth in high income countries, where intrapartum causes are responsible for only 8-10% of cases. These fetuses die in-utero prior to the onset of labour and associations include fetal abnormality, maternal diseases, congenital infections, isoimmunisation and complications of pregnancy such as placental abruption, gestational diabetes mellitus and pre-eclampsia. However, for many antepartum stillbirths, no specific cause is found, and these are referred to as unexplained. A large proportion of these unexplained deaths are associated with SGA/intrauterine growth restriction. Epidemiological risk factors for antepartum stillbirth include advanced maternal age, nulliparity, smoking, low socio-economic status, obesity, advanced gestational age, previous stillbirth, and multiple pregnancies. From all factors associated with antepartum stillbirth the major contributors, according to population attributable fraction, are maternal age, smoking, obesity and SGA. The most prevalent single condition associated with stillbirth is SGA, thus appropriate definition, detection and management of SGA fetuses is an important strategy to reduce the rate of stillbirths.

There are two methods commonly used to define an SGA fetus (ultrasound estimated fetal weight below the 10th centile): population centiles, which adjust for gestational age and fetal sex; and customised centiles, which adjust for maternal height and weight, ethnicity, parity, gestational age and fetal sex. Evidence from observational studies support SGA infants by customised, but not by population centiles, are at increased risk for perinatal adverse outcomes (including stillbirth). SGA infants by population, but not by customised centiles, are not at increased risk. This would suggest that the use of customised centiles better predicts fetuses at risk. However, the customisation process does not account for potential pathological influences on fetal growth such as maternal obesity recognised as a pathological variation of weight, and ethnicity which in some groups is associated with socioeconomic deprivation. Recently the INTERGROWTH 21st project has published a new international standard of fetal growth in line with the WHO principles of child growth charts. Pooled data from 8 different countries was used to create a standard to compare populations. However, the validity for applying this reference to individual patients and the association with adverse perinatal outcomes has not been established.

The key issue in reducing stillbirth associated with SGA is to improve detection irrespective of the definition used locally. It is recognised that antenatal identification of SGA fetuses can reduce the risk of stillbirth through appropriate follow up with Doppler ultrasound and timely delivery. The Grow Assessment Protocol (GAP) is a complex intervention for improved detection of SGA infants, which includes risk stratification in early pregnancy, serial fundal height measurement or ultrasound scans during second and third trimester, and use of customised charts for assessment of fetal growth. Studies suggest that the use of GAP can double the detection of SGA (from 16-20% to 38-42%). Another strategy to improve antenatal detection of SGA is universal screening with third trimester ultrasound. A recent cohort study reported universal third trimester ultrasound provides a detection rate of 67% compared to 20% with routine care. Health economic analysis comparing these two strategies should inform the most effective way to improve detection of SGA.

Maternal perception of reduced fetal movements is another established risk factor for stillbirth. The mechanism leading to death is not clear in this group but the related association with increased risk of growth restriction suggests placenta insufficiency may be involved. Induction of labour is recommended when repeated episodes of reduced fetal movement occur in term pregnancies, even if tests of fetal wellbeing are normal. It has been hypothesised that increasing awareness of reduced fetal movements could lead to earlier report of these episodes by pregnant women. Such early report of reduced fetal movements associated with clear management of these episodes has the potential to reduce rates of stillbirth. The AFFIRM trial is a stepped wedge trial which is testing this hypothesis and is due to complete in March 2017. Other strategies to reduce antepartum stillbirth include smoking cessation programmes, induction of labour for post-date pregnancies, and elective delivery of multiple pregnancies at or before 37 weeks' gestation. Cardiotocography and biophysical profiling are tools that are routinely used but their benefit in preventing antepartum stillbirth remains unproven.

