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Validation of second trimester miscarriages and spontaneous deliveries

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Objective: To validate the diagnosis of second trimester miscarriages/deliveries (16+0 weeks to 27+6 weeks of gestation) recorded as miscarriages in the Danish National Patient Registry or spontaneous deliveries in the Danish Medical Birth Registry, and asses the validity of risk factors, pregnancy complications, and cerclage by review of medical records.

Materials and methods: In a cohort of 2,358 women with a second trimester miscarriage/delivery in first pregnancy and a subsequent delivery during 1997–2012, we reviewed a representative sample of 682 medical records. We searched for clinically important information and calculated positive predictive values of the registry diagnoses stratified by type of registry, as well as sensitivity, specificity, positive predictive value, and kappa coefficients of risk factors, pregnancy complications, and cerclage.

Results: Miscarriage/spontaneous delivery in the second trimester was confirmed in 621/682 patients (91.1%). Pregnancy complications in second trimester miscarriages were underreported, resulting in low sensitivities and poor to moderate agreements between records and registries. There was a good agreement (kappa >0.6) between medical records and the registries regarding risk factors and cerclage. The diagnosis of cervical insufficiency had "moderate" kappa values for both miscarriages and deliveries (0.55 and 0.57).

Conclusion: Spontaneous second trimester deliveries and miscarriages recorded in the registers were confirmed by medical records in 91%, but register-based information on pregnancy complications need to be improved. We recommend that all pregnancies ending spontaneously beyond the first trimester are included in the national birth registry and described by appropriate variables.

Keywords: second trimester, miscarriage, preterm birth, prematurity, registries, reproducibility of results, cerclage, cervical insufficiency

Introduction

Preterm delivery at or near the limit of viability is associated with a high neonatal mortality and morbidity.[1] Survival rates increase progressively with each week gained between gestational week 23 and 28.[2] It has been suggested that the risk factors and causes of miscarriage in 16–19 weeks are similar to those of spontaneous deliveries at 20–26 weeks.[3,4] Therefore, we chose to define preterm delivery from 16 weeks, a cutoff previously used in a large-scale preterm birth classification study.[5]

Second trimester miscarriage/delivery is estimated to complicate approximately 0.5%–1% of all deliveries.[6–9] Causes are numerous and complex, and require different preventive strategies.[10–14] In cervical insufficiency, painless cervical dilation in the second trimester of pregnancy leads to expulsion of the fetus without uterine contractions.[15–17] The lack of objective findings and diagnostic tests make the diagnosis

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of cervical insufficiency elusive. Identification of women with cervical insufficiency is important as recurrence risk is high and prophylactic treatments exist: progesterone and cerclage.[18,19]

Studies on large populations are required to explore uncommon phenotypes of spontaneous second trimester deliveries and subsequent pregnancy outcomes. Population-based studies rely on valid identification of diagnoses in the registries. Therefore, we present the results of a validation study of the diagnoses of spontaneous second trimester deliveries, risk factors, pregnancy complications, and procedures of cerclage in two national registries.

Materials and methods

The Danish National Patient Registry (DNPR) contains all hospital admissions in Denmark since 1977. The registry also contains 99.4% of all discharge records from Danish hospitals.[20] All Danish citizens receive a ten-digit personal identification number, which is used as identification in the registries and medical records filed in the archives. Diagnoses are applied by physicians using the Danish version of the International Classification of Diseases 10th revision (ICD-10; 1994 onward). Outpatient contacts and visits to the emergency room have been recorded since 1995. All births and miscarriages are found in the DNPR, whereas only births are included in the Danish Medical Birth Registry (DMBR), which also includes variables that are not registered for the miscarriages (Apgar score, parity, birth weight, etc). Pregnancy characteristics and complications are integrated in DMBR. The DMBR includes all live births irrespective of gestational age and stillbirth from 22 weeks of gestation. This division is based on the WHO's universally adopted definition of a live birth as delivery of a fetus that subsequently shows any signs of life, such as movement, heartbeat, or pulsation of the umbilical cord, for however brief a time.[21] Fetal deaths before 22 weeks are regarded miscarriages and recorded in DNPR.

