Cause of intrauterine and neonatal Death in Twin Pregnancies (CoDiT)

Gulati, Nidhi; Mackie, Fiona; Cox, Phillip; Marton, Tamas; Heazell, Alexander; Morris, R. Katie; Kilby, Mark

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Cause of intrauterine and neonatal death in twin pregnancies (CoDiT): development of a novel classification system

N Gulati,[a,b] FL Mackie,[a,b] P Cox,[c] T Marton,[c] AEP Heazell,[d,e] RK Morris,[b,f] MD Kilby[a,b]

[a] Institute of Metabolism & Systems Research, College of Medical & Dental Sciences, University of Birmingham, Birmingham, UK [b] Fetal Medicine Centre, Birmingham Women's & Children's Foundation Trust, Birmingham, UK [c] Cellular Pathology Department, Birmingham Women's Hospital, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK [d] Maternal and Fetal Health Research Centre, University of Manchester, Manchester, UK [e] St Mary's Hospital, Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK [f] Institute of Applied Health Research, College of Medical & Dental Sciences, University of Birmingham, Birmingham, UK

Correspondence: Dr N Gulati, Institute of Metabolism and Systems Research, College of Medical & Dental Sciences, University of Birmingham, Birmingham B15 2TT, UK. Email: nidhigulati@nhs.net

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Objective Twin pregnancies have a significantly higher perinatal mortality than singleton pregnancies. Current classification systems for perinatal death lack twin-specific categories, potentially leading to loss of important information regarding cause of death. We introduce and test a classification system designed to assign a cause of death in twin pregnancies (CoDiT).

Design Retrospective cross-sectional study.

Setting Tertiary maternity unit in England with a perinatal pathology service.

Population Twin pregnancies in the West Midlands affected by fetal or neonatal demise of one or both twins between 1 January 2005 and 31 December 2016 in which postmortem examination was undertaken.

Methods A multidisciplinary panel designed CoDiT by adapting the most appropriate elements of singleton classification systems. The system was tested by assigning cause of death in 265 fetal and neonatal deaths from 144 twin pregnancies. Cause of death was validated by another obstetrician blinded to the original classification.

Main outcome measures Inter-rater, intra-rater, inter-disciplinary agreement and cause of death.

Results Cohen's Kappa demonstrated 'strong' (>0.8) inter-rater, intra-rater and inter-disciplinary agreement (95% CI 0.70–0.91). The commonest cause of death irrespective of chorionicity was the placenta; twin-to-twin transfusion syndrome (TTTS) was the commonest placental cause in monochorionic twins and acute chorioamnionitis in dichorionic twins.

Conclusions This novel classification system records causes of death in twin pregnancies from postmortem reports with high inter-user agreement. We highlight differences in aetiology of death between monochorionic and dichorionic twins.

Keywords Cause of death, classification system, dichorionic, monochorionic, multiple pregnancy, perinatal death, stillbirth, twins.

Tweetable abstract New classification system for #twin cause of death 'CoDiT' shows high rater agreement.

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Introduction

Multiple pregnancies occur in 1.6% of pregnancies in England and Wales; the commonest are twin pregnancies (98%).[1] Compared with singletons, monochorionic twins have a 13-fold increased risk of stillbirth and dichorionic twins a five-fold increased risk.[2–4] Twin pregnancies account for almost 6% of all stillbirths, 18% of neonatal deaths (NND) and 20% of preterm births (many of which occur <28 weeks' gestation).[5,6] Complex anastomoses connecting fetal circulations in monochorionic placentas leads to highly morbid conditions unique to these pregnancies, such as twin-to-twin transfusion syndrome (TTTS). Twin-specific risks of dichorionic pregnancies include prematurity, selective growth restriction and co-twin interventions. Although pathological causes of death in twin pregnancies are well established, a classification system specifically for twins does not exist.

