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European trends in mortality in children with congenital anomalies: 2000–2015

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Abstract

Objective: To investigate if the survival of children with congenital anomalies has improved from 2000 to 2015 and whether there is heterogeneity in the improvements across Europe.

Design: Population-based study of routine collected data from the WHO database on mortality and causes.

Setting: Data on 31 European countries from 2000 to 2015.

Main outcome measures: All-cause and congenital anomaly mortality rates for infants and children up to age 9 in countries and regions of Europe.

Results: The relative odds of all-cause mortality in 2015 compared with 2000 was 0.54 (95% CI: 0.50–0.59) for under 1, 0.48 (95% CI: 0.44–0.53) for ages 1–4, and 0.53 (95% CI: 0.49–0.56) for ages 5–9 with the relative odds of mortality from congenital anomalies being 0.49 (95% CI: 0.44–0.55), 0.51 (95% CI: 0.44–0.60), and 0.65 (95% CI: 0.53–0.80), respectively. The proportion of deaths from congenital anomalies remained relatively constant over time (26, 16, and 9% for under 1, ages 1–4, and ages 5–9, respectively) and was similar in all regions of Europe. For mortality from all causes and from congenital anomalies heterogeneity between countries and regions of Europe was high, with the countries in Eastern Europe having higher rates, but also experiencing greater relative reductions in mortality from 2000 to 2015.

Conclusion: There was a large geo-spatial disparity in all cause and congenital anomaly mortality for infants and children up to 9. However, all regions saw a significant decrease in all cause and congenital anomaly mortality rates, with the proportions of deaths from congenital anomalies remaining constant over this time.

KEYWORDS

all-cause mortality, childhood mortality, congenital anomalies, Europe, infant mortality

1 | INTRODUCTION

Congenital anomalies are defined by the World Health Organisation (WHO) as structural or functional abnormalities that occur prenatally and may be diagnosed prenatally or in early infancy (WHO, 2020b). They lead to high levels of disability and mortality (WHO, 2020b). The 2010 Global Burden of Disease study found congenital anomalies accounted for 6% of infant deaths and 2.5% of deaths in children aged 1–4 years globally (Lozano et al., 2012). Studies have suggested around 19.3% of neonatal deaths and 20.6% of infant deaths are due to congenital anomalies in more developed countries (Almli et al., 2020; Roncancio et al., 2018).

Mortality from any cause and particularly from congenital anomalies is much greater during infancy than childhood with over 80% of deaths in children under-5 actually occurring in infants under 1 (Zylbersztejn, Gilbert, Hjern, Wijlaars, & Hardelid, 2018). However, deaths in childhood, particularly among children with congenital anomalies, do occur and it is therefore important to monitor changes in mortality in children as well as infants. Recent studies (Göpfert, Sethi, Rakovac, & Mitis, 2015; Lyons & Brophy, 2005; Onambele et al., 2019) have shown that all-cause infant mortality has significantly decreased in Europe, with an annual percentage change of −3.8%; from 8.3 to 3.6 per 1,000 live births from 1994 to 2015 (Onambele et al., 2019). However, in Europe there is limited recent research in mortality of children post infancy. Lyons and Brophy (2005) showed a decrease in childhood mortality by 50% from 1969 to 1992. Of concern is that increased heterogeneity in mortality across Europe has been reported with, for example, all-cause mortality being lower in Scandinavian countries compared to Eastern Europe countries (Lyons & Brophy, 2005). Child injury deaths have been increasing in low-to-middle income countries (LMIC) compared with high income countries (HIC) by 31% (Göpfert et al., 2015).

Research has shown that the survival of infants with congenital anomalies has improved in recent years (Glinianaia et al., 2020; Schneuer et al., 2019; Tennant, Pearce, Bythell, & Rankin, 2010; Wang, Hu, Druschel, & Kirby, 2011). However, other studies have found no significant change in survival (Dastgiri, Gilmour, & Stone, 2003; Roncancio et al., 2018). Furthermore, some research has suggested that the proportion of congenital anomaly compared with all deaths increased slightly from 1976 to 1985 across the USA and UK but not in Sweden (Powell-Griner & Woolbright, 1990).

Therefore, this study used the WHO mortality database (WHO, 2020a) to examine if mortality from congenital anomalies and all-cause childhood mortality has continued to decrease in Europe from 2000 to 2015 and if the relative contribution of deaths from congenital anomalies to total mortality in childhood has changed significantly across Europe.