In the registries, we identified women hospitalized in Denmark with the diagnosis of miscarriage or spontaneous delivery in week 16–27 during 1997–2012, no prior deliveries, and a subsequent miscarriage/delivery after 16 weeks of gestation (Figure 1). Multiple pregnancies were included. Records with unregistered gestational age and birth weight <1,200 g (n=58) were included in the cohort by the calculated gestational age.[22]

Medical records for validation of information on the first pregnancy were retrieved from a total of 13 hospitals. We selected the four largest tertiary hospitals from the five regions in Denmark (the fifth region does not have a

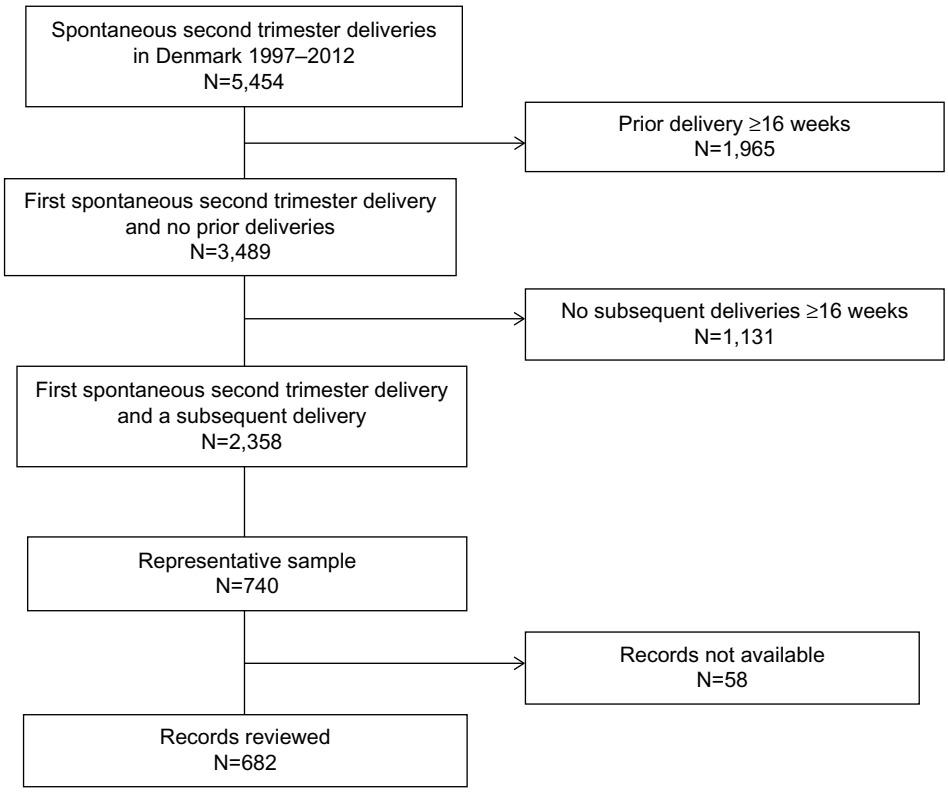

Figure 1 Flowchart of selection for validation.

tertiary hospital and all extremely preterm deliveries are therefore referred to another region). We randomly selected between one and three secondary hospitals from each of the five regions without knowledge of specific local routines or registration procedures. From the selected hospitals we retrieved the following samples from the registries: 1) second trimester spontaneous delivery/miscarriage in both first and second pregnancy beyond 16 weeks of gestation (n=88) and 2) second trimester spontaneous delivery/miscarriage in first pregnancy beyond 16 weeks and third trimester delivery in second pregnancy beyond 16 weeks (n=652).

The review of medical records included ultrasound and surgical descriptions, autopsy reports, blood samples and the birth chart with admission history, description of the delivery, and the outcome. For each record, we decided whether a diagnosis of spontaneous second trimester delivery could be confirmed. Data were collected from the records using Epidata Data Entry (EpiData Association, http://www.epidata.dk) by one of the authors (KS).

Validation of the diagnoses related to the first spontaneous second trimester delivery/miscarriage was carried out with the knowledge of the outcome of subsequent pregnancy, sometimes at the same hospital. However, the criteria for categorization by pathway to delivery (spontaneous vs caregiver-initiated) were explicit, and when in doubt the case was discussed with a second reviewer (n=25).

A spontaneous onset of delivery was defined by the presence of initial signs of delivery (contractions, bleeding, preterm premature rupture of membranes [PPROM], or painless cervical dilation), but contractions may be augmented and delivery may be by cesarean section. The definitions and ICD-10 codes were as follows: Spontaneous onset of delivery (DO800–DO809, DO840–DO842, DO821B/C, DO843B/C in the absence of the Danish code of induction of labor, BKHD2) and miscarriage (DO030–DO039) combined with the Danish codes for gestational week 16+0–27+6 (DU16D1–DU27D6). Duration of gestation was calculated from the 1st day of last period or estimated by an early ultrasound. From 2004, gestational age has been routinely measured by ultrasound screening at 11–13 weeks. Gestational age was evaluated in two categories: ±1 week and ±2 weeks of gestational age recorded in the medical records. We defined a correct diagnosis of second trimester delivery as a gestational age within weeks 16–27 regardless of errors in gestational age within this period.