Classification systems standardise recording of aetiology of mortality, inform public healthcare policies, clinical care

and research, and facilitate comparison of global rates.[7] Existing classification systems include limited acknowledgement of the complexity of multiple pregnancies. In Codac (Cause of Death and Associated Conditions), multiple pregnancies are classified as an associated perinatal cause of death, and TTTS is the only twin-specific cause cited in ReCoDe (Relevant Condition at Death).[7,8]

A 2016 systematic review identified 81 classification systems created, modified and/or used between 2009 and 2014, not including the World Health Organization (WHO) International Classification of Diseases 10th revision classification for perinatal deaths (ICD-PM).[9–11] A Delphi consensus identified the 17 most important characteristics required for a global classification system of perinatal deaths: (1) a sufficiently comprehensive list of categories to minimise the proportion of deaths classified as 'other', (2) accommodates stillbirths and NND, and (3) shows high inter- and intra-rater reliability.[12] Assessment of existing classification systems against the 17 characteristics found that 82% of systems aligned with fewer than five of these characteristics. The most aligned to these aims were Codac (9/17) and Tulip (7/17).[10] Despite overall poor performance, development of a globally effective system would benefit from referring to the most aligned systems.[13]

To address the need to record causes of mortality in twin pregnancies, we developed and validated a classification system to report causes of fetal or NND in twin pregnancies that aimed to meet as many of the characteristics of the Delphi study as possible.

Methods

Developing the classification system

A multidisciplinary panel of four obstetricians and two perinatal pathologists created a classification system for twin pregnancies by adapting and combining the two systems which scored highest against the Delphi consensus criteria: Codac and Tulip.[7,12,14] As Tulip resonates with the aim of our system to identify underlying aetiologies, the main categories of Tulip—congenital abnormality, placenta, prematurity, infection, other and unknown—feature in our system, named CoDiT (Cause of Death in Twins) (Appendix S1). Codac, unlike Tulip, recognises umbilical cord events as a main category for cause of death. As cord accidents are a specific risk for monochorionic monoamniotic (MCMA) pregnancies, umbilical cord is a main category in CoDiT.

Each of the seven main categories has subcategories drawn from singleton classification systems, with additional twin-specific subcategories. Conjoined twins and twin-reversed arterial perfusion (TRAP) were added to congenital abnormalities, with a distinction between the pump and acardiac twin. TTTS is a subcategory in placental causes of death, with a distinction between chronic and acute, intrapartum or antenatal variants (the latter with or without neurological damage) and treated and untreated TTTS. Combining pathological and clinical entities recognises the multi-dimensional causes of perinatal mortality in twins and acknowledges that there may be inherent differences between diagnosing TTTS antenatally and postmortem. The 'unknown' category has two subcategories allowing distinction between cases in which cause of death is unknown despite thorough postmortem investigation or unknown because important information was missing to determine the cause of death.

CoDiT is prefaced with a section to record the mother's demographics, medical and obstetric history, whether demise was of one or both twins, gestation at death, age at death if a NND, and gestation at delivery. Recording mode of death enables distinction between 'how' and 'why' the death occurred. For example, if a pregnancy was terminated for a lethal congenital abnormality, the classification system should reflect that the fetus(es) would have had a high chance of mortality because of the underlying anomaly irrespective of prenatal intervention.

Once agreement within the panel was achieved on the final classification system, it was used to classify causes of death from postmortem reports. It was determined a priori that the reliability of CoDiT would be determined by the level of inter-rater, inter-disciplinary and intra-rater agreement.

Testing CoDiT

Postmortems conducted at a West Midlands tertiary unit between 1 January 2005 and 31 December 2016 on fetuses and neonates from twin pregnancies were identified from a pre-existing database of all postmortems conducted at the unit (Figure 1). All postmortems had written parental consent and were performed by perinatal pathologists. Project development had no funding, patient involvement or core outcome set and was registered as a service evaluation project by the unit's clinical governance team. Each pregnancy was anonymised by assigning a case number, then the letter 'A' for twin 1 or 'B' for twin 2. Each postmortem report begins with a clinical summary provided by the referring hospital, from which all demographic and clinical data were obtained, including gestation at death and delivery (or age at death if NND). A summary of the main findings and a detailed description of macroscopic external and internal organ examination findings is provided, followed by a description of the placenta including chorionicity, vascular territories and findings from injection studies. An injection study was conducted if TTTS was suspected or there was significant weight discordance between twins. Injection studies were not possible if the placenta was too small or damaged. Individual organ and placental histology