2 | METHODS

We extracted data for 31 European countries for years 2000–2015 from the WHO database on cause of death (https://apps.who.int/healthinfo/statistics/mortality/causeofdeath_query/start.php). We used Detailed ICD-10 for deaths data, selected Cause-group as all causes and "17 Congenital malformations, deformations and chromosomal abnormalities" for the age categories <1, 1, 2, 3, 4, and 5–9 years. Where ICD 10 was not available, we used detailed ICD-9 with for all causes and "14 Congenital anomalies." For the Ukraine we used 101-ICD-10 Mortality Tabulation List 1 with all-causes and "1093 Congenital malformations, deformations, and chromosomal abnormalities". For Portugal 2004 and 2005 data, we used "UE1–ICD-10 special list for Portugal (data for 2004-2005)" and "CH00 ALL CAUSES OF DEATH" and "CH17 CONGENITAL MALFORMATIONS, DEFORMATIONS AND CHROMOSOMAL ABNORMALITIES." For Ireland pre 2006 we used "09A/09B–ICD9th revision, (Standard) Basic Tabulation List" with "B00 All causes" and "B44 Congenital anomalies" as causes. This gave us almost a complete set of data for all 31 countries from 2000 to 2015. We did not impute any deaths data not given. For population data we used the WHO database on population and selected the 31 countries for the years 2000–2015 where available and then selected <1, 1, 2, 3, 4, 5–9 years of age categories. Where 2014/2015 population data were not available, we used the previous year's population data (Finland, Switzerland, and Ireland).

To allow us to look for disparities across Europe we split the countries into four regions; Northern (Denmark, Finland, Ireland, Norway, and Sweden, UK), Eastern (Bulgaria, Croatia, Czech Republic, Estonia, Hungry, Latvia, Lithuania, Poland, Romania, Slovakia, Slovenia, and Ukraine), Southern (Greece, Italy, Portugal, Spain, Cyprus, and Malta), and Western (Austria, Belgium, France, Germany, Luxemburg, Netherlands, and Switzerland) based on the geographic location within Europe and as used by other studies (Bosetti et al., 2010; Onambele et al., 2019).

2.1 | Statistical analysis methods

Mortality was analyzed separately for infants, for children aged 1–4, and for children aged 5–9.

To examine trends in all-cause mortality over time we fitted multilevel negative binomial regression models with European region as the first level and within that country as a random effect and each two-year period was fitted independently as a fixed effect within country. This takes into account the correlations within a country. Negative binomial regression models were used instead of poisson regression models to allow for overdispersion. Robust variance estimators were used. For each region, the average marginal effects were calculated to estimate the overall all-cause mortality in each region for each

2-year period. Two-year periods were analyzed to be consistent with other analyses in the paper for deaths from congenital anomalies where displaying data by individual year results in a lack of clarity due to small numbers having wide sampling errors.

To illustrate the heterogeneity in trends over time between countries within regions negative binomial regression models were fitted within each country with year as a continuous variable (rather than as a categorical variable). A random-effects meta-analysis of the estimated percentage change in mortality rate from 2000 to 2015 by country within region was performed and the forest plot presented.

Similar models were fitted to analyze the trends in mortality from congenital anomalies over time.

Multilevel logistic regression models were used to investigate any changes over time in the relative proportion of deaths due to congenital anomalies in the different countries. European region was the first level and within that country as a random effect and each year was fitted independently as a fixed effect within country.

All analyses were performed in Stata version 15 (StatCorp, College Station, Texas).

3 | RESULTS

Table 1 shows for each country the average population size and the numbers of deaths from all causes and congenital anomalies across the three age categories. The countries differed in size with France having the biggest average population with over 765,000 infants under 1 year and Malta the smallest, with around 4,000 infants under 1 year.

3.1 | All-cause mortality

Figure 1 shows that infant all-cause mortality varied by region; countries in Eastern Europe had almost twice the mortality rate than those in the rest of Europe. Mortality decreased in all countries (except for Malta) with an average reduction of 46% (95% CI: 41–50%) (Table 2). On average Eastern Europe saw the greatest decrease of 56% (95% CI: 48–62%), and Western the smallest decrease of 31% (95% CI: 26–36%). Within each region of Europe there was considerable heterogeneity, with all regions having an I^2 over 88%, and there was also considerable heterogeneity between the regions in Europe ($I^2 = 98.3\%$).