Information regarding risk factors was collected until the date of the second delivery. In women with recurrent second trimester deliveries, data collection continued until a first third trimester delivery. Cerclage was placed either in the nonpregnant woman (prepregnancy abdominal cerclage) or in second pregnancy (vaginal cerclage, postconceptional abdominal cerclage). For vaginal cerclages we used the gestational age at the time of placement to distinguish between elective vaginal cerclage (applied before 16 weeks of gestation) and urgent cerclage (applied ≥16 weeks of gestations). Definitions and ICD-10 codes or Danish procedure codes of risk factors, pregnancy complications, and procedures of cerclage are presented in Table S1.

Statistical analysis

We compared the primary diagnoses in the registries with those obtained by review of the medical records (the gold standard). The main outcome was positive predictive value (PPV), defined as the proportion of patients with a diagnosis of second trimester preterm birth in the registries that had the diagnosis verified by medicals records. We calculated PPV with 95% confidence intervals (CI). PPV was calculated for the whole study population and stratified by registrations as miscarriage (DNPR) or birth (DMBR). Distributions in the registries were compared with the Fisher's exact test. We proceeded with 2×2 cross tables calculating specificity, sensitivity, and PPV for each of the diagnoses related to spontaneous second trimester delivery. Sensitivity is the proportion of patients with a true diagnosis captured by the registry. We calculated sensitivity as (+patient registry + records)/[(+patient registry + records) + (−patient registry + records)]. Specificity is the proportion of patients without a registered diagnosis, who truly do not have the diagnosis. We calculated specificity as (−patient registry − records)/[(−patient registry − records) + (+patient registry − records)]. Sensitivity and specificity were calculated with 95% CI. Sensitivity and specificity were calculated for the following risk factors, pregnancy complications, and types of cerclage: congenital uterine anomalies, uterine fibroids, thrombophilia, cervical conizations, cervical insufficiency, chorioamnionitis, antepartum fetal death, multiple pregnancies, congenital fetal anomalies, placental insufficiency/intrauterine growth retardation (IUGR), placental abruption, PPROM, antepartum bleeding, and cervical cerclage. Cohen's kappa was estimated as a measure of agreement between the validated and the register-based diagnoses.[23]

We used SPSS software (Version 22.0; IBM Corporation, Armonk, NY, USA). The study was approved by the Danish Data Protection Agency (journal number 2008-58-0028) and The Danish Health and Medicines Authority (journal number 3-3013-185/1/).

Table 1 Distribution and validity of the diagnoses of miscarriage and spontaneous preterm delivery in the second trimester in the Danish National Patient Registry and the Danish Medical Birth Registry

Registry	Sample, n	Available records, n (%)	Category	Confirmed diagnoses, n	Positive predictive value % (95% CI)
Danish National Patient Registry	408	369 (90.4)	Spontaneous onset	335	90.8 (87.9–93.8)
			Gestational age ±1 week	259	70.2 (65.5–74.9)
			Gestational age ±2 weeks	360	97.6 (96.0–99.2)
			Miscarriage weeks 16–27	330	89.4 (86.3–92.5)
Danish Medical Birth Registry	332	313 (94.2)	Spontaneous onset	298	95.2 (92.8–97.6)
			Gestational age ±1 week	280	89.5 (84.6–92.8)
			Gestational age ±2 weeks	306	97.7 (96.0–99.4)
			Spontaneous delivery weeks 16–27	291	92.9 (90.1–95.8)
Total	740	682 (92.3)	Miscarriage/spontaneous delivery weeks 16–27	621	91.1 (88.6–93.0)

Abbreviation: CI, confidence interval.

Results

Among 441,904 women with a first pregnancy progressing beyond 16 weeks in Denmark during 1997–2012, 3,489 (0.8%) had a spontaneous delivery or miscarriage before week 28 and 2,358 had a subsequent pregnancy ≥16 weeks (Figure 1). In the sample of 740 registry records from DNPR and DMBR, 682 (92.2%) were available in the hospital achieves. Records were unavailable in eleven of the 13 hospitals.