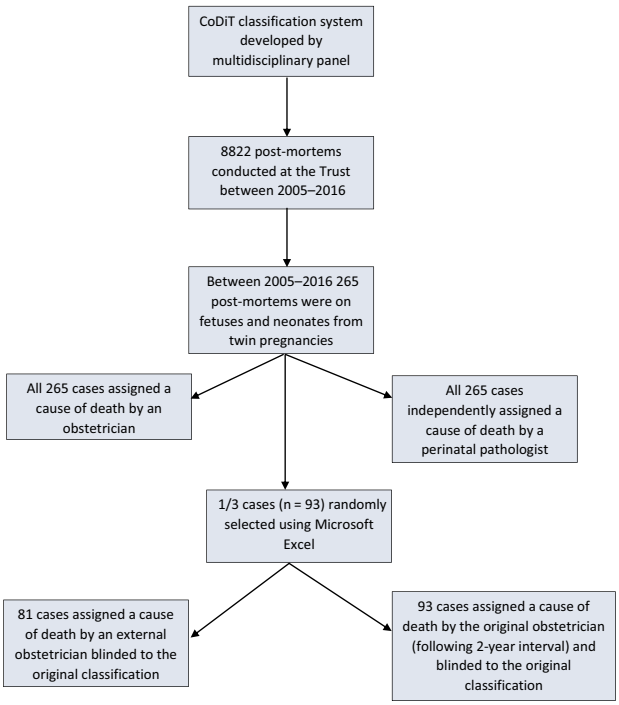

Figure 1. Flowchart demonstrating method of case identification following development of CoDiT classification and assignment of cause of death.

and microbiological and genetic testing results are then described. All postmortem reports of fetuses and neonates in this cohort were examined and a cause of death assigned independently by an obstetrician and perinatal pathologist. Although CoDiT enables users to capture all postmortem findings, users understood to select a single cause of death. Subsequent panel consensus was drawn to allow data analysis. One-third of cases were randomly selected for independent classification by an external obstetrician, who had the same information and case numbers as other raters, and re-classification by the initial obstetrician after a 2-year interval. Cohen's Kappa was used to calculate separately inter-rater agreement between the external and initial obstetrician, intra-rater agreement and inter-disciplinary agreement, using a hand-programmed matrix in Microsoft EXCEL. Qualitative interpretation of Kappa values was as follows: <0.4, minimal; 0.4–0.59, weak; 0.6–0.79, moderate; 0.8–0.9, strong; >0.9, almost perfect.[15]

Results

General findings

Between 1 January 2005 and 31 December 2016, 265 fetal and neonatal postmortems from 144 twin pregnancies were performed, referred from 14 hospitals throughout the West Midlands. Table 1 summarises maternal demographic and descriptive data. Forty-six per cent of deaths occurred in monochorionic twins (122/265 postmortems). Chorionicity was undesignated at postmortem in 18% (47/265) as the placenta was either not submitted or unsuitable (too fragmented or incorrectly fixed) for examination. Most demises were in utero (miscarriages and stillbirths); 7% were NND (18/265), of which 61% (11/18) were dichorionic pregnancies. Most deaths, irrespective of chorionicity, were double-twin deaths (246/265; 93%); a greater proportion of single twin deaths occurred in dichorionic than in monochorionic

Table 1. Demographic information of all postmortem reports from twin pregnancies between January 2005 and December 2016 at a West Midlands tertiary hospital