A similar pattern is seen for all-cause mortality in children over 1 year of age, where countries in Eastern Europe had almost twice the mortality of those in Northern Europe (Figure 1). In ages 1–4 mortality significantly reduced by an average of 52% (95% CI: 47–56%) with all countries apart from Greece seeing a significant reduction. Heterogeneity between countries and between regions was slightly lower with a range from 66.9% I^2 score in Northern Europe to 94.1% in Southern Europe and an overall I^2 score of 92.4%. In ages 5–9, Countries from Eastern Europe had much higher mortality rates, while countries from Southern Europe also had higher mortality rates than those in Western and Northern Europe but there was a similar overall reduction of 47% (95% CI: 44–51%) with all countries seeing a reduction. Heterogeneity remained relatively high but decreased slightly with an I-squared score of 76.7% between regions.

Overall, there was a significant decrease in mortality in almost all countries across all ages up to 9 years while the countries in Eastern Europe had the greatest decreases.

3.2 | Congenital anomaly mortality

Figure 2 shows that infant deaths from congenital anomalies varied by region of Europe, in particular Eastern Europe had higher mortality than the rest of Europe. However, infant mortality from congenital anomalies decreased in all countries (except for Malta) with an average reduction of 51% (95% CI: 45–56%) (Table 2 and Figure 3) across the 16 years. On average Eastern Europe saw the greatest decrease of 58% (95% CI: 52–63%), and Western Europe the smallest decrease of 32% (95% CI: 20–43%). Within each region of Europe there was considerable heterogeneity, with all regions having an I^2 over 85%, and there was also considerable heterogeneity between the regions in Europe ($I^2 = 95.3\%$).

A similar pattern is seen for mortality from congenital anomalies in children aged 1–4, where Eastern Europe had the highest rates and all countries (apart from Malta and Luxembourg) saw a reduction, varying from 56% (95% CI: 40–68%) in Southern Europe to 34% (95% CI: 23–43%) in Western Europe but with an average overall reduction of 49% (95% CI: 40–56%). Heterogeneity within regions decreased as well as between the regions ($I^2 = 81.5\%$). In addition, Eastern Europe still had much higher mortality rates for ages 5–9 and there was an overall significant reduction of 35% (95% CI: 20–47%) across Europe. However, most individual countries did not see a statistically significant reduction. Heterogeneity between regions decreased ($I^2 = 67.95$) as well as heterogeneity within some regions, which was as low as 17.2 and 23.6% in Western and Northern Europe, respectively.

Overall there was a significant decrease in mortality from congenital anomalies in Europe across all age