For the second trimester miscarriage/spontaneous delivery diagnoses, we examined gestational age and pathway to delivery independently and in combination (Table 1). A spontaneous pathway to delivery occurring between 16 weeks and 27 weeks of gestation was observed in 621 cases resulting in an overall PPV of 91.1% (95% CI: 88.6–93.0; Table 1). The PPVs were similar in DMBR and DNPR (P=0.08). The level of agreement of gestational age within 2 weeks between registries and medical records were 97.6% for DNPR and 97.7% for DMBR. Among the 61 women in whom the registry diagnosis was not confirmed, 38 were recorded in DNPR. Three women had an early miscarriage, and 37 had induced labor due to fetal or maternal conditions (antepartum fetal death [n=28], malformations [n=3], IUGR [n=2], or maternal conditions [n=2]). Of the 23 women whose registry diagnosis was not confirmed in DMBR, 15 women had induced labor due to antepartum fetal death (n=5), fetal malformations (n=2), and preeclampsia (n=8) and eight women had erroneous gestational recordings (seven term deliveries and one preterm delivery). We found no difference in PPV in tertiary hospitals compared to secondary hospitals.

Table 2 lists frequencies of risk factors and pregnancy complications. No difference was detected in frequencies of risk factors recorded in DNPR and medical records. Cervical insufficiency had a higher frequency in DNPR compared to

Table 2 Frequencies of risk factors and pregnancy complications in the first spontaneous second trimester delivery/miscarriage

	National Patient Registry (n=682)	*P*-value	Medical records (n=682)	Medical Birth Registry[a] (n=313)	*P*-value
Uterine congenital anomaly	23 (3.4)	0.29	31 (4.5)	–	
Uterine fibroids	22 (3.2)	0.48	27 (4.0)	–	
Thrombophilia	15 (2.2)	0.73	17 (2.5)	–	
Cervical conization	50 (7.3)	0.46	58 (8.5)	–	
Cervical insufficiency	198 (29.0)	0.02	149 (21.8)	–	
Antepartum fetal death	10 (1.5)	<0.001	41 (6.0)	–	
Multiple pregnancies	63 (9.2)	0.002	106 (15.5)	30 (9.5)	0.003
Major fetal anomaly	5 (0.7)	0.04	14 (2.1)	6 (1.9)	0.89
Placental insufficiency/intrauterine growth retardation	16 (2.3)	0.10	27 (4.0)	–	
Placental abruption	25 (3.7)	0.05	41 (6.0)	24 (7.6)	0.36
Antepartum vaginal bleeding	36 (5.3)	<0.001	119 (17.4)		
Preterm premature rupture of membranes	82 (12.0)	<0.001	169 (24.7)	61 (19.5)	0.14

Note: [a]Incidences are based on deliveries recorded in The Danish Medical Birth Registry.

Table 3 Sensitivity, specificity, positive predictive value, and kappa scores of pregnancy complications recorded in the Danish National Patient Registry and the Danish Medical Birth Registry

Pregnancy complication	Danish National Patient Registry				Danish Medical Birth Registry			
	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive predictive value, % (95% CI)	Kappa (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive predictive value, % (95% CI)	Kappa (95% CI)
Antepartum fetal death								
Miscarriages	22.7 (12.0–38.2)	100 (98.5–100)	100 (65.6–100)	0.34 (0.18–0.50)	–	–	–	–
Deliveries	–	–	–	–	–	–	–	–
Multiple pregnancies								
Miscarriages	40.9 (30.0–53.7)	99.3 (97.6–99.9)	93.1 (77.2–99.2)	0.52 (0.39–0.64)	–	–	–	–
Deliveries	78.0 (62.0–88.9)	99.3 (97.2–99.9)	94.1 (78.9–99.0)	0.83 (0.74–0.93)	82.4 (65.7–93.2)	99.3 (97.4–99.8)	93.3 (77.9–99.2)	0.86 (0.77–0.96)
Major fetal anomaly								
Miscarriages	27.2 (7.3–60.9)	100 (98.7–100)	100 (30.9–100)	0.42 (0.10–0.75)	–	–	–	–
Deliveries	70.0 (35.4–91.9)	100 (98.4–100)	100 (56.1–100)	0.82 (0.62–1.00)	60.0 (27.4–86.3)	100 (98.4–100)	100 (51.9–100)	0.74 (0.50–0.99)
Placental insufficiency/intrauterine growth retardation								
Miscarriages	50.0 (17.4–82.6)	100 (98.7–100)	100 (39.6–100)	0.66 (0.35–0.97)	–	–	–	–
Deliveries	52.6 (29.5–74.8)	99.3 (97.3–99.9)	83.3 (50.9–97.1)	0.63 (0.43–0.83)	–	–	–	–
Placental abruption								
Miscarriages	14.2 (0.7–58.0)	100 (98.7–100)	1 (5.4–100)	0.25 (–0.15–0.64)	–	–	–	–
Deliveries	65.7 (47.7–80.3)	99.6 (97.6–100)	95.8 (76.9–99.8)	0.76 (0.63–0.88)	62.9 (44.9–78.0)	99.6 (97.7–100)	95.6 (92.2–97.5)	0.74 (0.60–0.87)
Preterm premature rupture of membranes								
Miscarriages	22.8 (15.0–33.0)	99.6 (97.7–100)	95.5 (75.1–99.8)	0.30 (0.20–0.41)	–	–	–	–
Deliveries	68.8 (57.1–78.6)	97.0 (93.7–98.7)	88.3 (76.8–94.8)	0.71 (0.62–0.81)	71.4 (59.8–80.9)	97.9 (94.8–99.2)	91.7 (80.9–96.9)	0.75 (0.66–0.84)
Cervical insufficiency								
Miscarriages	76.3 (64.5–85.4)	86.9 (82.0–90.3)	58.5 (47.9–68.0)	0.57 (0.47–0.67)	–	–	–	–
Deliveries	77.9 (66.5–86.4)	81.4 (75.7–86.0)	57.7 (47.6–67.1)	0.55 (0.45–0.65)	–	–	–	–