	Monochorionic	Dichorionic	Total
No. pregnancies	66	78	144
Mean maternal age	29.1 (95% CI 27.4–30.7)	30.2 (95% CI 28.2–32.1)	29.6 (95% CI 28.5–30.7)
Mean maternal BMI	27.7 (95% CI 25.6–29.8)	26.3 (95% CI 24.4–28.3)	26.7 (95% CI 25.4–28.1)
% Nulliparity	31/66 (47%)	32/78 (41%)	73/144 (51%)
Total perinatal deaths	122	96	265 (unknown chorionicity in 47)
No. fetal deaths	117/122 (96%)	85/96 (89%)	247/265 (93%)
No. NNDs	5/122 (4%)	11/96 (11%)	18/265 (7%)
No. Single deaths	6/122 (5%)	8/96 (8%)	19/265 (7%)
No. Double deaths	116/122 (95%)	88/96 (92%)	246/265 (93%)
Mean gestation at death (weeks)	19.6 (95% CI 18.3–20.8)	19.7 (95% CI 18.5–21.0)	19.6 (95% CI 18.8 - 20.5)
No. spontaneous deaths	95/122 (78%)	85/96 (89%)	219/265 (83%)
No. terminations of whole pregnancy	9/66 (14%)	6/78 (8%)	17/144 (6%)
No. selective reductions	4/122 (3%)	0	4/265 (2%)
No. deaths within 7 days of medical intervention	7/122 (6%)	0	9/265 (3%)

The chorionicity of 47 cases was unknown and therefore the total does not reflect the sum of monochorionic and dichorionic deaths.

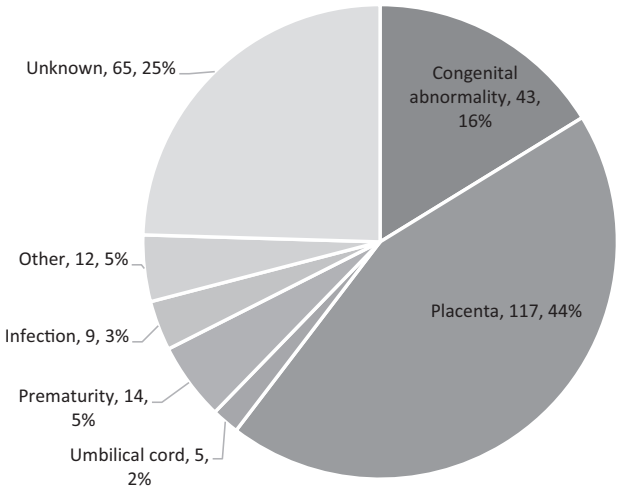

Figure 2. Distribution of causes of perinatal death in twin pregnancies between 2005 and 2016 in the West Midlands irrespective of chorionicity who had undergone a postmortem.

pregnancies (8 versus 5%). Mean gestation at death was 19–20 weeks (range 8–37 weeks). Most deaths were spontaneous (219/265; 83%); selective reduction and death within a week of medical intervention solely affected monochorionic pregnancies (9% of monochorionic deaths (11/122).

Irrespective of chorionicity, the most commonly assigned main category was 'placental' (117/265) (Figure 2), followed by 'unknown' (65/265), of which 80% (52/65) were unknown 'despite thorough postmortem investigation'. The remaining 20% (13/65) were subcategorised as unknown due to 'important information missing', most commonly referring to the placenta not being submitted.

Inter-rater, intra-rater and inter-disciplinary agreement

The Kappa coefficient for the main cause of death was 'strong' for all measured combinations of agreement; inter-rater 0.80 (95% CI 0.70–0.91), intra-rater 0.80 (95% CI 0.71–0.90) and an inter-disciplinary agreement 0.81 (95% CI 0.75–0.87). This indicates that the main cause of death can be reproducibly categorised by different users. However, agreement was 'minimal' and 'weak' when all 51 subcategories were considered, with a Kappa co-efficient of 0.39 (95% CI 0.27–0.51) for inter-rater, 0.33 (95% CI 0.22–0.43) for intra-rater, and 0.4 (95% CI 0.34–0.47) for inter-disciplinary agreement. This may be influenced by the large number of subcategories. Nevertheless, percentage agreement in the main and subcategories for all combinations was high; 86% (70/81) inter-rater main category agreement and 83% (67/81) subcategory agreement, 86% (80/93) intra-rater main category agreement and 76% (71/93) subcategory agreement and 86% (228/265) inter-disciplinary main category agreement and 82% (216/265) subcategory agreement. The commonest subcategory disagreement was acute chorioamnionitis versus ascending infection, representing 29% (4/14) of inter-rater, 18% (4/22) of intra-rater and 16% (8/49) of inter-disciplinary disagreement. Although user guidance states that ascending infection should only be assigned when there is proven birth canal colonisation, users argued that acute chorioamnionitis often derives from ascending infection.

