# Termination of pregnancy for fetal anomaly after 23 weeks of gestation: a European register-based study

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**Objective** To determine the prevalence of termination of pregnancy for fetal anomaly (TOPFA) after 23 weeks of gestation in European countries, and describe the spectrum of anomalies for which late TOPFA is recorded.

Design Population-based study.

Setting Twelve European countries.

**Population** Nineteen registries of congenital anomaly in 12 European countries between 2000 and 2005. The number of total births covered was 2 695 832.

**Methods** TOPFAs in singleton pregnancies from the European Surveillance of Congenital Anomalies and Twins (EUROCAT) database.

**Main outcome measures** The prevalence of TOPFA and type of anomaly.

**Results** There were 10 233 TOPFAs, 678 (6.6%) of which were performed at 24 weeks or more. The rate of TOPFA before 24 weeks was 3.4 per 1000 births, at 24–25 weeks 0.14 per 1000 births and at 26 weeks or more 0.11 per 1000 births. There was

significant variation in the prevalence of TOPFA at  $\geq$ 24 weeks between countries (P < 0.001), with all countries in the range 0–0.55 per 1000 births, except France (Paris) at 2.65 per 1000 births. The large majority of late TOPFAs had a gestational age of 24–27 weeks (516/678, 76%). The proportion of TOPFAs from 24 weeks or more varied by type of anomaly, with 4% of all TOPFAs for chromosomal anomalies and 9% of all TOPFAs for nonchromosomal anomalies resulting in late TOPFA (P < 0.001). For transposition of the great arteries, single ventricle, hypoplastic left heart and hydrocephaly, the percentage of late TOPFA was 12–23%. The median time interval between diagnosis and late TOPFA was 2 weeks for most anomalies, but longer ( $\geq$ 5 weeks) for diaphragmatic hernia, omphalocoele, arthrogryposis multiplex and Turner's syndrome.

**Conclusion** Late TOPFA is rare in Europe, and varies in prevalence between countries. Compared with earlier TOPFA, late TOPFA is more often performed for a nonchromosomal isolated major structural anomaly and less often for a fetus with a chromosomal syndrome or multiple anomalies.

Keywords Fetal anomaly, termination of pregnancy.

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## Introduction

Most terminations of pregnancy for fetal anomaly (TOP-FAs) occur during the second trimester of pregnancy, before fetal viability. In rare circumstances, TOPFA is performed late in pregnancy. The laws on performing TOPFA vary between countries within Europe,<sup>1</sup> and may specify no upper gestational age (GA) limit for any TOP-FA, no upper GA limit for lethal anomalies, a GA limit for any TOPFA or no TOPFA at any GA.

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There are few published data on the prevalence of TOPFA at a GA of 24 weeks or more, beyond the viability limit and the type of anomalies diagnosed in these pregnancies. A French study<sup>2</sup> described the termination of pregnancy after 12 weeks of gestation from 1989 to 2000 for all fetal and maternal indications. In 74% of all terminations, the indication was fetal anomaly (39% with strucmalformations and 35% with chromosomal tural anomalies). Although the percentage of TOPFA after 24 weeks was stable over time, an increasing prevalence of late TOPFA reflected an increase in the prevalence of all TOPFA. A British study from 1995 to 2004<sup>3</sup> found that 8.4% of TOPFAs were performed with a GA of 24 weeks or more.

In this article, we determine the prevalence of TOPFA from a GA of 24 weeks in 19 regions in 12 European countries in which TOPFA is legal, and describe the spectrum of congenital anomalies for TOPFA.

# **Materials and methods**

The study was based on routinely collected data from 19 European Surveillance of Congenital Anomalies and Twins (EUROCAT) registries in 12 European countries in which TOPFA is legal:<sup>1</sup> Austria (Styria), Belgium (Hainault and Antwerp), Denmark (Odense), France (Paris), Germany (Saxony-Anhalt), Italy (Tuscany, Emilia-Romagna, Campania), the Netherlands (Groningen), Norway, Portugal (South Portugal), Switzerland (Vaud), Ukraine, and England and Wales (East Midlands & South Yorkshire, Northern England, Thames Valley, Wales and Wessex).

The study years were 2000–05, except for France and Ukraine where only 2005 data were available. The total number of registered births (live and stillbirths) covered in the study period for the 19 regions was 2 695 832.