Placental function is determined early in pregnancy and requires extensive uterine remodelling to accommodate deep trophoblast invasion. Markers of placentation have been

investigated and incorporated into clinical practice. Low levels of pregnancy-associated plasma protein A (PAPP-A) at 11-13 weeks (< 0.415 MoM) are associated with both SGA fetus and other adverse obstetric outcomes, therefore serial growth scans are indicated. An abnormal uterine artery Doppler measurement at 20-24 weeks' gestation is defined as a pulsatility index (PI) above the 95th centile and/or notching. If this occurs in a high risk pregnancy, the Royal College of Obstetricians and Gynaecologists (RCOG) recommends serial ultrasound scans from 26-28 weeks' gestation to assess fetal size and umbilical artery Doppler measurements.

Intrapartum Stillbirth and Early Neonatal Death

Overall, prematurity is the leading cause of intrapartum stillbirth and neonatal deaths and it is therefore difficult to disentangle the effect of prematurity from the effects of the care provided in labour. Studies from high income countries have reported more than a 50% reduction in delivery related perinatal deaths over the last four decades. In recent years, improvements in neonatal care have significantly improved the rates of survival in pre-term infants. Therefore it is difficult to determine the relative contribution of changes in obstetric and neonatal care on the trend of perinatal mortality in analyses which include pre-term births.

Term Delivery Related Perinatal Death

At term, intrapartum stillbirth accounts for approximately 15% of all stillbirths. Most neonatal deaths in normally formed fetuses at term are due to intrapartum related events (intrapartum anoxia and mechanical causes). These deaths are collectively referred to as delivery related perinatal death at term, and the rate of these deaths can be used as a marker for the quality of intrapartum care.

1. Studying delivery related perinatal death

There are a number of factors that make the study of delivery related perinatal deaths problematic. Firstly, in high income countries, the incidence of term intrapartum stillbirth and neonatal death is rare, being only 1 in 1000 for primiparous, and 1 in 2000 for multiparous, women. Therefore, large numbers of women are required to study factors

determining these events. Secondly, detailed information is required on perinatal mortality in order to define the event, and exclude antepartum stillbirths.

2. Epidemiology

Even with a falling perinatal mortality rate in high income countries wide variations exist even within a nation. For example in England in 2013, Yorkshire and the Humber had the highest adjusted stillbirth rate (4.7 per 1,000 total births) and the East of England had the lowest (3.9 per 1,000 total births). Unfortunately, such data does not always distinguish the specific causes of perinatal mortality and in particular how these relate to labour. In a detailed population based analysis from Scotland of term singleton fetuses with cephalic presentation, the incidence of both intrapartum stillbirth and neonatal death declined between 1985 and 2004. This was wholly due to a reduction in the incidence of intrapartum anoxic related deaths. Changes in obstetric care may have resulted in a shift in the timing of perinatal mortality in relation to labour. A reduction in intrapartum stillbirth may be associated with an increased incidence of neonatal death. The decline observed in the Scottish study coincides with the observed rising rate of caesarean section, however it may also be attributed to other aspects of improved obstetric care such as better multidisciplinary education training and senior clinical supervision. The association between rates of cesarean delivery and neonatal mortality is known and a recent ecological study including data from 194 WHO member states suggested that rates up to 19% were associated with lower neonatal mortality, which is higher than the 15% previously recommended.

3a. Risk factors for delivery related perinatal death – maternal characteristics

In most high income countries there has been a marked shift in maternal demographics in the last few decades, including age, obesity and family size. Women are choosing to delay childbirth. The association of advanced maternal age and the incidence of adverse pregnancy outcomes such as miscarriage, pre-eclampsia, gestational diabetes and antepartum stillbirth have been well described. Increasing maternal age is also found to be associated with intrapartum complications, including dysfunctional labour and operative birth. The association between maternal age and the risk of delivery related perinatal death

is less clear, although there is now evidence that women aged 40 and above are at greater than two-fold increased risk of delivery related perinatal death at term. This excess is secondary to deaths due to intrapartum anoxia and was independent of parity. The biological basis of this association is unclear. There are two main hypotheses; firstly, older women may have abnormal placental function, thus increasing the risk of anoxic related events. Secondly, there is a linear increase in the risk of operative delivery with increasing maternal age. This may be attributed in part to a reduction in spontaneous contractility of myometrial muscle fibres as evidenced by *in vitro* studies.

