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## Title

Perinatal deaths in twin and singleton infants in Ireland: a comparison of characteristics and causes

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## Introduction

Perinatal mortality (PM) is defined as a stillbirth (a viable baby born without signs of life) or an early neonatal death (death of a live born baby occurring within 7 completed days of birth) (1–3). Twin pregnancies are associated with a three to seven times higher risk of perinatal mortality compared to singletons, largely due to increased rates of fetal growth restriction, preterm birth, and congenital anomalies (4–6). PM is one of the most devastating pregnancy outcomes for parents, families and healthcare professionals (3,7). The complexity of grief can be particularly pronounced in twin pregnancies, especially with the loss of one twin (8,9).

The perinatal mortality rate (PMR) of a country is one of the key indicators reflecting maternal health and the quality of obstetric and neonatal care (10,11). In Ireland the PMR for 2022 is 5.87/1000, and there has been no significant change to this figure over the past few years (12). The PMR for babies in multiple pregnancies was 4.45 times higher in 2021 compared to babies in singleton pregnancies (12). Overall, developing countries report falling PMRs, despite this, the burden of perinatal mortality remains a public health priority (10,13). Each year, Ireland's National Perinatal Epidemiology Centre

(NPEC) perinatal mortality audit highlights the disproportionate number of twin pregnancies within the perinatal mortality population (24,25).

The disproportionate rate of perinatal mortality in twins has been highlighted in international reports and perinatal audits (2,14,15), while the global twins and multiples priority setting partnership has developed research priorities addressing the health and wellbeing of multiple pregnancies (16).

In response to the risk factors and unique challenges associated with multiple pregnancies, targeted efforts to reduce their occurrence following assisted reproductive treatment (ART) in some countries have included restrictions on numbers of embryos transferred, in countries such as Belgium, the U.K and U.S.A, who later reported a decline in their multiple pregnancy rate (17–20). This decline, however, is not observed in the Republic of Ireland (ROI), where the twin birth rate has remained largely unchanged despite a significant overall decline in birthrate over the last 10 years, and where twin pregnancies remain an important issue for healthcare providers (2). In 2019, Ireland and Spain had joint fourth highest rate of twins in the E.U (17.9/1000 maternities) (21).

In 2021, the UK report on ‘Confidential Enquiry into Stillbirth and Neonatal Death in Twin Pregnancies’ found that in over half of twin pregnancies the care provided was poor, and better care ‘may have prevented the baby from dying’ (22). This report demonstrated that deficiencies in care should be addressed, including appropriate early referral on identification of complications, and multidisciplinary team involvement with effective communication and staff education on the management of complications in a twin pregnancy (22,23). Examining and evaluating characteristics of twin pregnancies is crucial for identifying necessary targets and improvements for twin pregnancy care. This is particularly important in Ireland, where, as outlined, the twin birth rate has remained largely unchanged and contributes significantly to the country's perinatal mortality rates.

This study aimed to examine characteristics associated with PM (stillbirth and early neonatal death) in twin pregnancies. It also aimed to compare maternal and obstetric factors and cause of death among twins and singletons in the Republic of Ireland.

## Materials and Methods

### Study population and design

Data for this study were originally collected for the National Perinatal Epidemiology Centre (NPEC) PM annual audit which analyses perinatal mortalities in the Irish maternity hospitals and identifies modifiable factors to generate national clinical recommendations to improve maternity services. This study is a secondary analysis of the PM data. The study population consisted of perinatal deaths, within all 19 maternity hospitals (or associated Neonatal units) in the ROI between January 1, 2011,

and December 31, 2022. NPEC's perinatal death notification dataset includes the standardised collection of data on maternal and infant characteristics including number of fetuses in a pregnancy, chorionicity and the cause of death. Data were validated directly with the respective maternity units to ensure accuracy of information on perinatal mortality. Causes of death were classified in accordance with the NPEC perinatal mortality audit data collection tool and classification system (2).

To calculate risk within the general pregnancy population, the Hospital In Patient Enquiry (HIPE) data was used. HIPE data is an anonymous, national health computer based system of coded discharge summaries from acute public hospitals within the ROI (24). It captures demographic and clinical data of maternity discharges from all 19 maternity units in the ROI and is representative of the overall pregnancy population, capturing approximately 98% of all births nationally. Access to the HIPE maternity discharges from January 1st, 2011, to Dec 31st, 2022, were obtained from the Healthcare Pricing Office (HPO). HIPE uses the International Classification of Diseases, tenth revision, Australian modification (ICD-10-AM) for both diagnosis and procedure coding since 2020, with regular updates to ensure international comparability and quality.

Maternity units in the ROI are classified as tertiary (n=4), regional (n=4), or peripheral (n=11) based on the number of births per annum and the neonatal consultant cover in their associated neonatal units. Each tertiary centre has more than 7,000 births per annum and a dedicated level III neonatal intensive care unit (NICU). Regional hospital units have 2,000-7,000 births per annum, dedicated NICUs but without 24-hour neonatal consultant cover and peripheral hospital units have <2000 births per annum, special care baby units (SCBUs) and infants are cared for by general pediatricians (25).

Stillbirth (SB), defined in accordance with the Civil Registration Act 2004, is a child born weighing 500 grammes or more, or having a gestational age of 24 weeks or more who shows no sign of life (26). This definition is applied by both NPEC and HIPE databases. Early neonatal death (ENND) is defined as the death of a live born baby occurring within 7 completed days of birth (2). There were 4,697 SBs and ENNDs during 2011-2022. There were 4,514 perinatal deaths after excluding terminations of pregnancy. Of these, 4,494 infants were either a singleton (n=4,025) or a twin (n=469).