Cause of death by chorionicity

Figure 3 summarises cause of death by chorionicity and amnionicity. Chi-square testing demonstrated that cause of death was significantly different between monochorionic and dichorionic twins ($P < 0.01$). Significantly more monochorionic twins died of congenital abnormalities ($P < 0.05$) or umbilical cord events ($P < 0.05$) compared with dichorionic twins, and significantly more dichorionic twins died of infection compared with monochorionic twins ($P < 0.001$).

Dichorionic twins

Placental causes represented 47% (45/96) of deaths in dichorionic pregnancies, with acute chorioamnionitis being the commonest subcategory (40/45; 89%). An 'unknown' cause of death was the second commonest classification (19/96; 20%), all 'despite thorough investigation', except one, classified as unknown due to important information missing because parental consent was for a limited postmortem.

Prematurity, the third commonest cause (10/96; 10%), was secondary to preterm prelabour rupture of membranes (PPROM) in 6/10 cases, spontaneous preterm labour in 3/10 and complications of prematurity in one 22-day-old neonate, born at 31 weeks' gestation. The eight deaths due to infection (8/96; 8%) were double twin deaths from four pregnancies, three of which were ascending infections and one transplacental infection. Congenital abnormalities affected eight fetuses, of which two were co-twins affected by lethal urogenital anomalies. All but one of the dichorionic pregnancies affected by congenital abnormalities resulted in death of the co-twin within 2 weeks of death of the abnormal twin. The five deaths categorised as 'other' were from three dichorionic pregnancies; two sets of twins that died secondary to maternal diseases and a NND at 17 minutes of age at 25 weeks' gestation due to fetal trauma at birth.

Monochorionic twins

Placental causes of death were most common in monochorionic twins (53/122; 43%); TTTS was the commonest subcategory (36/53; 68%). In total, 51 deaths were categorised as TTTS, but in 15/51 (29%), the placenta was not

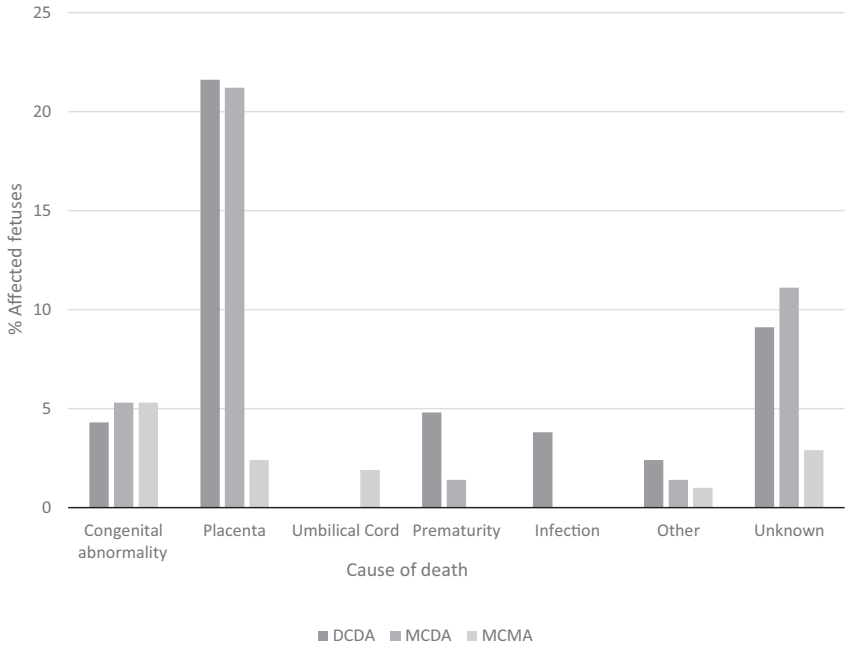

Figure 3. Distribution of causes of death by chorionicity and amnionicity, as a percentage of the total number of fetuses about which chorionicity was known (n = 208). DCDA = dichorionic diamniotic; MCDA = monochorionic diamniotic; MCMA = monochorionic monoamniotic.