Abbreviation: CI, confidence interval.

Table 4 Sensitivity, specificity, positive predictive value, and kappa scores of risk factors of spontaneous second trimester delivery/miscarriage

Risk factor	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive predictive value, % (95% CI)	Kappa (95% CI)
Uterine congenital anomaly	71.5 (51.7–85.2)	99.8 (98.9–100)	95.0 (95.0–98.0)	0.81 (0.69–0.92)
Uterine fibroids	74.1 (53.7–88.9)	99.7 (98.9–100)	90.9 (70.8–99.6)	0.81 (0.69–0.93)
Thrombophilia	88.2 (63.6–98.5)	100 (99.5–100)	100 (78.2–100)	0.94 (0.85–1.00)
Cervical conization	84.5 (72.6–92.7)	99.8 (99.1–100)	98.0 (89.4–99.9)	0.90 (0.84–0.96)

Abbreviation: CI, confidence interval.

the records (29.0% vs 21.8%, P=0.02). All other pregnancy complications except placental insufficiency/IUGR were underreported in DNPR (up to 70%).

Sensitivities, specificities, and PPVs of pregnancy complication are presented in Table 3. The 2×2 tables of diagnoses in registries and medical records are available in Tables S2 and S3. Most sensitivities of pregnancy complications recorded in DNPR were <50% in miscarriages and 65%–90% in deliveries. Generally, strength of agreements between registries and medical records described by kappa coefficients was "fair" to "moderate" for miscarriages (kappa coefficients 0.21–0.60) and "good" for births (kappa coefficients 0.61–0.80). Specificity was >90% for all diagnoses except cervical insufficiency (81%–86%). The diagnoses of cervical insufficiency had "moderate" kappa coefficients for both miscarriages and deliveries (0.55–0.57). We found no difference in sensitivity of variables available in both registries.

Table 4 lists sensitivities, specificities, and PPVs of risk factors of spontaneous second trimester delivery. The number of diagnoses recorded in DNPR and medical records are available in 2×2 tables in Table S4. Most of the kappa values showed good agreement (≥0.6) between each registry and the medical record.

Sensitivity, specificity, PPVs, and kappa scores of the cervical cerclage are summarized in Table 5. The 2×2 tables of diagnoses in registries and medical records are available in Table S5. All kappa scores were >0.80, corresponding to a "very good" agreement between registry and medical records. Distinguishing between elective and urgent vaginal cerclage by gestational age at cerclage placement (cutoff was 16 weeks) resulted in a decrease in sensitivity, specificity, PPV, and kappa score.

Discussion

Medical records confirmed 91% of register-based spontaneous second trimester deliveries. The PPVs were similar in DMBR and DNPR. Kappa coefficients for risk factors associated with second trimester deliveries were ≥0.61, indicating good agreement. Most pregnancy complications in second trimester miscarriage were underreported in DNPR, resulting in low sensitivities and poor to moderate kappa values. The diagnosis of cervical insufficiency had a "moderate" kappa value of 0.55.