### **Statistical analysis**

PM data were analysed to explore the differences in maternal and infant characteristics using descriptive statistics and frequencies. Pearson's chi-square analyses studied associations between variables and are presented as absolute values and percentages. Independent samples t-test were presented as the mean and standard deviation (SD). A p-value of  $\leq 0.005$  was considered significant. We derived unadjusted relative risks and corresponding 95% confidence intervals (CIs) to compare the

distribution of risk factors between singletons and twin perinatal deaths. The analysis utilised HIPE data as the denominator for these calculations. Analysis was conducted using SPSS Version 28.0 and STATA version 8.0.

### **Ethical approval**

Ethical approval for the national perinatal mortality audit in NPEC was granted by the Clinical Research Ethics Committee of the Cork Teaching Hospitals (Ref. No: ECM 4 (g) 05/08/08, ECM 3 (GG) 13/08/19). Additional ethical approval for the current secondary data analysis of the NPEC perinatal mortality data and the HIPE data was also obtained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals (Ref: ECM 4 (cc) 11/5/2021).

## **Results**

During the 12-year period, from January 2011 to December 2022, HIPE recorded 684,785 births in Ireland. Among these, there were 24,572 twin births, which account for 3.5% of all births and relates to 1.8% of twin pregnancies. During the same timeframe twins accounted for 469 deaths (10.4%) of all perinatal deaths (n=4514). Of these twin perinatal deaths, 215 (45.8%) were stillbirths and 254 (54.2%) were early neonatal deaths (ENND). Within the singleton perinatal deaths, a higher percentage (68.6%) were stillbirths while 31.1% were early neonatal deaths. Therefore, a higher percentage of twin deaths were ENNDs in contrast to singletons. Additionally, when analysing perinatal mortality in twins by their chorionicity, dichorionic twins accounted for 52.7% (164/203) stillbirths while monochorionic twins accounted for 47.3% (79/243). Among the twin ENNDs, 67.5% (129/243) were dichorionic and 32.5% (57/186) monochorionic.

### *Risk of perinatal mortality in twins and singletons (Table 1)*

Table 1 shows that the perinatal mortality rate (PMR) for infants from a twin pregnancy was 17.3 per 1000; this was 3.1 times higher than that of singletons (95% CI: 2.84-3.48, <.001). The stillbirth rate was 8.1 per 1000 which was 2.1 times higher than singletons (95% CI: 1.85-2.47, <.001), and the ENND rate was 9.2 per 1000 for twins, or 5.4 times higher (95% CI: 4.67-6.22, <.001) compared to singletons. The risk of stillbirth and ENND was highest in the youngest maternal age category (Table 1), with 15–24-year-olds being 2.8 times more likely to have a stillbirth (95% CI: 1.7-4.64, <.001) and 8.3 times more likely to have a ENND (95% CI: 5.43-12.86, <.001) compared to the same age group with a singleton pregnancy. The risk for stillbirth and ENND in twin pregnancies decreased with increasing

age, however in all age categories the risk of PM remained higher compared to singletons. Nulliparous women with twin pregnancies were 2.35 times more likely to have a stillbirth (95% CI:1.9-2.91, <.001) and 5.5 times more likely to have a ENND (95% CI:4.43-6.85, <.001) compared to nulliparous women with a singleton pregnancy. The stillbirth and ENND rate decreased with higher parity, but the risk of death across all categories of parity remained higher in twins compared to singletons.

#### *Maternal characteristics of perinatal mortality in twins and singletons (Table 2)*

Comparison of maternal characteristics for stillbirths and ENNDs in infants from twin and singleton pregnancies are shown in table 2. Among early neonatal deaths, a significantly higher proportion of twins were born to White Irish mothers (81.8% vs. 72.7% of singletons,  $p=0.005$ ). Analysis of BMI revealed there was a difference in early neonatal deaths, with a greater percentage of underweight mothers in twin pregnancies compared to singletons (2.7% vs. 0.9%,  $p=0.007$ ). The proportion of mothers with a healthy BMI was higher in twins for both stillbirths (44.8% vs. 42.4%) and early neonatal deaths (50.5% vs. 41.1%). Conversely, the proportion of mothers classified as overweight or obese was slightly lower in twin pregnancies, with 26.5% of twin stillbirths being overweight compared to 31.3% of singletons, and 18.6% of twin early neonatal deaths being obese compared to 27.3% in singletons.

Among twin perinatal deaths, the type of hospital where the birth occurred varied significantly. The majority of twin stillbirths occurred in tertiary hospitals, accounting for 59.2% of cases. Regional hospitals were the site of 26.3% of twin stillbirths, while 14.6% of twin stillbirths occurred in peripheral hospitals ( $p<0.001$ ). For early neonatal deaths, the role of tertiary hospitals was even more pronounced, with 72.8% of twin early neonatal deaths occurring in these specialised facilities ( $p=0.006$ ). Regional hospitals accounted for 13.6%, while 13.6% of twin early neonatal deaths took place in peripheral hospitals. In twin pregnancies, a higher proportion of in-utero transfers to another hospital occurred for both stillbirths (10.9% vs. 4.3%,  $p<0.001$ ) and early neonatal deaths (27.7% vs. 18.2%,  $p=0.006$ ) compared to singleton pregnancies.

Twins had their anatomy scans at slightly earlier gestations than singletons, with the average gestational age for stillbirths being 20.4 weeks for twins compared to 21.1 weeks for singletons. Although this difference was statistically significant ( $p=0.010$ ). It's important to note that this variable was only collected from 2017 onwards, and not all hospital units were offering anatomy scans prior to this. Therefore, this may not fully reflect earlier practices or the adoption of routine anatomy scans across all facilities. As such, these findings should be interpreted with caution when considering their broader application.