The EUROCAT registries are all population based, recording all live births, stillbirths and TOPFA with congenital anomaly in their populations. A description of the geographically defined populations and the methods of case ascertainment for EUROCAT is given at www.eurocatnetwork.eu.

The registries are based on multiple sources of information, including hospital records, birth and death certificates, and postmortem examinations, and include information about live births, fetal deaths at  $GA \ge 20$  weeks and terminations of pregnancy after prenatal diagnosis of fetal anomaly at any GA (TOPFA). All structural malformations, syndromes and chromosomal anomalies are included in the database, except for minor anomalies specified on a list for exclusion. Case information includes type of birth (live birth, fetal death or termination of pregnancy), GA at prenatal diagnosis (at first suspicion or positive test) and GA at delivery (birth or termination). Up to eight anomalies per case and syndrome, if present, are coded according to the International Classification of Diseases v9 (ICD9)/British Paediatric Association (BPA) or ICD10/BPA, and the cases are allocated to subgroups of anomalies based on the ICD codes. All cases not diagnosed with a chromosomal anomaly are classified as nonchromosomal, and this includes cases that have not been karyotyped. All TOPFA cases with GA  $\geq$  24 weeks with multiple anomalies (more than one organ system, excluding associations, chromosomal anomalies and monogenic syndromes) were identified using the EUROCAT multiple anomaly computer algorithm, followed by manual review by a panel of medical geneticists.

All terminations of pregnancy in singletons only were included in the study. Data were extracted from the central database, and local registries then confirmed GA at termination for all TOPFA with a GA of 24 weeks or more.

We defined late TOPFA to be  $GA \ge 24$  weeks of gestation, because of general agreement on a viability limit at 24 weeks.

We calculated the prevalence of TOPFA at <24 and  $\geq$ 24 weeks of gestation for each country (based on the corresponding registry data) with 95% Poisson exact confidence intervals (CIs); the denominators were the total number of births in the population base for the EURO-CAT areas within each country. The proportion of terminations at <24 and  $\geq$ 24 weeks of gestation were estimated with 95% binomial exact CIs for each country, as well as for the overall study population. For the latter, clustering by country was taken into account in the calculation of binomial Wald CIs. The median GAs at diagnosis and at termination, as well as the median difference between GAs at diagnosis and termination, were calculated with 95% linear interpolation binomialbased CIs.

# Results

During the study period, there were 10 233 TOPFAs reported in singleton pregnancies. GA was unknown for 451 of these cases (4.4%). Among the 9782 TOPFAs with known GAs, 5396 (55%) were diagnosed with nonchromosomal anomalies and 4386 (45%) were diagnosed with a chromosomal anomaly.

TOPFA with GA of less than 24 weeks accounted for 93% of all TOPFAs, a rate of 3.4 per 1000 births (range, 1.4–7.1 per 1000 births) (Table 1). TOPFA with GA  $\geq$  24 weeks accounted for 7% (678 cases).

Eleven countries performed TOPFAs at 24–25 weeks of gestation [prevalence, 0.14 per 1000 births (range, 0.03–0.97 per 1000 births)]. Ten countries reported TOPFA at 26 weeks of gestation or more [prevalence, 0.11 per 1000 births (range, 0.03–1.68 per 1000 births)]. The total rate of