submitted or too fragmented to confirm chorionicity, and TTTS was diagnosed from supporting information using the clinical history and ultrasound findings provided by the referring hospital and examining the fetuses. Most TTTS deaths were chronic and untreated (40/51; 78%). Only 20 of the 36 cases of TTTS with a placenta sent to pathology underwent injection studies, representing 39% (20/51) of the total number of fetuses categorised as TTTS. Of the four fetal deaths secondary to chronic treated TTTS, one set of twins died at 27^{+2} weeks' gestation following amnioreduction, one fetus died spontaneously more than 7 days after fetoscopic laser ablation (FLA), with survival of its co-twin, and the other died within 4 days of FLA with subsequent death of its co-twin due to acute TTTS. In 47% (24/51) of TTTS cases, clinical information from the referring hospital provided no information about possible evidence of TTTS antenatally and, as such, TTTS was diagnosed solely based on postmortem findings. For 13 of these 24 cases diagnosed with TTTS solely postmortem, the diagnosis was made without a suitable placenta to examine and was based on features noted on fetal examination such as body or organ weight discordance. Of the 20 cases in which injection studies were performed, TTTS was diagnosed solely from injection studies in 20% (n = 4).

An 'unknown' cause of death was the second commonest category (29/122; 24%), all of which were categorised as such 'despite thorough investigation'. A third of these 'unknown' cases underwent injection studies (10/29; 34%), all demonstrating a balanced circulation.

The third commonest cause was congenital abnormalities, representing 23% of monochorionic twin deaths (28/122), of which TRAP (acardiac and pump) was the commonest abnormality (13/28; 46%). There were 28 MCMA pregnancies, representing 23% of the monochorionic pregnancies in this cohort with a gestational age at death ranging from 8 to 28 weeks' gestation. The commonest cause of death in MCMA twins was congenital abnormalities (11/28), of which almost two-thirds were twin-specific (7/11) (i.e. TRAP or conjoined twins). All deaths due to umbilical cord events (4/122; 3%) occurred in MCMA pregnancies.

Cause of death by double- and single-twin demise

In monochorionic pregnancies, 95% were double-twin deaths (116/122), with 44% (51/116) classified as placental, 24% (28/116) due to congenital abnormalities, 22% (25/116) as unknown and the remaining due umbilical cord events (n = 4), prematurity (n = 3) and 'other' (n = 5). In TTTS, 98% of deaths were double-twin deaths (50/51). In dichorionic pregnancies, 92% of deaths were double-twin deaths (88/96), with 50% (44/88) classified as placental and 15% (13/88) as unknown. All deaths due to prematurity, infection, 'other' causes and congenital abnormalities in dichorionic twins were double-twin deaths.

Of the 19 single-twin deaths, 58% had an unknown cause of death (11/19), all of which were spontaneous fetal losses with a mean gestational age at death of 23 weeks (range 12–20^{+3} weeks' gestation). Four of these single-twin deaths with an unknown cause were from monochorionic

pregnancies, six from dichorionic pregnancies and one did not have a placenta submitted to confirm chorionicity.

Gestation at death and delivery

Table 2 outlines the causes of death by gestational age and chorionicity. The most common gestation for death irrespective of chorionicity was before 24 weeks' gestation (129/218; 59%), representing 60% of deaths in monochorionic (73/122) and 58% of deaths in dichorionic twins (56/96). In both chorionicities, the most common cause of death before 24 weeks was placental, affecting 41% of monochorionic twins (30/73) that died before 24 weeks and 43% of dichorionic twins (24/56).

Gestation at death and delivery was specified in 59% of cases, of which 11% delivered more than 4 weeks after death ($n = 17$). In most of these, cause of death was unknown (65%; $n = 11$) and 76% were <24 weeks' gestation (13/17). Of the four deaths >24 weeks' gestation that were delivered more than 4 weeks after death, three were single intrauterine deaths in dichorionic pregnancies, delivered with the surviving co-twin between 34^{+0} and 40^{+2} weeks, and one was a monochorionic twin that died at 24 weeks' gestation with termination of the co-twin at 32 weeks when both twins were delivered together.