### *Causes of death in twins and singletons (Table 3-5)*

In terms of gestational age, twin stillbirths occurred most frequently between 33-36 weeks gestation (34%) and <28 weeks (33.5%). For early neonatal deaths, 61.0% of twin deaths occurred at less than 28 weeks gestation ( $p<0.001$ ). Regarding birthweight, a significant proportion of twin stillbirths were of extremely low birth weight (<500 grams), representing 24.3% of cases ( $p<0.001$ ), compared to 58.7% of twin early neonatal deaths with a birthweight of 500-999 grams ( $p<0.001$ ).

For major congenital anomalies (MCAs), the incidence was relatively lower in twins compared to singletons; the difference was more notable in ENNDs (58.6% vs 31.3%,  $p\text{ value}<.001$ , Table 3). Twin infants with MCAs were managed across all types of units (tertiary  $n=88$ , regional  $n=21$  and peripheral  $n=13$ ). At least 51.9% of the MCAs were confirmed or suspected antenatally by consultant fetal medicine specialists, however this variable was only recorded from 2016 onwards. The most common type of MCA in twins were chromosomal disorders (9.8% of SB and 7.5% in ENND). A significantly higher proportion of dichorionic twins had a MCA compared to monochorionic twins (Table 5).

Preterm rupture of membranes (PROM) was significantly higher in twin ENNDs (24.5%), compared to 12.9% in singletons ( $p<0.001$ ). Most twin perinatal deaths associated with PROM occurred before 28 weeks gestation (81.8% of SB and 82.3% of ENNDs) (Table 3).

Twins had a lower rate of intrapartum stillbirths than singletons (5.2% vs 6.3%,  $p<.001$ ). There were eleven intrapartum deaths in twin pregnancies, the majority of which occurred in twin 1 ( $n=5$ ), and in dichorionic twins ( $n=6$ ). X of the eleven intrapartum stillbirths in twins were extremely preterm (<28 weeks gestation) and the others occurred at 33-36 weeks gestation. X of the eleven had extremely low birthweight (500-999g). The cause of death was infection (7 chorioamnionitis and 1 Group B streptococcus). Additionally, 26.7% of twin stillbirths occurred in mothers who never went into labor.

Specific placental conditions such as maternal and fetal vascular malperfusion and chorioamnionitis were responsible for 22.3% of all twin stillbirths (Table 4). These conditions were more frequent in dichorionic twins, with 14% of cases attributed to maternal vascular malperfusion compared to 2.1% in monochorionic twins (Table 5). Chorioamnionitis was more common in dichorionic pregnancies (9.3%) than in monochorionic pregnancies (5.2%) (Table 5).

Spontaneous preterm labour was the leading cause of early neonatal death in twins, accounting for 32.7% of all cases (Table 4). The occurrence was the same for both dichorionic and monochorionic twins (33% in each group) (Table 5). The vast majority of spontaneous preterm labour occurred <28 weeks gestation ( $n=80/83$ ), with one occurring >32 weeks gestation. Of the twin infants who died due

to spontaneous preterm labor, born at less than 28 weeks' gestation (n = 80, with 6 cases where the hospital type was unknown), 48 infants (60%) were delivered in tertiary centers, while 15 infants (18.8%) were born in peripheral units, and 11 infants (13.8%) were delivered in regional hospitals.

TTTs was also a leading cause of death in monochorionic pregnancies (45.8% of SB and 24.1% of ENND) Table 5). Of the infants who died due to TTTS (ENND and SB, n=67) 26.9% were born in non-tertiary units, with a significant majority (61% of this subset) born before 32 weeks gestation.

## Discussion

During the study period (2011 - 2022), infants from twin pregnancies constituted 10.4% of all perinatal mortalities, despite representing only 3.6% of total births (equivalent to 1.8% of pregnancies). This highlights a clear over-representation of twins in the perinatal deaths occurring in Ireland. The overall perinatal mortality rate for twins was 17.3 per 1000 births, which was 3.14 times higher than the singleton rate. Among perinatal deaths in twin pregnancies, a greater proportion (54.2%) were early neonatal deaths (ENND). Most perinatal deaths in twins occurred in extremely preterm (<28 weeks gestation) and extremely low birthweight infants (<1000g).

In Ireland, the PMR for twins in 2022 was 16.1 per 1000 births, with twins accounting for 3.6% of all births (1.8% of all pregnancies). Furthermore, the PMR in twin pregnancy was 7.8 per 1000 for SB and (8.3 per 1000 for ENND. However, detailed data on perinatal mortality for twins is not readily available across many countries (5). Additionally, a comparative analysis of twin PMRs, where such data does exist, has not been widely explored in relation to Ireland. When comparing Ireland's twin PMR with other countries, the U.K and the Netherlands report significantly lower PMRs while Australia and New Zealand have higher rates (27–30). The UK's twin PMR stands at 13.5 per 1,000 births, broken down into 7.3 per 1,000 for stillbirths and 6.2 per 1,000 for neonatal deaths (31). The U.K have reported a reduction in twin perinatal mortality, which they attribute in part to the recognition of twin-related obstetric risks compared to singletons and the emphasis on managing twin pregnancies based on chorionicity (5,32). They published the Royal College of Obstetricians and Gynaecologists (RCOG) Green-top Guideline for managing monochorionic twin pregnancies, first published in 2008, revised in 2016 (33). This was further supported by the National Institute for Health and Care Excellence (NICE) guideline on twin and triplet pregnancies, first published in 2019 and revised in 2024 (34). Despite the recommendation to manage twin pregnancies based on chorionicity, there is no specific guideline in the UK for managing DCDA twin pregnancies. In the Netherlands, the most recent (2021) figures show a PMR for multiples of 16.9 per 1,000 births, with twins accounting for 2.9% of all births. In contrast,

perinatal mortality rates for multiples in Australia and New Zealand are much higher, at 35 per 1,000 and 35.09 per 1,000, respectively. However, these figures include deaths from 20 weeks gestation onward, which may explain the higher rates. Kilby et al. point out that perinatal mortality in twins doubles before 22 weeks, particularly in monochorionic pregnancies, describing this as "hidden mortality (5)." Notably, these early losses are not captured in Ireland's data.