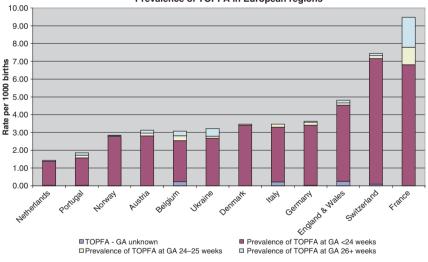
Country*	GA < 24 weeks	GA = 24–25 weeks	GA = 26 + weeks	GA NK	Total TOPFA cases	Total births	Prevalence of TOPFA < 24 weeks per 1000 births (95% CI)	Prevalence of TOPFA at 24–25 weeks per 1000 births (95% CI)	Prevalence of TOPFA from 26 weeks per 1000 births (95% Cl)	Total TOPFA prevalence per 1000 births
Austria	176	10	10	0	196	62 667	2.8 (2.4–3.3)	0.16 (0.08–0.29)	0.16 (0.08–0.29)	3.1 (2.7–3.6)
Belgium	422	49	48	42	561	182 467	2.3 (2.1–2.5)	0.27 (0.20-0.36)	0.26 (0.19–0.35)	3.1 (2.8–3.3)
Denmark	109	2	0	0	111	32 003	3.4 (2.8–4.1)	0.06 (0.00-0.23)	0.0	3.5 (2.9–4.2)
England & Wales	4075	119	143	241	4578	951 001	4.3 (4.2–4.4)	0.13 (0.10–0.15)	0.15 (0.13–0.18)	4.8 (4.7–5.0)
France**	182	26	45	0	253	26 715	6.8 (5.9–7.9)	0.97 (0.64–1.42)	1.68 (1.23–2.26)	9.5 (8.4–10.7)
Germany	359	17	6	3	385	106 257	3.4 (3.0–3.7)	0.16 (0.09–0.26)	0.06 (0.02-0.12)	3.6 (3.3–4.0)
Italy	2115	116	0	151	2382	686 894	3.1 (2.9–3.2)	0.17 (0.14–0.20)	0.0	3.5 (3.3–3.6)
Netherlands	161	0	6	3	170	118 971	1.4 (1.2–1.6)	0.0	0.05 (0.02–0.11)	1.4 (1.2–1.7)
Norway	958	11	12	4	985	346 838	2.8 (2.6–2.9)	0.03 (0.02–0.06)	0.03 (0.02-0.06)	2.8 (2.7–3.0)
Portugal	175	17	15	3	210	113 310	1.5 (1.3–1.8)	0.15 (0.09–0.24)	0.13 (0.07–0.22)	1.9 (1.6–2.1)
Switzerland	303	7	5	4	319	42 874	7.1 (6.3–7.9)	0.16 (0.07–0.34)	0.12 (0.04-0.27)	7.4 (6.7–8.3)
Ukraine**	69	3	11	0	83	25 835	2.7 (2.1–3.4)	0.12 (0.02–0.34)	0.43 (0.21–0.76)	3.2 (2.6–4.0)
Total	9104	377	301	451	10 233	2 695 832	3.4 (3.3–3.4)	0.14 (0.13–0.15)	0.11 (0.10–0.13)	3.8 (3.7–3.9)

**Table 1.** Number of terminations of pregnancy for fetal anomaly (TOPFAs) by country, and prevalence of TOPFA before and after 24 weeks of gestation, 2000–05 (for regions covered within the countries, see Materials and methods)

CI, confidence interval; GA, gestational age; NK, not known.

\*Legal situation regarding late TOPFA: no GA limit for severe anomalies (Austria, Belgium, England and Wales, France, Germany); no GA limit if lethal (Netherlands, Norway, Portugal, Switzerland, Denmark); upper GA limit [Italy (24 weeks/fetal viability), Ukraine (28 weeks)].

\*\*For France and Ukraine, only 2005.



Prevalence of TOPFA in European regions

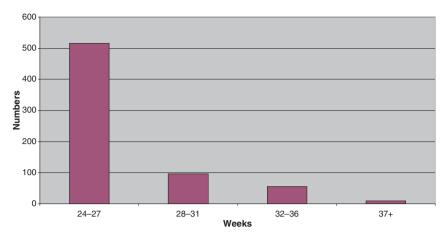
Figure 1. Prevalence of terminations of pregnancy for fetal anomaly (TOPFAs) in 12 European countries, 2000–5.

TOPFA at 24 weeks or more varied from 0 to 2.65 per 1000 births in the 12 countries: the variation between countries was highly statistically significant (P < 0.001) (Figure 1).

The large majority of late TOPFAs had a GA at 24–27 weeks (516/678, 76%) and 162 TOPFAs had a GA of 28 weeks or more (Figure 2).

For structural anomalies, 498/5396 (9%) of TOPFAs had a GA of 24 weeks or more, whereas, for cases with chromosomal anomalies, 180/4386 (4%) had a GA of 24 weeks or more (P < 0.001).