In high income countries, increasing obesity is a major public health issue and it is associated with adverse pregnancy outcomes, including gestational diabetes mellitus, pre-eclampsia, fetal macrosomia, caesarean delivery and antepartum stillbirth. Compared to multiparous women, nulliparity carries an increased risk of most adverse obstetric outcomes, including stillbirth. This also extends to delivery related perinatal death at term, with a 56% increase in the risk in nulliparous women. A linear association between antepartum stillbirth and neonatal death and socioeconomic status has been identified. However, no such association has been found between delivery related perinatal death at term and other maternal characteristics such as smoking and sociodemographic characteristics.

3b. Risk factors for delivery related perinatal death – Fetal characteristics

SGA and intrauterine growth restriction are associated with intrapartum stillbirth and neonatal death at term. There is a greater than two-fold risk of intrapartum stillbirth and neonatal death in SGA infants. It is estimated that SGA contributes to 17% of delivery related perinatal death. Conversely, there has been mounting concern regarding the trend of increasing birthweight in high income countries. Term pregnancies with a birthweight greater than 4500g or the 97th percentile were associated with more than a two-fold risk of infant death secondary to asphyxia. Despite compromising a smaller proportion of delivery related perinatal death (Population Attributable Factor 2.8-3.5%), there is a potential for improvement in intrapartum complications related to delivery of overgrown fetus. A recent randomised controlled trial assessed the effect of early term induction of labour in women

with a suspected large for gestational age (LGA) infant (ultrasound estimated fetal weight above the 95th centile at 36-38 weeks). Induction of labour at 37-39 weeks reduced the risk of shoulder dystocia and associated neonatal morbidity (RR 0.32; 95%CI 0.15-0.71) without increasing caesarean section rates (RR 0.89; 95%CI 0.72-1.09). One remaining challenge is how to accurately identify fetal overgrowth before labour. Reports suggest that antenatal identification of LGA in routine clinical practice is 9.7-16.6% which is similarly poor to the figures described for SGA (16.4-26.4%). This highlights the importance of improved antenatal estimation of birthweight and identification of infants at the extremes of birthweight percentiles as a strategy to reduce delivery related perinatal death.

Breech presentation is associated with a higher risk of labour related perinatal mortality and morbidity. The Term Breech Trial demonstrated a three-fold greater risk of perinatal morbidity and mortality associated with vaginal breech delivery compared to planned caesarean delivery. This resulted in an immediate shift in clinical practice with most advocating planned caesarean delivery for breech presentation. However the debate on the appropriate management of breech pregnancies has continued. It has been demonstrated that despite exclusion of deaths due to congenital abnormalities, not all perinatal deaths in the Term Breech Trial were due to breech labour and delivery. However, in a cohort study between 1985 and 2004, the absolute risk of anoxic or mechanical death in infants delivered by vaginal breech delivery was 25.5 per 10,000 births. In multivariate analysis, this risk was five times the risk in infants delivered by caesarean delivery following the onset of labour. There were no events among infants delivered by planned caesarean delivery. This analysis provides more precise risk estimation associated with breech delivery and labour.