Twin pregnancies exhibited an elevated risk of SB and ENND when compared to singleton pregnancies across all maternal age groups. Our study indicates that younger maternal age, particularly under 25 years, is associated with a significantly higher risk of perinatal mortality in twin pregnancies. This finding aligns with existing literature, which highlights that younger mothers are at greater risk for adverse perinatal outcomes in twin pregnancies due to several factors (35–38). One of the main contributors to the increased PM in younger mothers is the higher rate of preterm births and low birth weight in twin pregnancies (35,37). Zhang et al. highlights that younger mothers from lower socioeconomic backgrounds were more likely to have poor perinatal outcomes due to fewer prenatal visits and less frequent surveillance (35). Similarly, another study emphasized that insufficient prenatal care is a significant factor in the elevated neonatal death rates observed in younger mothers (37). Interestingly, psychosocial and nutritional challenges were also identified as potential contributing factors. Younger women, particularly adolescents, often experience increased stress during pregnancy, which was linked to higher rates of preterm birth (37). Additionally, younger mothers, may not have fully developed physically, leading to poorer nutritional status, which can further increase the risk of preterm birth and low birth weight (37). Inexperience and lower health literacy among younger mothers may also play a role in their higher risk for adverse perinatal outcomes (36). Prapas et al. speculate younger mothers may be less equipped to recognise or manage pregnancy complications and may make delayed decisions regarding medical care (36). Considering these findings, there is a clear need to address potential social barriers, increase engagement in antenatal education for twin pregnancies relevant to this age category and chorionicity and increase antenatal surveillance as recommended in a previous study from McLennan et al (34,37).

It is widely reported that preterm birth and low birth weight are the most important factors in determining perinatal deaths (4,6,39–42). This is also reflected in our findings as most of twin pregnancy perinatal deaths occurred in extremely preterm and extremely low birthweight infants. Spontaneous preterm birth was the leading cause of ENND in monochorionic twin pregnancies and the second main cause in dichorionic twin pregnancies. These findings reinforce the need for effective screening and interventions for preterm birth. The current Irish multiple pregnancy guideline does not

recommend routine screening for preterm birth due to the absence of effective management of this issue. Before 2024 the UK's Twin and Triplet National Institute for Health Care Excellence (NICE) guideline did not either (43–45). However, the revised NICE guideline now recommends 'a single cervical length scan between 16-20 weeks to woman or pregnant people with a twin pregnancy' (46). This change in recommendation comes from the availability and review of clinical studies supporting the use of vaginal progesterone as an intervention(46). Progesterone was shown to reduce preterm birth and serious neonatal complications in women with a cervix of <25mm (44,47). Screening for the risk of spontaneous preterm birth in twins, using a cervical length threshold of <25 mm and treating pregnancies identified as being at higher risk of preterm birth was found to be a cost-effective use of NHS resources (46). While the most effective tool for spontaneous preterm birth prediction is a mid-trimester cervical length measurement (transvaginal) (44,48,49), there are conflicting recommendations for twin pregnancies regarding the use of cervical length screening, at exactly what gestation screening should be performed and the measurements to define a short cervical length evident across international clinical practice guidelines (50,51). Standardisation of definitions and identification of effective methods for the prevention of preterm birth in twin pregnancies could have a significant impact on the perinatal mortality rate. The ROI also needs an up-to-date guideline regarding the management of twin pregnancies according to chorionicity, reflecting the most current evidence.

A higher proportion of twin early neonatal deaths occurred in underweight mothers compared to singletons, while a greater number of singleton ENNDs were associated with mothers with obesity. This suggests that low maternal BMI might be more strongly associated with early neonatal deaths in twins, whereas higher BMI may have a stronger link to outcomes in singleton pregnancies. These results align with the findings of other studies, in which they highlight that underweight women are at increased risk for adverse perinatal outcomes in twin pregnancies (42,52,53). They also suggest that the association between BMI and adverse outcomes appears to differ in twin pregnancies compared to singleton pregnancies (52,53). This underscores the need for tailored twin pregnancy counseling and prenatal care, particularly for underweight women carrying twins.

Obstetric ultrasound is essential for the appropriate management of twin pregnancies (43,46,54,55). An Irish study from 2016 highlighted a variation across maternity units regarding the provision of these scans (55). It showed only 35% of maternity units offered fetal anomaly ultrasounds to all women (55). Furthermore, only 47% of women nationwide had access to a routine first-trimester ultrasound conducted in a dedicated ultrasound department by a qualified sonographer and an additional 26% of

women had a first-trimester ultrasound in an antenatal clinic or by a doctor who may lack formal ultrasound training (55). Fetal anomaly ultrasounds are now available for every pregnancy within the ROI (since 2023) and the national clinical practice guideline recommends chorionicity should be assigned at the earliest opportunity (43).