TABLE 1 Population and deaths from 2000 to 2015 in 31 European countries

		Average population (per 1,000)			Total deaths from 2000 to 2015			Total congenital anomaly deaths from 2000 to 2015			Percentage of deaths from congenital anomalies (%)		
Country	**Region**	**Under 1**	**Age 1–4**	**Age 5–9**	**Under 1**	**Age 1–4**	**Age 5–9**	**Under 1**	**Age 1–4**	**Age 5–9**	**Under 1**	**Age 1–4**	**Age 5–9**
Bulgaria[a]	Eastern	64	258	320	10,892	2,148	1,302	2,169	274	76	20	13	6
Croatia	Eastern	42	174	231	3,587	639	476	1,099	162	43	31	25	9
Czech Republic	Eastern	105	411	503	5,283	1,256	935	1,109	169	85	21	14	9
Estonia	Eastern	14	56	68	1,068	309	221	286	58	20	27	19	9
Hungary	Eastern	94	383	507	9,113	1,653	1,060	2,232	306	124	25	19	12
Latvia	Eastern	21	81	103	2,507	561	474	690	86	37	28	15	8
Lithuania	Eastern	31	124	168	2,968	787	625	1,059	140	57	36	18	9
Poland	Eastern	376	1,539	2010	35,437	5,921	4,514	11,869	1,424	470	34	24	10
Romania	Eastern	208	849	1,099	43,431	8,051	5,080	9,716	1,070	218	22	13	4
Slovakia[b]	Eastern	55	220	291	4,998	1,078	743	1,454	200	58	29	19	8
Slovenia	Eastern	20	78	95	953	222	168	275	51	20	29	23	12
Ukraine	Eastern	416	1,627	2069	64,968	16,027	10,334	17,050	3,169	1,150	26	20	11
	Eastern	1,445	5,799	7,463	185,205	38,652	25,932	49,008	7,109	2,358	27	18	9
Cyprus[c]	Southern	9	36	45	335	76	71	55	13	2	16	17	3
Greece	Southern	105	425	532	6,515	1,254	982	2,468	357	150	38	29	15
Italy	Southern	538	2,186	2,762	31,624	5,726	4,103	8,290	958	313	26	17	8
Malta	Southern	4	17	22	375	63	27	150	9	5	40	14	19
Portugal[b]	Southern	81	334	431	4,705	1,263	932	1,118	191	70	24	15	8
Spain	Southern	450	1789	2,179	25,200	5,602	3,707	6,803	873	335	27	16	9
	Southern	1,188	4,786	5,971	68,754	13,984	9,822	18,884	2,401	875	28	17	9
Austria	Western	78	322	426	4,814	983	652	1,411	215	102	29	22	16
Belgium	Western	121	487	608	7,593	1749	998	1979	196	56	26	11	6
France[b]	Western	765	3,042	3,779	43,275	9,077	5,408	9,256	936	333	21	10	6
Germany	Western	700	2,879	3,781	42,019	9,001	5,696	11,303	1,507	604	27	17	11
Luxembourg	Western	6	23	30	234	60	28	36	6	2	15	10	7
Netherlands	Western	188	769	983	12,702	2,490	1,501	3,848	321	116	30	13	8
Switzerland[d]	Western	76	309	397	5,165	857	583	1,587	133	60	31	16	10
	Western	1933	7,832	10,003	115,802	24,217	14,866	29,420	3,314	1,273	25	14	9
Denmark	Northern	63	260	337	3,947	739	436	965	131	49	24	18	11

TABLE 1 (Continued)

Country	Region	Average population (per 1,000) Under 1	Age 1–4	Age 5–9	Total deaths from 2000 to 2015 Under 1	Age 1–4	Age 5–9	Total congenital anomaly deaths from 2000 to 2015 Under 1	Age 1–4	Age 5–9	Percentage of deaths from congenital anomalies (%) Under 1	Age 1–4	Age 5–9
Finland[a]	Northern	58	235	301	2,491	621	509	819	103	51	33	17	10
Ireland[b,e]	Northern	61	235	275	3,800	698	414	1,551	124	47	41	18	11
Norway	Northern	59	241	306	2,796	686	469	826	132	42	30	19	9
Sweden	Northern	106	416	523	4,615	1,047	707	1,324	149	78	29	14	11
United Kingdom[f]	Northern	750	2,952	3,608	52,597	8,869	5,234	12,484	1,268	482	24	14	9
	Northern	1,096	4,339	5,349	70,246	12,660	7,769	17,969	1907	749	26	15	10
All regions		5,663	22,756	28,786	440,007	89,513	58,389	115,281	14,731	5,255	26	17	9

[a]2015 population data replaced with 2014.
[b]2015 data missing (2011 too for Slovakia).
[c]2000, 2001, 2002, 2003 data missing.
[d]2014 and 2015 population data replaced with 2013.
[e]2014 population data replaced with 2013.
[f]2000 data missing.