The proportion of late TOPFA varied by type of anomaly (Table 2). Those that were difficult to diagnose by ultrasound (hydrocephalus, severe cardiac malformations)



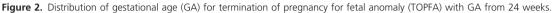


Table 2. Number of terminations of pregnancy for fetal anomaly (TOPFAs) by selected types of nonchromosomal anomaly, proportion of TOPFAs with gestational age (GA) of 24 weeks or more, median GA at diagnosis and median GA at TOPFA

Congenital anomaly type*	Total TOPFA cases (n)	Percentage of anomalies with TOPFA ≥ 24 weeks (95% Cl)	Median GA at diagnosis in weeks, TOPFA ≥ 24 weeks** (95% CI)	Median GA in weeks at TOPFA ≥ 24 weeks (95% CI)
All anomalies excluding diagnosed	5396	9.2 (8.5–10.0)	23 (23–23)	25 (25–25)
chromosomal anomalies	064	$2 \in (1 \in 2, 0)$	22 (22, 24)	25 (24 20)
Anencephalus and similar	864	2.5 (1.6–3.8)	23 (22–24)	25 (24–28)
Encephalocoele	180	2.2 (0.6–5.6)	24.5 (22–29)	26.5 (24–30)
Spina bifida***	754	7.3 (5.5–9.4)	23 (23–24)	25 (24–26)
Hydrocephaly***	560	14.3 (11.5–17.5)	23 (23–24)	26 (25–27)
Arhinencephaly/holoprosencephaly	138	12.3 (7.3–19.0)	24.5 (23–28)	26 (25–32)
Congenital heart disease	976	12.2 (10.2–14.4)	23 (22–24)	25 (24–25)
Transposition of great vessels	51	15.7 (7.0–28.6)	22.5 (22–29)	24 (24–30)
Single ventricle	43	23.3 (11.8–38.6)	23.5 (22–29)	25 (24–28)
Atrioventricular septal defect	88	13.6 (7.2–22.6)	22 (20–23)	24.5 (24–26)
Hypoplastic left heart	282	12.1 (8.5–16.4)	23 (22–24)	24 (24–25)
Oesophageal atresia	38	10.5 (2.9–24.8)	23.5 (19–28)	26 (24–29)
Diaphragmatic hernia	95	9.5 (4.4–17.2)	21 (17–29)	26 (24–29)
Gastroschisis	72	2.8 (0.3–9.7)	23.5 (23–24)	25 (24–26)
Omphalocoele	234	3.4 (1.5–6.6)	18 (13–33)	24.5 (24–34)
Bilateral renal agenesis	216	8.8 (5.4–13.4)	23 (22–25)	25 (24–26)
Arthrogryposis multiplex congenita	64	14.1 (6.6–25.0)	20.5 (18–25)	26 (25–26)
Thanatophoric skeletal dysplasia	74	1.4 (0.03–7.3)	24 (24–24)	24 (24–24)
Monogenic syndromes + microdeletions	250	9.2 (5.9–13.5)	24 (21–26)	26 (25–28)

CI, confidence interval.

\*Cases with more than one major anomally may be presented in more than one group.

\*\*GA at diagnosis not available for 17% at late TOPFAs.

\*\*\*Cases with spina + hydrocephalus counted in the spina bifida subgroup only.

had a higher proportion of late TOPFAs than those that were more easily seen on ultrasound, such as anencephalus and abdominal wall defects. For chromosomal anomalies, the highest proportion of late TOPFAs was for trisomy 13, with 6.4% of all TOPFAs with a GA of 24 weeks or more (Table 3).

Table 3. Diagnosed chromosomal anomalies: number of terminations of pregnancy for fetal anomaly (TOPFAs), proportion of TOPFAs with
gestational age (GA) of 24 weeks or more, median GA at diagnosis and median GA at TOPFA

	Total TOPFA chromosomal cases with known GA	Percentage of chromosomal anomalies with TOPFA ≥ 24 weeks (95% CI)	Median GA in weeks at diagnosis, TOPFA ≥ 24 weeks* (95% CI)	Median GA in weeks at TOPFA (95% Cl)
All chromosomal cases	4386	4.1 (3.5–4.7)	23 (22–23)	25 (25–26)
Down's syndrome	2285	2.3 (1.7–3.0)	23 (22–23)	24 (24–25)
Patau syndrome/trisomy 13	298	6.4 (3.9–9.8)	24 (22–27)	26 24–27)
Edward syndrome/trisomy 18	749	6.0 (4.4-8.0)	23 (23–24)	25 (24–26)
Turner's syndrome	344	2.3 (1.0-4.5)	18 (12–26)	25 (24–26)

CI, confidence interval.

\*GA at diagnosis not known for 17% of all late TOPFA cases.