While most perinatal deaths were observed in tertiary hospitals, a notable proportion occurred in non-tertiary units and of these, 28% had an MCA – with more than half detected antenatally. According to the Irish multiple pregnancy guideline (2012), referral of twin pregnancies with an MCA to a tertiary level Fetal Medicine Unit should be considered in the presence of intertwin growth discordance or a fetal structural abnormality (46). The newly published fetal anatomy ultrasound guideline recommends referring patients with a suspected anomaly to a Fetal Medicine Consultant or if none is available the woman or couple should be referred to a tertiary centre (56). Specialised care for twin pregnancies is not available in all Irish maternity units, especially those without specialised neonatal facilities and staff experienced in twin birth and management. Previous studies have highlighted the importance of having experienced and trained clinicians in the management of twins (41,57). The NICE twin and triplet pregnancy guideline state that multiple pregnancies should be cared for by specialist teams, with early referral of complicated pregnancies to a tertiary level fetal medicine centre (45). In total 42.8% of twin SBs and 31.5% of twin ENND occurred in non-tertiary units. Among all twins who died due to spontaneous preterm birth and were born at less than 28 weeks gestation, 32.6% were delivered outside of tertiary hospitals (18.8% in peripheral hospital and 13.8% in regional hospitals). This contrasts with the model of care for Neonatal Services, which recommends that infants born < 28 weeks should ideally be born in tertiary centers where specialised neonatal services are available (43,44). This recommendation was further reinforced by the 2018 Neonatal Intensive Care Outcomes Research and Evaluation (NICORE) Report, which examined mortality risks among very low birth weight infants in the Republic of Ireland from 2014-2018 (45). The study found that infants born at 24-27 weeks' gestation in tertiary units in the ROI had mortality rates in line with expectations (45). However, infants born in non-tertiary units faced a 70% higher risk of mortality, with the majority of these deaths occurring in peripheral hospitals (45). Our findings might indicate that these practices may not be consistently followed at national level. Further research is needed to thoroughly examine the care pathways for twin pregnancies in Ireland and to assess the extent to which guideline recommendations are being applied in clinical practice.

The MBRRACE twin pregnancy confidential enquiry report showed that the lack of a specialist core team contributed to pregnancy loss in several cases (22). Better definition of twin pregnancy

complications requiring management in tertiary hospital units could improve care, potentially reducing perinatal mortality rates in twins (5). In Ireland, efforts should be made to optimise the referral system for twin pregnancies within established networks and encourage planning for delivery in tertiary centres where obstetricians experienced in twin births are immediately available, particularly when pregnancy complications are anticipated or diagnosed, as outlined in the current clinical practice guideline (43).

Centralising care to tertiary units and timely referrals to maternal fetal medicine specialists for complicated twin pregnancies, such as monochorionic twins, discordant fetal growth and single fetal demise and the presence of fetal anomalies, could also be effective for preterm birth prevention as highlighted by various authors (4,58). An algorithm describing appropriate referral pathways to fetal medicine expertise in the event of an abnormal finding in a twin pregnancy should be identified. Due to the risk of preterm birth in twin pregnancies, timely specialist counselling on this issue is an important aspect of care (59). Antenatal counselling on the risk of preterm labour associated with twin pregnancies does not feature in the current Irish multiple pregnancy guideline (43), however the MBRRACE twin pregnancy confidential enquiry report noted that the lack of a discussion surrounding this issue constitutes deficient care (22).

National perinatal mortality statistics contribute to improving perinatal care (5) and special attention should be focused on the cause of death for twins. A major cause of death for infants from a twin pregnancy was placental conditions which is a major contributor to birth weight discordance (60). National assessment of perinatal mortality in twins by chorionicity is important and may improve counselling and management of twin pregnancies for conditions such as twin-to-twin transfusion syndrome (TTTS) (5). This highlights the importance of early chorionicity determination, closer ultrasound monitoring and timely referral of these cases (within 24-48hours) in hospitals specialised in the management of TTTS as emphasized in previous research (4,61,62). There is a clear necessity for the formulation of dedicated twin pregnancy guidelines within Ireland. These should be specific according to chorionicity in recognition of the distinct differences in management pathways required for dichorionic and monochorionic twins (33).

The MBRRACE-UK enquiry of stillbirths and neonatal deaths in twin pregnancies found that TTTS went unrecognised in some cases of emergency assessment within the maternity triage, despite presentation with classical TTTS signs and symptoms. Therefore, the report recommended that all clinical staff working in emergency assessment should undergo training to recognize the signs of TTTS and women should be educated on the symptoms and advised to seek immediate assessment should they present (22). Early detection of chorionicity and improved practice in chorionicity diagnosis would

help streamline care pathways for antenatal care. Improved practice for monochorionic twins would also better direct antenatal care.

Our findings show that more can be done in Ireland to improve care in twin pregnancies to optimise outcomes and ultimately, prevent perinatal deaths. Targeted measures and clinical guidance should be put in place to ensure continuous improvement and the provision of best care in the management of twin pregnancies.

### Strengths and limitations

The data did not allow calculations of adjusted risk ratios because required variables were not available at the population level. Therefore, we were able to report some crude risk ratios in addition to comparing the distribution of risk factors in singleton and twin perinatal deaths.

Our study has additional limitations: the available PM data did not allow for the analysis of cases where both twins died as twin pairs could not be matched. Moreover, limitations were identified regarding the data's potential underestimation of maternal conditions like hypertension and fetal conditions such as accurate reporting of fetuses who were small for gestational age (SGA). To capture relevant sociodemographic determinants of health and previous relevant histories, additional data is needed.

The availability of chorionicity data within the perinatal mortality population was a strength of this study, however this data was not available for the national population of all twins (within the HIPE data). This study's main strength is its comprehensive inclusion of data from the entire national twin population, combined with a national perinatal mortality database. It has national representativeness, and the utilisation of two national datasets enabled the calculation of rates and risks specific to this population, a novel approach for Ireland. Additionally, the study's ability to conduct detailed analyses of twin perinatal mortalities contributes to its relevance, novelty and learning.