This validation study is the first on spontaneous second trimester miscarriages and deliveries described by risk factors and pregnancy complications. We examined a representative segment of the population from hospitals in each of the five Danish regions without knowledge of specific local routines or registration procedures. We have no reason to believe that registration practice in selected hospitals was different from that in other hospitals. Therefore, we assume that the results are generalizable. Unavailable or missing records were less likely to bias the results, as they were missing in small numbers in most of the selected hospitals.

A prior study validated the diagnosis of miscarriage in the DNPR and found a PPV of 97.4%.[24] In contrast to our study, the authors used the same code for missed abortions and miscarriages arguing that the two are different presentations of the same conditions. In this study, we have chosen to distinguish between the two diagnoses, as we consider

Table 5 Sensitivity, specificity, positive predictive value, and kappa scores of different types of cervical cerclage

	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive predictive value, % (95% CI)	Kappa (95% CI)
Elective vaginal cerclage	82.7 (73.8–89.2)	99.5 (98.4–99.9)	96.6 (89.8–99.1)	0.87 (0.82–0.93)
Urgent cerclage	90.3 (75.9–96.8)	98.2 (96.8–99.1)	77.1 (62.3–87.5)	0.82 (0.73–0.91)
All vaginal cerclages	92.2 (86.1–95.8)	100 (99.1–100)	100 (96.4–100)	0.95 (0.92–0.98)
Abdominal cerclage	85.7 (66.4–95.3)	100 (99.3–100)	100 (82.5–100)	0.92 (0.84–1.00)

Abbreviation: CI, confidence interval.

miscarriages and intrauterine fetal death in the absence of symptoms of delivery as different entities.

By using Danish medical registries, we found an incidence of 0.8% of spontaneous second trimester delivery/miscarriage in first time pregnancies beyond 16 weeks, which is comparable to the rates presented in previous publications.[6–9,25] We did not search for spontaneous second trimester deliveries among induced deliveries, pregnancy terminations, and miscarriages with unrecorded gestational age, which is a limitation. Our findings of high PPVs indicate that the DNPR and DMBR can be used to identify spontaneous second trimester deliveries/miscarriages for the purpose of register-based cohort studies.

The gestational age registered in DMBR has been evaluated in a previous study.[26] Kristensen et al compared a review of medical records of 1,662 preterm deliveries with registry information and found a large number of errors in the length of gestational age. We found agreement between DMBR and medical records within 1 week of 89.4% and within 2 weeks of 97.7%. Implausible combinations of gestational age and birth weight may identify errors in gestational age, but it can be difficult to determine which measure is reliable.

We used a cutoff at 16 gestational weeks to distinguish between elective and urgent vaginal cerclage. Since 30% of miscarriages had at least 1 week difference in gestational age in the medical records compared to the register, some elective cerclages might have been recorded as urgent/emergency, and vice versa.

According to WHO definitions, presence of signs of life at delivery/miscarriage determines whether a delivery of a fetus <22 weeks will be recorded as a miscarriage in DNPR or a delivery in DMBR. There are several problems related to this definition. It may be difficult to distinguish stillborn infants from liveborn infants who are extremely preterm, asphyxiated, or neurologically depressed and who die soon after birth. Even if the fetus is clearly stillborn, it is not possible in registries to distinguish peripartum fetal deaths caused by the preterm delivery from antepartum fetal death. In 2004, in Denmark, the gestational age classifying intrauterine fetal deaths as births was lowered from 28 weeks to 22 weeks. Recent studies, however, have suggested similar causes and risk factors in miscarriages at 16–19 weeks and births at 22–25 weeks.

There is no agreement about the definition of cervical insufficiency.[27,28] Traditionally, the diagnosis has been made based on an obstetric history of recurrent second trimester delivery following painless cervical dilation.[28] In the absence of recurrence, the term can be applied to a single event with painless cervical dilation after exclusions of other possible causes of preterm delivery.[16] The main problem of the diagnosis of cervical insufficiency is that it is not associated with specific symptoms and that there are no diagnostics tests. A low specificity, as observed in this study, indicates that the diagnosis may be applied to a variety of patients that do not suffer from cervical insufficiency. Some use the diagnosis of cervical insufficiency in women with a short cervix measured by ultrasound. For a correct diagnosis of cervical insufficiency, a classification system based on objective components would be beneficial. In particular, we need information on cervical length, dilation, and clinical presentation at admission to hospital in the second trimester.