**Table 4.** Distribution by organ system for terminations of pregnancy for fetal anomaly (TOPFAs) with a gestational age (GA) of 24 weeks or more (n = 678). All cases only counted once in the table

Type of anomaly	Number of cases	Percentage of total	
Neural tube defects*	76	11	
Hydrocephalus*	59	9	
Other cerebral anomalies*	44	6	
Cardiac defects*	73	11	
Respiratory*	10	<1	
Gastrointestinal anomalies*	11	<1	
Abdominal wall defects*	8	<1	
Renal anomalies*	49	7	
Other isolated anomalies	52	8	
Multiple anomalies	67	10	
Monogenic syndrome or microdeletion	43	6	
Down's syndrome	53	8	
Trisomy 13	19	3	
Trisomy 18	42	6	
Other chromosomal	72	11	
Total	678	100	

\*As isolated anomaly.

The types of anomaly diagnosed for all 678 TOPFAs with a GA of 24 weeks or more are presented in Table 4. Twenty-seven percent of all late TOPFAs were caused by chromosomal anomalies and 73% were caused by major structural anomalies. Ten percent of late TOPFAs were for multiple anomalies, 6% for monogenic syndromes and the remaining 57% for isolated major structural anomalies.

For all 678 TOPFAs with a GA of 24 weeks or more, the median GA at diagnosis was 23 weeks and the median GA at TOPFA was 25 weeks. For four anomalies, the median

time interval between diagnosis and late TOPFA was more than 5 weeks: diaphragmatic hernia, omphalocoele, arthrogryposis multiplex and Turner's syndrome.

#### Discussion

In our study population of 12 European countries in which TOPFA is legal, we found, on average, approximately one late TOPFA per 4000 births (0.25 per 1000 births) for the period 2000–05. More than one-half of these terminations of pregnancy were performed following the diagnosis of a major anomaly of a single organ system. We do not know from our registry data whether the anomaly diagnosed was the sole reason for the termination. There may also have been other conditions contributing to a poor prognosis, such as severe fetal growth restriction, severe hydrops, severe oligohydramnios or additional maternal factors.

The rate of TOPFA with a GA of 24 weeks or more varied considerably between countries, from less than 0.1 per 1000 births in the Netherlands (Groningen), Denmark (Odense) and Norway, to 2.65 per 1000 in France (Paris), with all countries other than France having rates under 0.6 per 1000. There was a poor relationship between the prevalence of early terminations and the prevalence of late terminations—a point illustrated by the fact that both France (Paris) and Switzerland (Vaud) showed high rates of termination before 24 weeks (6.8 and 7.1 per 1000, respectively), whereas Paris had a much higher rate of termination after 24 weeks than Vaud. Several other studies have reported previously a high prevalence of late TOPFA in France.<sup>2,4,5</sup> The variations in TOPFA rates in Europe have been reported previously.<sup>1,5,6</sup>

In Paris, the second trimester anomaly scan tends to be performed later than in other European countries. An earlier analysis of EUROCAT registry data showed the median GA at diagnosis for structural anomalies was 22 weeks in Paris, compared with 19–20 weeks in registries in Belgium, Italy and the UK.<sup>6</sup> As our data suggest that the median time from prenatal diagnosis to termination is 2 weeks, having a relatively late GA for the anomaly scan would result in more TOPFA after 24 weeks. Nevertheless, Paris also had a higher TOPFA rate from 26 weeks of gestation, suggesting a higher acceptability of late termination in this population. Paris, like some but not all European countries, also has a recommended third trimester scan.<sup>1</sup>

There are some limitations to our data. The areas covered by EUROCAT are not necessarily representative of the entire country. Furthermore, it is possible that some late TOPFAs were recorded in the EUROCAT registers as stillbirths or live births (i.e. early birth inductions) rather than TOPFA, depending on local medical practice. In some areas, TOPFA performed outside the registry area may not be known to the registry, as in Saxony-Anhalt, Germany. This may also be the case in countries with an upper GA limit for TOPFA. In the Ukraine, the legal limit for TOPFA was 28 weeks during the study period (2005), but was reduced to 22 weeks in 2006.