### Conclusion

Despite existing guidelines and advancements in managing twin pregnancies, our study highlights the need for more consistent application of best practices and improvements in antenatal care. Key areas for improvement include enhanced screening for preterm birth and establishing a clear referral pathway to ensure that high-risk twin pregnancies are directed to specialised facilities with the necessary expertise and resources for optimal care.

Our findings also emphasise the importance of tailored care for twin pregnancies, particularly in younger women and those underweight, who face an elevated risk of perinatal mortality. This underscores the need for early identification of risk factors and prompt intervention to mitigate complications such as preterm birth and low birth weight.

Twin-specific guidelines are crucial for improving outcomes in twin pregnancies by providing tailored care that addresses the distinct risks involved. Ireland needs updated guidelines that consider chorionicity and ensure clear referral pathways to fetal medicine specialists for complex cases. Additionally, enhanced staff training, public awareness, and optimised referral systems can help reduce perinatal mortality. Managing twin pregnancies in specialised centers with experienced clinicians will better address these challenges and improve outcomes for both mothers and infants.

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## Authors' contributions:

COC: Conceptualization, data analysis, methodology and writing and editing

SL: Conceptualization, supervision, data analysis, methodology & reviewing the paper

PC: Conceptualization, data analysis & methodology

KOD: Conceptualization, methodology, supervision & reviewing the paper

## References

1. Lawn JE, Blencowe H, Pattinson R, Cousens S, Kumar R, Ibiebele I, et al. Stillbirths: Where? When? Why? How to make the data count? *The Lancet*. 2011;377(9775):1448–63. doi:10.1016/S0140-6736(10)62187-3
2. San Lazaro Campillo I, Manning E, Corcoran P, Keane J, O'Farrel I, McKernan J, et al. Perinatal Mortality National Clinical Audit in Ireland Annual Report 2020. 2022;
3. Helps A, Leitao S, Greene R, O'Donoghue K. Perinatal mortality audits and reviews: Past, present and the way forward. *European Journal of Obstetrics and Gynecology and Reproductive Biology*. 2020;250:24–30. doi:10.1016/j.ejogrb.2020.04.054
4. Chitrit Y, Filidori M, Pons JC, Duyme M, Papiernik E. Perinatal mortality in twin pregnancies: A 3-year analysis in Seine Saint-Denis (France). *European Journal of Obstetrics and Gynecology and Reproductive Biology*. 1999;86(1):23–8. doi:10.1016/S0301-2115(99)00037-8
5. Kilby MD, Gibson JL, Ville Y. Falling perinatal mortality in twins in the UK: organisational success or chance? *BJOG An International Journal Obstetrics Gynaecology*. 2019;126(3):341–7. doi:10.1111/1471-0528.15517
6. Herruzo AJ, Martínez L, Biel E, Robles R, Rosales MA, Miranda JA. Perinatal morbidity and mortality in twin pregnancies. *International Journal of Gynecology & Obstetrics*. 1991 Sep;36(1):17–22. doi:10.1016/0020-7292(91)90172-2
7. O'Connell O, Meaney S, O'Donoghue K. Caring for parents at the time of stillbirth: How can we do better? *Women and Birth*. 2016;29(4):345–9. doi:10.1016/j.wombi.2016.01.003
8. Wilson AL, Fenton LJ, Stevens DC, Soule DJ. The death of a newborn twin: an analysis of parental bereavement. *Pediatrics*. 1982 Oct;70(4):587–91.
9. Richards J, Graham R, Embleton ND, Campbell C, Rankin J. Mothers' perspectives on the perinatal loss of a co-twin: A qualitative study. *BMC Pregnancy Childbirth*. 2015;15(1):1–12. doi:10.1186/s12884-015-0579-z
10. Ravelli ACJ, Eskes M, Van Der Post JAM, Abu-Hanna A, De Groot CJM. Decreasing trend in preterm birth and perinatal mortality, do disparities also decline? *BMC Public Health*. 2020;20(1):1–10. doi:10.1186/s12889-020-08925-w

11. Sherman M. The neonatal intensive care unit. *Psychiatric Clinics of North America*. 1982;5(2):433–43. doi:10.1016/s0193-953x(18)30879-7
12. San Lazaro Campillo I, Manning E, Corcoran P, Keane J, O’Farrell I, McKernan J, et al. Perinatal mortality national clinical audit in Ireland annual report 2021. 2023;
13. Boerma T, Lawn JE. Delivering data on pregnancy outcomes through prospective studies in high-burden settings. *The Lancet Global Health*. 2018;6(12):e1256–7. doi:10.1016/S2214-109X(18)30419-4
14. Mortality P. 65,904. 2017;1–2.
15. ROURKE AJ. Evaluating the quality of medical care. *Hospital progress*. 1957;38(9):72–3. doi:10.1056/nejm197306212882509
16. Lam JR, Liu B, Bhate R, Fenwick N, Reed K, Duffy JMN, et al. Research priorities for the future health of multiples and their families: The Global Twins and Multiples Priority Setting Partnership. *Ultrasound in Obstetrics and Gynecology*. 2019;54(6):715–21. doi:10.1002/uog.20858
17. Horon I, Martin JA. National Vital Statistics Reports Volume 71, Number 09, December 7, 2022. *National Vital Statistics Reports*. 2022;71(9):1–11.
18. Human Fertilisation & Embryology Authority. Multiple births in fertility treatment 2019. 2022.
19. Debrock S, Spiessens C, Meuleman C, Segal L, De Loecker P, Meeuwis L, et al. New Belgian legislation regarding the limitation of transferable embryos in in vitro fertilization cycles does not significantly influence the pregnancy rate but reduces the multiple pregnancy rate in a threefold way in the Leuven University Fertility Center. *Fertility and Sterility*. 2005 May 1;83(5):1572–4. doi:10.1016/J.FERTNSTERT.2005.01.087
20. Chambers GM, Keller E, Choi S, Khalaf Y, Crawford S, Botha W, et al. Funding and public reporting strategies for reducing multiple pregnancy from fertility treatments. *Fertility and Sterility*. 2020;114(4):715–21. doi:10.1016/j.fertnstert.2020.08.1405
21. Euro-Peristat Project. *European Perinatal Health Report*. 2022.
22. Draper ES, Gallimore ID, Kurinczuk JJ, Kenon S, (Eds.) on behalf of MMBRACE-UK. MMBRACE-UK 2019 Perinatal Confidential Enquiry Stillbirths and neonatal deaths in twin pregnancies. The Infant Mortality and Morbidity Studies, Department of Health Sciences, University of Leicester; 2021.