It is well recognised that twin pregnancies are associated with an increase in the risk of all causes of perinatal mortality. Labour and delivery are however a time of significant risk to twin pregnancies and in particular to the second twin. One study of twin pregnancies beyond 24 weeks demonstrated an excess in the risk of delivery related perinatal mortality associated with the second twin, which was only observed in pregnancies beyond 36 weeks. At term the absolute risk of delivery related perinatal death in the second twin was approximately 1 in 270 for all causes, 1 in 350 for deaths due to intrapartum anoxia and 1

in 500 for mechanical causes of death. Birthweight discordance was associated with an increased risk of death in the second twin. Observational studies have suggested that planned caesarean section could reduce the risk of perinatal death of twins which made the case for a randomised controlled trial. The Twins Birth Study was designed to test this hypothesis and randomised 2804 women for a planned caesarean delivery or a planned vaginal birth. In twin pregnancies with the first twin in cephalic presentation, planned caesarean delivery did not decrease the risk of fetal or neonatal death or serious neonatal morbidity (RR 1.16; 95%CI 0.77 – 1.74, p=0.49).

3c. Risk factors for delivery related perinatal death – Obstetric and service

The increase in the rate of caesarean section is partly attributed to the decline in vaginal birth after caesarean delivery (VBAC). This is driven, in part, by the concern of uterine rupture and the consequent perinatal mortality and morbidity. A systematic review has reported an increased perinatal mortality associated with an attempt of VBAC (13/10,000 births) compared to elective repeated caesarean section (5/10,000 birth). However, the absolute risk is very low and risks and benefits of VBAC should be discussed with all women. Previous uterine rupture and classical uterine scar are particular risk factors for subsequent uterine rupture and consideration should be given to avoid VBAC in these situations. A large scale population based cohort study from Scotland reported that delivery in an obstetric unit with less than 3000 births per year was a risk factor for perinatal death following uterine rupture. Additional factors identified include prostaglandin induction and no previous vaginal delivery.

It has been suggested that there might be associations between perinatal mortality rates and both the time and day of delivery and the place of birth. Births in the evening and night time were associated with almost a two-fold risk of both intrapartum stillbirth and neonatal death, although some reports have failed to demonstrate this association. It has been suggested this could be related to the presence of senior obstetricians on the birth units during day time. However a recent study exploring this hypothesis has shown no difference perinatal morbidity, low Apgar score at 5 min and low cord pH in relation to the presence of senior obstetricians in the labour ward. Differences in access to emergency care such as

“crash” caesarean delivery, resuscitation facilities and service provision out of hours may be responsible for the difference in the incidence observed. Regarding the place of birth, a systematic review and meta-analysis of home versus hospital birth failed to show any difference in the incidence of perinatal mortality. However, the Birthplace study has identified that in term cephalic pregnancies, the incidence of perinatal mortality and morbidity was higher in nulliparous women delivering at home compared to those delivering in an obstetric unit (9.3 per 1000 compared to 5.3 per 1000). This was not the case for multiparous women. The overall safety of births at home, in midwifery units, free standing or alongside obstetric units compared to births in hospitals has been demonstrated.

4. Prevention of delivery related perinatal death

Much of the intrapartum interventions such as electronic fetal monitoring (EFM), fetal blood sampling and operative delivery are aimed at reducing the risk of perinatal mortality and morbidity associated with labour and delivery. EFM in labour is a screening test aimed at identifying infants at risk of asphyxia. The sensitivity, specificity and prevalence of the outcome influence the positive predictive value of the test. The outcome of interest is rare, and this screening test has a high false positive rate and poor predictive value. Continuous EFM versus intermittent auscultation is associated with an increase in the risk of obstetric intervention including caesarean delivery, with no difference in the incidence of perinatal mortality having been demonstrated. However, in order to test the hypothesis that continuous EFM can reduce the incidence of delivery related perinatal death a study would have to randomize more than 50,000 women in each arm. Therefore the absence of evidence is largely an issue of power and may not truly reflect a negative result. Currently, the use of EFM is only advocated in the presence of risk factors for intrapartum hypoxia. In those cases where EFM is indicated it has been suggested that the use of computer-based decision-support would earlier indicate the possibility of a poor outcome therefore improving outcomes through earlier intervention. The INFANT trial addresses this hypothesis and is due to report soon.