Discussion

Main findings

CoDiT is a classification system designed specifically for twin pregnancies using postmortem reports as the primary source of information. Initial testing demonstrates high inter- and intra-rater reliability for main cause of death. The commonest cause of death overall was placental conditions, with acute chorioamnionitis the commonest subcategory in dichorionic twins and TTTS in monochorionic twins. Most deaths were double demises and, irrespective of chorionicity, most occurred before 24 weeks' gestation. Delivery more than 4 weeks after death was associated with an increased likelihood of the cause of death being unknown.

Strengths and limitations

As parents had to consent to postmortem examination, this introduces a potential source of case selection bias. As such, our cohort may include disproportionately fewer terminated pregnancies due to a known abnormality, single deaths with prolonged in utero retention or a higher number of spontaneous deaths without an obvious antenatal cause. Pre-existing classification systems rely on clinical information, yet postmortems provide new information to change the diagnosis in 9–11%, and additional information in 22–76%.[16–21] However, pathological causes of twin demise remain unknown in 25%. Postmortem reports are not standardised and depend upon availability of local expertise in perinatal pathology and the quality of clinical information received. A standardised approach to submitting clinical information, postmortem procedure, reporting and criteria for conducting injection studies may improve the accuracy of assigning cause of death.

In the 2017 UK Perinatal Mortality Surveillance Report, only 50% of parents of stillborn babies and 28% of parents affected by NND consented to a postmortem.[22] Restricting CoDiT to cases in which a postmortem was undertaken limits its general useability.

CoDiT already aligns with six of the essential characteristics in the Delphi study—accommodates fetal death, stillbirths and NND; distinguishes between NND and stillbirth; has a small number of main categories; shows strong inter- and intra- rater agreement; allows associated factors such as placental descriptions to be recorded and distinguished

Table 2. Distribution of gestational age at death by cause and chorionicity with numbers and percentage within each group

Cause of Death	<24 weeks' gestation		>24 weeks' gestation		Neonatal death		Unknown gestation at death	
	MC *n* (%)	DC *n* (%)	MC *n* (%)	DC *n* (%)	MC *n* (%)	DC *n* (%)	MC *n* (%)	DC *n* (%)
Congenital Abnormality	23 (32%)	5 (9%)	1 (5%)	1 (11%)	1 (20%)	1 (9%)	3 (13%)	2 (10%)
Placental	30 (41%)	24 (43%)	9 (43%)	4 (44%)	2 (40%)	4 (36%)	12 (52%)	13 (65%)
Umbilical cord	3 (4%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Prematurity	0 (0%)	4 (7%)	0 (0%)	0 (0%)	1 (20%)	5 (45%)	2 (9%)	1 (5%)
Infection	0 (0%)	8 (14%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Other	4 (5%)	2 (4%)	1 (5%)	2 (22%)	0 (0%)	1 (9%)	0 (0%)	0 (0%)
Unknown	13 (18%)	13 (23%)	9 (43%)	2 (22%)	1 (20%)	0 (0%)	6 (26%)	4 (20%)
Total	73	56	21	9	5	11	23	20

from the cause of death; requires the single most important factor to be recorded.[12] CoDiT requires external validation to meet other criteria—ease of use; clear guidelines; produces easily understood data; has a sufficiently comprehensive list of categories to minimise the proportion of deaths classified as 'unknown'.[12] An important characteristic we were unable to assess was the ability of CoDiT to distinguish between antepartum and intrapartum deaths, as our cohort contained no intrapartum deaths.[12] As a higher proportion of twin pregnancies are delivered electively by caesarean section, a lack of intrapartum deaths may reflect the reduced number of women who go into labour with twin pregnancies.