23. Khalil A, Reed K. Confidential Enquiry into Stillbirth and Neonatal Death in Twins: key messages for obstetricians and fetal medicine specialists. *Ultrasound in Obstetrics & Gynecology*. 2021; doi:10.1002/uog.23594
24. Wiley MM. Using HIPE data as a research and planning tool: Limitations and opportunities: A response. *Irish Journal of Medical Science*. 2005;174(2):52–7. doi:10.1007/BF03169130
25. Leitaio, S. Corcoran, P. Greene, RA. Murphy, BP. Twomey. A on behalf of NR of I. Very Low Birth Weight Infants in the Republic of Ireland Annual Report 2019. Cork: National Perinatal Epidemiology Centre. 2021.
26. Irish Statute Book. Civil Registration Act 2004 [Internet]. 2024. Available from: <https://www.irishstatutebook.ie/eli/2004/act/3/enacted/en/pdf>
27. Manktelow BN Prunet C, Smith PW, Boby T, Hyman-Taylor P, Kurinczuk JJ, Field DJ, Draper ES on behalf of the MUC. MBRRACE-UK Perinatal Mortality Surveillance Report, UK Perinatal Deaths for Births from January to December 2020. 2022.
28. Perined. Perinatale audit [Internet]. Available from: <https://www.perined.nl/>
29. Australian Institute of Health and Welfare. National Perinatal Data Collection Annual Update [Internet]. Available from: <https://www.aihw.gov.au/reports/mothers-babies/australias-mothers-babies/data>
30. PMMRC. Twelfth Annual Report of the Perinatal and Maternal Mortality Review Committee Reporting mortality 2016. 2018. 1–181 p.
31. Draper, Elizabeth S. Gallimore, Ian D. Smith, Lucy K. Matthews, Ruth J. Fenton, Alan C. Kurinczuk, Jennifer J. Smith, Peter W. Manktelow BN. MBRRACE-UK Perinatal Mortality Surveillance Report, UK Perinatal Deaths for Births from January to December 2020. Leicester;
32. Kilby, MD. Baker, PN. Critchley, H. Field D. Multiple Pregnancy Study- Group Statement: Consensus views arising from the 50th study group. Royal College Obstetricians Gynaecologists, RCOG.
33. Royal College of Obstetricians & Gynaecologists: RCOG. Management of Monochorionic Twin Pregnancy: Green-top Guideline No. 51. *BJOG An International Journal Obstetrics Gynaecology*. 2017 Jan;124(1):e1–45. doi:10.1111/1471-0528.14188
34. Excellence NI of H. Twin and triplet pregnancy. Twin triplet pregnancy. 2024;(April).
35. Zhang J, Meikle S, Grainger DA, Trumble A. Multifetal pregnancy in older women and

- perinatal outcomes. *Fertility and Sterility*. 2002;78(3):562–8. doi:10.1016/S0015-0282(02)03272-7
36. Prapas N, Kalogiannidis I, Prapas I, Xiromeritis P, Karagiannidis A, Makedos G. Twin gestation in older women: Antepartum, intrapartum complications, and perinatal outcomes. *Archives of Gynecology and Obstetrics*. 2006;273(5):293–7. doi:10.1007/s00404-005-0089-8
  37. McLennan AS, Gyamfi-Bannerman C, Ananth C V., Wright JD, Siddiq Z, D’Alton ME, et al. The role of maternal age in twin pregnancy outcomes. *American Journal of Obstetrics and Gynecology*. 2017;217(1):80.e1-80.e8. doi:10.1016/j.ajog.2017.03.002
  38. Lisonkova S, Joseph KS, Bell R, Glinianaia S V. Effect of advanced maternal age on perinatal outcomes in twins: The impact of chorionicity. *Annals of Epidemiology*. 2013;23(7):428–34. doi:10.1016/j.annepidem.2013.05.005
  39. Glinianaia S V., Obeyesekere MA, Sturgiss S, Bell R. Stillbirth and neonatal mortality in monochorionic and dichorionic twins: A population-based study. *Human Reproduction*. 2011;26(9):2549–57. doi:10.1093/humrep/der213
  40. Gardner MO, Goldenberg RL, Cliver SP, Tucker JM, Nelson KG, Copper RL. The origin and outcome of preterm twin pregnancies. *Obstetrics and Gynecology*. 1995;85(4):553–7. doi:10.1016/0029-7844(94)00455-M
  41. Rizwan N, Abbasi RM, Mughal R. Maternal morbidity and perinatal outcome with twin pregnancy. *Journal Ayub Medical College, Abbottabad JAMC*. 2010;22(2):105–7.
  42. Santana DS, Silveira C, Costa ML, Souza RT, Surita FG, Souza JP, et al. Perinatal outcomes in twin pregnancies complicated by maternal morbidity : evidence from the WHO Multicountry Survey on Maternal and Newborn Health. 2018;9:1–11.
  43. Institute of Obstetricians and Gynaecologists, Royal College of Physicians of Ireland (RCPI) and Directorate of Strategy and Clinical Care HSE (HSE). Clinical practice guideline No. 14: Management of Multiple Pregnancy. 2014;
  44. Khalil A, Prasad S. Screening and prevention of preterm birth in twin pregnancies. *Best Practice Research Clinical Obstetrics Gynaecology*. 2022;84:179–93. doi:10.1016/j.bpobgyn.2022.08.008
  45. National Institute for Health and Care Excellence (NICE). Twin and triplet pregnancy. NICE guidelines (NG 137). 2019;(September):1–61.