The rate of caesarean delivery in most countries has increased significantly in the last twenty years and this has coincided with a decline in intrapartum stillbirth. The real effect

of mode of delivery on the risk of delivery related perinatal death associated with labour and delivery is not a question that can be studied easily. Firstly, it is not appropriate to randomize low risk women to caesarean section, therefore available evidence comes from observational studies. Secondly, the choice for a woman is not between planned caesarean delivery and vaginal birth but rather an attempt of vaginal birth and most studies have not taken that into account. This is an extension of the intention to treat principle. This approach was used in two large scale cohort studies on the risks of trial of labour in women with previous caesarean delivery. In both these studies, the risk of delivery related perinatal death associated with planned caesarean delivery at term was approximately 1 per 10,000. The additional risk associated with the decision of trial of vaginal delivery was 3 per 10,000. This risk was comparable to the risk for women having their first birth.

Conclusion

Globally, although the rate of perinatal mortality is falling, a slower rate of reduction has been observed in stillbirth compared to neonatal death. Low and middle income countries contribute to the vast majority of perinatal deaths and there is a need for effective pregnancy, childbirth and postnatal care to reach all mothers and their babies in these nations.

In the UK and in other high income countries, antenatal stillbirth is the major contributor to perinatal mortality. Risk factors for antenatal stillbirth have been identified such as advanced maternal age, smoking, obesity and SGA fetuses, but the clinical applicability of interventions has been limited. Ongoing studies may clarify which interventions are more cost-effective in reducing antenatal stillbirths. Despite the low incidence of delivery related perinatal death in these countries, it remains a severe adverse obstetric outcome. Identification of risk factors and preventative strategies are limited by precise case ascertainment and issues of power. However, a number of risk factors for delivery related perinatal death have been identified, including multiple pregnancy, breech labour and previous caesarean delivery. Future research needs to target individual risk estimation, thereby directing intervention to women at high-risk of delivery related perinatal death.

Practice points

- It is estimated that 98% of perinatal mortality occur in low income countries.
- Antenatal stillbirth accounts for two thirds of perinatal mortality globally.
- In the UK and in other high income countries, antenatal stillbirth represent at least 85% of all stillbirths.
- Risk factors for antenatal stillbirth include, but are not limited to, advanced maternal age, smoking, obesity and small for gestational age fetuses.
- Maternal characteristics of risk factors for term delivery related perinatal death include advanced maternal age, obesity, nulliparity and low socioeconomic status.
- Fetal characteristics of risk factors for term delivery related perinatal death include small for gestational age, intrauterine growth restriction, macrosomia (in diabetic mothers), breech presentation and multiple pregnancy.
- Obstetric and service determinants of risk factors for term delivery related perinatal death include uterine rupture associated with vaginal birth after caesarean section, small obstetric units and place of birth.
- In practice, prevention of term delivery related perinatal death depends largely on electronic fetal monitoring and caesarean section. However, these are likely to only be of benefit in situations where there is a high risk of intrapartum hypoxia.

Further Reading

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Table 1. Summary of definitions related to perinatal mortality in UK.

Stillbirth	A baby delivered at or after 24 ⁺⁰ weeks gestational age showing no signs of life, irrespective of when the death occurred.
Antenatal Stillbirth	A baby delivered at or after 24 ⁺⁰ weeks gestational age showing no signs of life and known to have died before the onset of care in labour.
Intrapartum stillbirth	A baby delivered at or after 24 ⁺⁰ weeks gestational age showing no signs of life and known to be alive at the onset of care in labour.
Neonatal death	A live born baby (born at 20 ⁺⁰ weeks gestational age or later, or with a birthweight of 400g or more where an accurate estimate of gestation is not available) who died before 28 completed days after birth
Early neonatal death	A live born baby (born at 20 ⁺⁰ weeks gestational age or later, or with a birthweight of 400g or more where an accurate estimate of gestation is not available) who died before 7 completed days after birth.
Late neonatal death	A live born baby (born at 20 ⁺⁰ weeks gestational age or later, or with a birthweight of 400g or more where an accurate estimate of gestation is not available) who died from 7 completed days but before 28 completed days after birth.
Perinatal mortality	A stillbirth or early neonatal death.