Terminations after 24 weeks, although a small proportion of all TOPFAs, nevertheless constitute a potentially large proportion of perinatal deaths or stillbirths. Countries vary in terms of the legal requirement to register late TOPFA as a live or stillbirth, and in terms of whether perinatal mortality associated with TOPFA can be distinguished from other perinatal mortality.<sup>5</sup> The Models of Organising Access to Intensive Care for very preterm babies (MOSAIC) study<sup>5</sup> published termination of pregnancy rates for European regions for a GA of 22-31 weeks for 2003 for any indication (fetal and maternal). The data sets are not completely comparable but, given the high rates of termination of pregnancy after 22 weeks in the MOSAIC study, it may be that there is some under-reporting of TOPFA as stillbirths in the current study. Until there is harmonisation of recording practices, late TOPFA creates difficulties in the interpretation of the variation between countries in stillbirth and perinatal mortality rates. On the one hand, late TOPFA may decrease perinatal mortality rates when it is not civilly registered, but may also increase perinatal mortality rates when it is performed for nonlethal anomalies and is civilly registered.<sup>5,7</sup>

The spectrum of anomalies in late TOPFA differs from that of early TOPFA, with a higher proportion of structural anomalies and a lower proportion of chromosomal anomalies. We also found that 57% of TOPFAs with a GA of 24 weeks or more are performed after prenatal diagnosis of an isolated major structural anomaly, and the proportion of multiple anomalies was only 10% (Table 4). The proportion of multiple malformed cases is lower than that found in two other studies from single centres.<sup>4,8</sup> Single-centre studies may be biased towards tertiary referral centres.

Certain anomalies were particularly likely to be associated with late termination, including single ventricle, transposition of the great vessels, arthrogryposis multiplex and hydrocephaly, for which more than 14% of all terminations were at 24 weeks or later. The distribution of the isolated major anomalies in late TOPFA, with a high proportion of cerebral anomalies in our European multicentre study, is comparable with that of other regional studies published in France (Isere, Paris), UK (Northern Region) and Israel.<sup>2,4,8,9</sup> Two of these studies presented data on third trimester terminations (GA  $\geq$  28 weeks).<sup>4,8</sup>

The median time interval from diagnosis to termination was 2 weeks. A reasonable time interval is needed between diagnosis and termination of pregnancy to allow referral to specialists and prenatal counsellors, to wait for karvotype results, to allow parents to reach an informed decision, and to obtain permission for termination from a committee or more than one doctor. In four anomalies, we found a median time interval of more than 1 month from prenatal diagnosis to termination: diaphragmatic omphalocoele, arthrogryposis multiplex and hernia, Turner's syndrome. Turner's syndrome is an example in which termination is most frequently performed when severe fetal hydrops is diagnosed late in gestation. In the case of diaphragmatic hernia, liver herniation suggests a poor prognosis and may influence the decision to terminate. Other indications, such as lung hypoplasia in diaphragmatic hernia and fetal akinesia in arthrogryposis late in pregnancy, may also influence the prognosis and the decision to terminate.

It was not our purpose in this article to discuss the ethical or psychological aspects of late termination. We note, however, that the general consensus is that ethical and psychological acceptability of TOPFA is greater the earlier in pregnancy in which it is performed.<sup>10</sup>

There is a balance to be reached, which takes into account cultural and ethical considerations, between having an earlier anomaly scan policy which allows earlier TOPFA or a later scan policy with a higher and sometimes more accurate prenatal detection rate, but resulting in later TOPFA. There may be situations in which it is necessary to follow the development of an anomaly to see if the fetus deteriorates in the weeks following a diagnosis, for example after a prenatal diagnosis of less severe hydrocephalus. The availability of late TOPFA may allow parents to make a decision on the basis of more accurate information from a later investigation.

## Addendum

TOPFA rates and rates before and after 20 weeks of gestation, for the most recent 5 years, can be found at the EUROCAT website: www.eurocat-network.eu. These data are updated annually.

#### Disclosure of interest

None.

#### Contribution to authorship

EG defined the research question, wrote the study description, wrote the paper, contacted local registries and is the corresponding author.

BK performed the statistical analysis, revised all versions of the paper and gave final approval.

ML wrote the study description, managed the data, performed statistical analysis, contacted local registries, revised all versions of the paper and gave final approval.

TB wrote the study description, revised all versions of the paper and gave final approval.

HD defined the research question, revised all versions of the paper and gave final approval.

#### Details of ethics approval

This was a central database study based on data from local registries. Ethics approval was performed by local registries.

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