Placental abruption, PPROM, multiple pregnancies, major fetal anomalies, and antepartum bleeding in miscarriages were underreported DNPR. Without information on pregnancy characteristics and complications, we risk lumping together different phenotypes of second trimester deliveries. A recently published series of clinical opinions described the purpose, challenges, and considerations for a preterm birth classification system.[3,4,29] The authors emphasize that precise classification of subtypes of preterm delivery from gestational week 16 will improve understanding of causes of preterm delivery and improve research in treatment and preventive interventions.

Data on three pregnancy complications (placental abruption, PPROM, and fetal anomaly) and multiplicity were available in both DNPR and DMBR and there were no difference in sensitivity, specificity, and kappa coefficients. DMBR is superior due to the readily accessible structure and the linkage between pregnancy characteristics, complications, neonatal outcomes, and maternal demographic data.

Conclusion

In conclusion, we found acceptable diagnostic validity of Danish medical registries in spontaneous second trimester deliveries and miscarriages. Kappa values were good for risk factors for second trimester miscarriage/delivery and cervical cerclage. The diagnosis of cervical insufficiency had "moderate" kappa coefficients for both miscarriages and deliveries (0.55–0.57). Most other pregnancy complications in miscarriages were underreported, resulting in low incidences, sensitivities, and kappa scores compared to cases recorded as deliveries. DNPR and DMBR were equally accurate regarding pregnancy complications in deliveries, but the advantages of DMBR are the readily accessible structure and linkage between pregnancy characteristics, maternal demographic data, and neonatal outcomes. We recommend improved data collection to the national birth registries with detailed information on pregnancies ending after the first

trimester – operationally after ultrasound scan showing live fetus at 12 weeks scan. For now, we can use combined data from the Danish patient and the birth registers to identify spontaneous second trimester deliveries and miscarriages. In order to obtain valid information about the etiology based on pregnancy characteristics and complications, we need to retrieve medical records.

Disclosure

The authors report no conflicts of interest in this work.

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Supplementary materials

Table S1 Definitions and codes of risk factors, pregnancy complications, and cerclage

	Definition	Codes
Fetal anomaly	Lethal or major fetal anomalies classified by complexity classification system:[30] anencephalus, microcephalus, encephalocele, esophageal atresia, bilateral multicystic renal disease, renal agenesia, omphalocele, pentagology of Cantrell, Pierre Robin sequence, trisomy 9,13,18, and 21,22q11 syndrome, 45×0 high and lethal complex cardiac malformations: truncus arteriosus communis, complete transposition of the great arteries, Isomeric auricularum atriorum, tetralogy of Fallot, hypoplastic left heart, dextrocardia, levocardia, congenital heart block, acardia	DO350–DO351, DQ00, DQ01, DQ02, DQ04, DQ390, DQ60–DQ61, DQ792, DQ85–DQ87, and DQ90–DQ900
Multiple pregnancies	≥2 fetuses	DO30–DO309, DO31, and DO84
Antepartum fetal death	Intrauterine fetal death before the onset of labor	DO021
Placental abruption	Premature separation of the placenta from the uterine wall that is diagnosed by 1. Ultrasonic retroplacental hematoma 2. Macroscopic hematoma 3. Histological evidence of abruption	DO45 and DO450–DO459
Placental insufficiency/intrauterine growth retardation	Histological evidence of vasculitis/infarction/necrosis/other stated in the placental pathology report or impaired fetal growth stated in the medical record	DO438–DO438E and DO365
Cervical insufficiency	Painless cervical shortening and/or dilation in singleton pregnancies after exclusion of major fetal anomalies, placental abruption, and other causes of spontaneous second trimester delivery	DO343, DO343A, DO343B, and DZ875A
Preterm premature rupture of membranes	Rupture of the amniotic membranes before the onset of labor	DO42–DO429
Antepartum vaginal bleeding	Extensive fresh vaginal bleeding without regular contractions, with or without PPROM	DO46–DO469
Thrombophilia	Abnormality of blood coagulation that increases the risk of thrombosis 1. Inherited: factor V Leiden and protrombin mutations and antithrombin III, protein S, and protein C deficiencies 2. Acquired: antiphospholipid syndrome	DD685, DD685A–DD685M, DD686D, and DD686E
Congenital uterine anomaly	Uterine agenesis, uterus didelphys, bi- and unicornuate uerus and arcuate, subseptate, and septate uterus	DQ51–DQ519
Uterine fibroid	Submucosal or intramurale uterine fibroids	DD250–DD251
Cervical conization	Excision of a conus of the cervix by cold knife or loop excision before the first second trimester delivery	KLDC00–13, KLDC20–23, and KLDC96[a]
Vaginal cerclage	The vaginal placement of cervical stitches on the pregnant uterus either electively in patients with a history of cervical insufficiency or urgent/emergency cerclage patients with short or dilated cervix	KMAB00[a]
Abdominal cerclage	Surgical procedure in which a band is placed on the cervico-isthmic junction via laparoscopy or laparoscopy	KLDD10, KLDD10A, and KLDD10B[a]

Note: [a]Danish codes for surgical procedures.
Abbreviation: PPROM, preterm premature rupture of membranes.