The proportion of cases classified as unknown (25%) is comparable to Codac but higher than Tulip (11%), which captured late fetal losses, stillbirths, NNDs and infant deaths, and ReCoDe (15%), which only applies to stillbirths.[8,14] CoDiT was designed to be used across all gestations including those in the first trimester. In our cohort, 20% (54/265) of fetuses were <16 weeks' gestation. Determining cause of death from early gestation fetal postmortems can be extremely difficult. However, we have shown the value of incorporating these early gestations, as the commonest cause of death <24 weeks' in our cohort was placental (54/129; 42%).

The high number of placental causes of deaths in this cohort highlights the importance of submitting the placenta for histopathological examination in twin deaths. In our view, it should be a mandatory component of postnatal investigation.[23] It is crucial that obstetricians provide high-quality clinical information to inform a postmortem. Ultrasound designation of chorionicity in the first trimester has high sensitivity and specificity.[24] Such data are vital to inform the pathologist when no placenta is submitted. A systematic review concluded that placental examination was useful to determine cause of stillbirth in 60% of studies.[25] Placental examination is associated with a significant reduction in 'unexplained' deaths in singleton pregnancies (odds ratio [OR] 0.17, 95% CI 0.04–0.70) and is more cost-effective than a postmortem of the baby or cytogenetics.[26,27] For twins, placental examination confirms chorionicity and amnionicity, and in monochorionic twins, injection studies determine whether inter-twin transfusional processes contributed to demise.[28] Lopriore et al. suggest that injection studies should be performed on all monochorionic placentas, irrespective of birth outcome, to evaluate the effect of any FLA and to understand the pathophysiology of disorders affecting monochorionic pregnancies, potentially uncovering patterns associated with fetal demise.[29–32]

Interpretation

CoDiT is the first classification system designed specifically for perinatal deaths in twin pregnancies. One study concluded that no existing classification system was suitable to classify causes of death in twin pregnancies, as they did not reflect the diversity of diagnoses in twins; at best, they identified twin pregnancies as subcategories under 'other conditions'.[33] Another study identified that a major risk factor for double fetal deaths in twins was monochorionicity, which is reflected in the higher proportion of double monochorionic twin deaths than dichorionic deaths in our cohort.[34] When Codac was used to assign cause of death in twins and singletons, a higher prevalence of twin pregnancies was found in cases with a placental and unknown cause of death, aligning with the overall top two causes in our cohort.[35] A large retrospective cohort analysis comparing the risks and causes of stillbirths in singletons and twins using ReCoDe, found that stillbirths were mainly due to TTTS in monochorionic twins, as in our cohort; however, unlike our cohort, congenital anomalies were the biggest cause of death in dichorionic twins and singletons.[4]

Future work

The guidelines require modification to clarify how users should distinguish infection from acute chorioamnionitis. Adding a subcategory to distinguish between deaths due to prematurity from PPROM with or without evidence of infection may be useful. Furthermore, comparative studies to evaluate the performance of CoDIT against other classification systems in twin pregnancies will determine whether the system employed affects the classification of cause of death and the frequency of unexplained deaths.

CoDiT has undergone testing in one tertiary UK hospital with a dedicated perinatal pathology service, by a small panel, with limited external validation. To determine its suitability as a global classification system, CoDiT requires large-scale validation using external cohorts and panels.

Conclusion

We introduce the first classification system specifically designed for twin pregnancies. Although external validation and modifications are required, preliminary testing demonstrates that CoDiT has the potential to be a powerful tool in furthering our understanding of deaths in twin pregnancies and a catalyst to improve management.

Disclosure of interests

FLM is a *BJOG* editor. The remaining authors have no disclosures. Completed disclosure of interest forms are available to view online as supporting information.

Contribution to authorship

NG, FLM, RKM, PC, MDK co-designed the classification system. NG, FLM, PC, TM tested the classification system by assigning cause of death to cases in the cohort to assess

inter-disciplinary agreement. AEH independently assigned cause of death to a subset of cases to assess inter-rater agreement. NG reclassified a subset of cases to determine intra-rater agreement. All authors contributed to the write-up and approval of the final manuscript.

Details of ethical approval

The project was registered as a service evaluation project by the unit's clinical governance team in 2017.

Funding

None.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Appendix S1. Cause of death of twins (CoDiT) classification system. ■

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