Table 2. Global estimates stillbirth rates and proportion of intrapartum stillbirth according to region. Adapted from Lawn JE et al. Lancet 2016 Jan;387(10018):587-603.

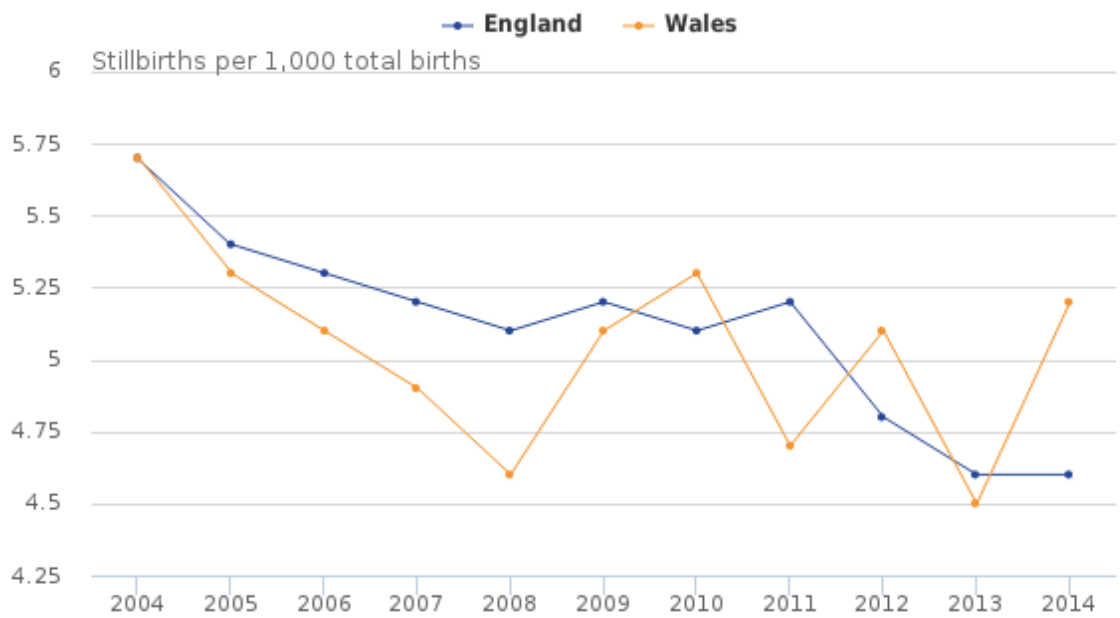
	Rate of all stillbirth (per 1,000 births)	Number of stillbirths	Number of intrapartum stillbirths	Proportion of Intrapartum stillbirths
Developed regions	3.4 (3.4-3.5)	46700	4700	10.0 (5.5-18.4)
Eastern Asia	7.2 (5.6-9.7)	129000	25700	19.9 (6.6-32.3) *
Latin America	8.2 (7.5-9.2)	91000	15300	16.8 (15.8-41.1)
Caucasus and central Asia	11.9 (9.8-15.6)	23400	4700	19.9 (6.6-32.3) *
Southeast Asia and Oceania	12.2 (10.7-14.6)	154900	70800	45.7 (31.3-74.5)
Northern Africa and western Asia	14.5 (12.9-17.6)	148300	62300	42.0 (22.9-57.9)
Southern Asia	25.5 (22.5-29.1)	966600	573200	59.3 (32.0-84.0)
Sub-Saharan Africa	28.7 (25.1-34.2)	1059700	541500	51.1 (33.8-81.8)

* Estimation of proportion of stillbirth calculated together.