46. National Institute of Health and Care Excellence. Twin and Triplet Pregnancy NG 137. NICE guidelines (NG 137). 2024. 1–61 p.
47. Romero R, Conde-Agudelo A, Rehal A, Da Fonseca E, Brizot ML, Rode L, et al. Vaginal progesterone for the prevention of preterm birth and adverse perinatal outcomes in twin gestations with a short cervix: an updated individual patient data meta-analysis. *Ultrasound in Obstetrics and Gynecology*. 2022;59(2):263–6. doi:10.1002/uog.24839
48. Conde-Agudelo A, Romero R, Hassan SS, Yeo L. Transvaginal sonographic cervical length for the prediction of spontaneous preterm birth in twin pregnancies: A systematic review and metaanalysis. *American Journal of Obstetrics and Gynecology*. 2010;203(2):128.e1-128.e12. doi:10.1016/j.ajog.2010.02.064
49. Lim AC, Hegeman MA, Huis In 't Veld MA, Opmeer BC, Bruinse HW, Mol BWJ. Cervical length measurement for the prediction of preterm birth in multiple pregnancies: A systematic review and bivariate meta-analysis. *Ultrasound in Obstetrics and Gynecology*. 2011;38(1):10–7. doi:10.1002/uog.9013
50. Roman A, Ramirez A, Fox NS. Screening for preterm birth in twin pregnancies. *American Journal Obstetrics Gynecology MFM*. 2022;4(2):100531. doi:10.1016/j.ajogmf.2021.100531
51. Tsakiridis I, Giouleka S, Mamopoulos A, Athanasiadis A, Dagklis T. Management of Twin Pregnancies: A Comparative Review of National and International Guidelines. *Obstetrical & Gynecological Survey*. 2020 Jul;75(7):419–30. doi:10.1097/OGX.0000000000000803
52. Bone JN, Joseph KS, Magee LA, Wang LQ. Pre-pregnancy body mass index and adverse maternal and perinatal outcomes in twins : A population retrospective cohort study. 2023;(April). doi:10.1038/s41366-023-01320-6
53. Greatholder I, Tomlinson E, Wilkinson J, Higgins LE, Kilby MD, Heazell AEP. Evaluating antenatal risk in twin pregnancies—A feasibility study to identify modifiable factors associated with adverse pregnancy outcomes. *Acta Obstetrica Gynecologica Scandinavica*. 2023;(October 2022):585–96. doi:10.1111/aogs.14540
54. Khalil A, Rodgers M, Baschat A, Bhide A, Gratacos E, Hecher K, et al. ISUOG Practice Guidelines: role of ultrasound in twin pregnancy. *Ultrasound in Obstetrics & Gynecology*. 2016 Feb;47(2):247–63. doi:10.1002/uog.15821
55. Hayes-Ryan D, McNamara K, Russell N, Kenny L, O'Donoghue K. Maternity ultrasound in the Republic of Ireland 2016; A review. *Irish Medical Journal*. 2017;110(7):598.

56. Fleming A, Corbett G, McParland P. National Clinical Practice Guideline: The Fetal Anatomy Ultrasound. National Women and Infants Health Programme and The Institute of Obstetricians and Gynaecologists. 2023;1–132.
57. Deruelle P, Coulon C, Vaast P, Houfflin-Debauge V. Twin pregnancies: Where should we manage them? Where should they deliver? *Journal Gynecologie Obstetrique Biologie la Reproduction*. 2009;38(8 SUPPL. 1):S56–60. doi:10.1016/S0368-2315(09)73561-6
58. Lewi L, Gucciardo L, Van Mieghem T, De Koninck P, Beck V, Medek H, et al. Monochorionic diamniotic twin pregnancies: Natural history and risk stratification. *Fetal Diagnosis Therapy*. 2010;27(3):121–33. doi:10.1159/000313300
59. Du L, Du X, Wang W, Hu L, Qiao C, Shi R. Clinical analysis on the influencing factors related to preterm twin pregnancy. *Revista da Associacao Medica Brasileira*. 2022;68(12):1651–6. doi:10.1590/1806-9282.20220447
60. Victoria A. Perinatal outcome, placental pathology, and severity of discordance in monochorionic and dichorionic twins. *Obstetrics & Gynecology*. 2001 Feb;97(2):310–5. doi:10.1016/S0029-7844(00)01111-X
61. Gulati N, Mackie FL, Cox P, Marton T, Heazell AEP, Morris RK, et al. Cause of intrauterine and neonatal death in twin pregnancies (CoDiT): development of a novel classification system. *BJOG An International Journal Obstetrics Gynaecology*. 2020;127(12):1507–15. doi:10.1111/1471-0528.16291
62. O’Farrel,I IB. Manning,E. Corcoran, P. White,E. Greene R on behalf of the PMG. Perinatal Mortality in Ireland Biennial Report 2018/2019. National Perinatal Epidemiology Centre 2021. doi:10.1007/BF02949658