Table S2 Diagnoses recorded in The Danish National Patient Registry (DNPR) by the presence of the condition in medical records

Diagnosis recorded in DNPR	Presence of condition in medical records		
	Yes	No	Total
Multiple pregnancies, miscarriages (030)			
Yes	27	2	29
No	38	302	340
Total	65	304	369
Multiple gestations, deliveries (030)			
Yes	7	0	7
No	34	272	306
Total	41	272	313
Major fetal anomaly, miscarriages			
Yes	2	0	32
No	6	361	367
Total	8	361	369
Major fetal anomaly, deliveries			
Yes	1	2	3
No	8	302	310
Total	9	304	313
Placental insufficiency/intrauterine growth retardation miscarriages (O438/O365)			
Yes	4	0	4
No	4	361	365
Total	8	361	369
Placental insufficiency/intrauterine growth retardation, deliveries (O438/O365)			
Yes	10	2	12
No	9	292	301
Total	19	294	313
Placental abruption, miscarriages (O45)			
Yes	1	0	1
No	5	363	368
Total	6	363	369
Placental abruption, deliveries (O45)			
Yes	23	1	24
No	12	277	289
Total	35	278	313
Antepartum fetal deaths, miscarriages (O021)			
Yes	10	0	10
No	34	325	359
Total	44	325	369
Antepartum bleeding, miscarriages (O46)			
Yes	7	0	7
No	64	298	362
Total	81	298	369
Antepartum bleeding, deliveries (O46)			
Yes	28	1	29
No	20	264	284
Total	48	265	313
Preterm premature rupture of membranes, miscarriages (O42)			
Yes	21	1	22
No	71	276	347
Total	92	277	369
Preterm premature rupture of membranes, deliveries (O42)			
Yes	53	7	54
No	24	229	259
Total	77	236	313
Cervical insufficiency, miscarriages (Z875A, O343, and O343A/B)			
Yes	55	39	94
No	17	258	275
Total	72	297	369
Cervical insufficiency deliveries (Z875A, O343, and O343A/B)			
Yes	60	44	104
No	17	192	209
Total	77	236	313

Table S3 Diagnoses recorded in The Danish Medical Birth Registry (DMBR) by the presence of the condition in medical records

Diagnosis recorded in DMBR	Presence of condition in medical records		
	Yes	No	Total
Multiple pregnancies (030)			
Yes	28	2	30
No	6	277	283
Total	34	279	313
Major fetal anomaly			
Yes	6	0	6
No	3	304	307
Total	9	304	313
Placental abruption (O45)			
Yes	22	1	23
No	13	277	290
Total	35	278	313
Preterm premature rupture of membranes (O42)			
Yes	55	5	60
No	22	231	253
Total	77	236	313

Table S4 Diagnoses recorded in the Danish National Patient Registry (DNPR) by the presence of the risk factor/surgical intervention observed in medical records

Diagnosis recorded in DNPR	Presence of risk factor in medical records		
	Yes	No	Total
Congenital uterine anomaly (Q510–Q519)			
Yes	22	1	23
No	9	650	659
Total	31	651	682
Uterine fibroids (D25–D259)			
Yes	20	2	22
No	7	653	660
Total	27	655	682
Thrombophilia (D680–D682 and D685–D686)			
Yes	15	0	15
No	2	665	667
Total	17	665	682
Cervical conization (KLDC)			
Yes	49	1	50
No	9	623	632
Total	58	624	682

Table S5 Diagnoses recorded in The Danish National Patient Registry (DNPR) by the presence of the procedure in medical records

Diagnosis recorded in DNPR	Presence of procedure in medical records		
	Yes	No	Total
Elective vaginal cerclage (KMAB00)			
Yes	86	3	89
No	18	596	593
Total	102	599	682
Urgent/emergent cerclage (KMAB00)			
Yes	37	11	48
No	4	630	634
Total	41	642	682
All vaginal cerclages (KMAB00)			
Yes	130	0	130
No	11	541	552
Total	141	541	682
Abdominal cerclage (KLDD10)			
Yes	24	0	24
No	4	354	358
Total	28	354	382