Table 3. Commonly reported maternal risk factors and causes of stillbirth, reported by ranking of importance and developed status of the country Obtained from McClure EM et al. Int J Gynaecol Obstet 2006 Aug;94(2):82-90

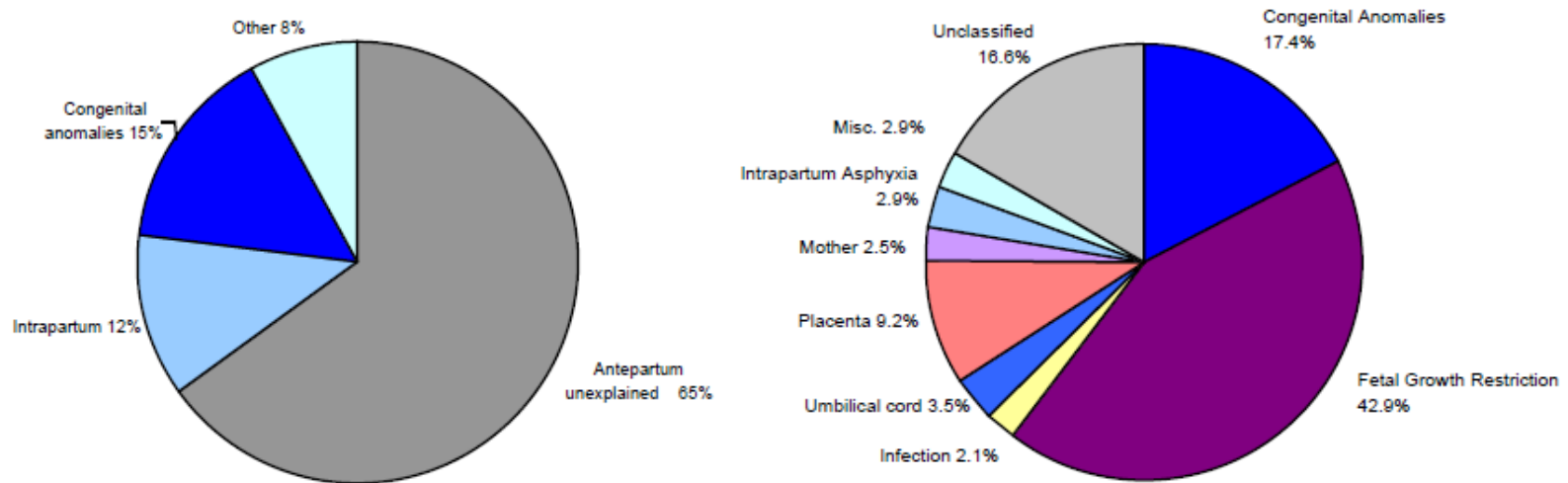
Developing Countries	Developed Countries
Obstructed/prolonged labour and associated asphyxia, infection and birth injury (low availability of caesarean section).	Congenital / karyotypic anomalies
Congenitally acquired infections especially syphilis and gram negative infections.	Growth restriction / placental thrombosis
Hypertensive disease, especially poor management of pre-eclampsia and eclampsia.	Medical disease such as diabetes, systemic lupus erythematosus, renal disease, thyroid disorders, thrombophilias, cholestasis of pregnancy, hypertensive disease/pre-eclampsia.
Poor nutritional state	Congenital acquired infections, especially group B Streptococcus and Parvovirus 19
Previous stillbirth	Smoking
Congenital anomalies	Multiple gestation
Malaria	-----
Sickle cell disease	-----

Figure 1. Trend of stillbirth rates in UK between 2004 and 2014.



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Figure 2. Causes of stillbirth according to Wigglesworth (left) and ReCoDe (right) classifications.



Obtained from Gardosi J, et al. Public Health. 2014;128(8):698-702.