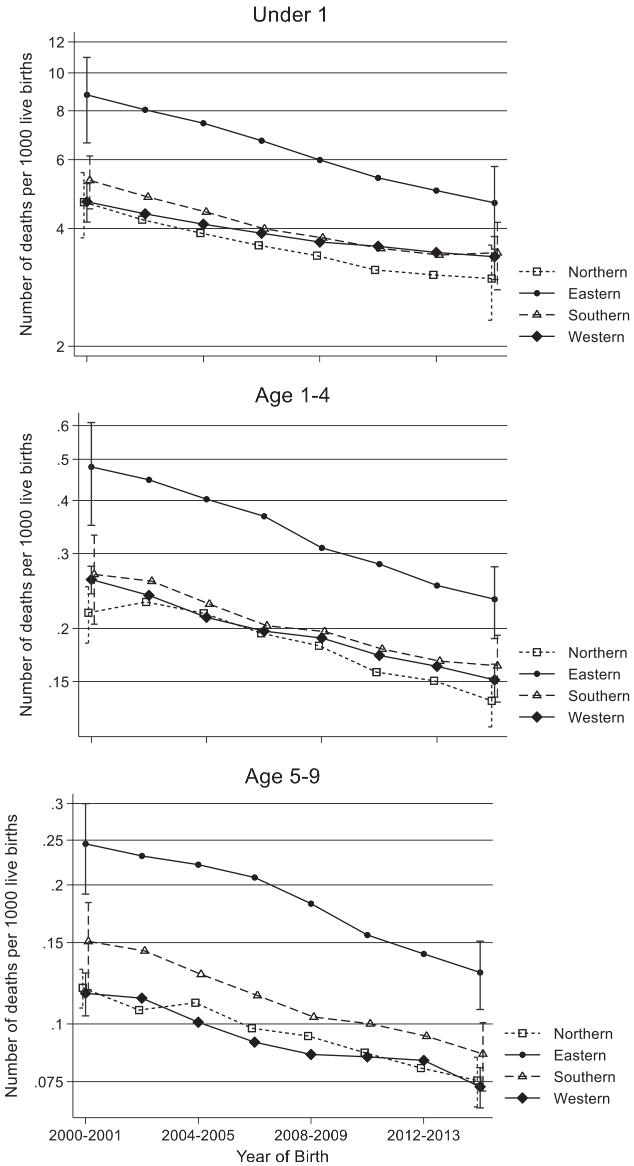

FIGURE 1 All-cause mortality in four regions of Europe (95% CI): 2000–2015 for ages under 1 year, 1–4 years, and 5–9 years

groups up to nine with greater decreases at younger ages. However, the decreases were not statistically significant in all individual countries. Heterogeneity was high but decreased as age increased.

3.3 | Congenital anomaly mortality compared with all-cause mortality

The proportion of all deaths due to congenital anomalies did not vary from 2000 to 2015 (data not shown). Table 1 shows congenital anomaly deaths as a proportion of all deaths for children up to age nine across four regions of Europe for the whole time period. As age increased, the proportion of deaths due to congenital

TABLE 2 Odds of death in 2015 compared to 2000: All-cause mortality and congenital anomaly mortality in 31 European countries within four regions

		All-cause mortality: Relative odds (95% CI)			Congenital anomaly mortality: Relative odds (95% CI)		
Country	Region	Under 1	Age 1–4	Age 5–9	Under 1	Age 1–4	Age 5–9
Bulgaria[a]	Eastern	0.46 (0.43-0.50)	0.45 (0.39–0.53)	0.60 (0.49–0.73)	0.32 (0.27–0.38)	0.51 (0.33–0.80)	1.86 (0.82–4.22)
Croatia	Eastern	0.51 (0.46–0.58)	0.61 (0.46–0.79)	0.60 (0.44–0.82)	0.47 (0.38–0.58)	0.93 (0.55–1.57)	0.52 (0.18–1.49)
Czech Republic	Eastern	0.51 (0.46–0.56)	0.47 (0.38–0.57)	0.49 (0.39–0.60)	0.43 (0.35–0.53)	0.52 (0.31–0.88)	0.46 (0.22–0.94)
Estonia	Eastern	0.23 (0.18–0.28)	0.34 (0.23–0.51)	0.29 (0.18–0.46)	0.20 (0.13–0.31)	0.24 (0.09–0.60)	0.09 (0.02–0.48)
Hungary	Eastern	0.47 (0.43–0.50)	0.49 (0.42–0.58)	0.52 (0.42–0.64)	0.58 (0.50–0.67)	0.55 (0.37–0.82)	0.39 (0.21–0.73)
Latvia	Eastern	0.36 (0.32–0.42)	0.29 (0.22–0.39)	0.39 (0.29–0.54)	0.27 (0.20–0.35)	0.38 (0.18–0.81)	0.75 (0.26–2.23)
Lithuania	Eastern	0.41 (0.36–0.46)	0.31 (0.24–0.40)	0.54 (0.41–0.72)	0.37 (0.30–0.46)	0.28 (0.16–0.51)	0.89 (0.37–2.19)
Poland	Eastern	0.49 (0.47–0.51)	0.51 (0.47–0.56)	0.50 (0.45–0.55)	0.53 (0.50–0.57)	0.82 (0.69–0.99)	1.28 (0.94–1.73)
Romania	Eastern	0.36 (0.34–0.37)	0.36 (0.33–0.39)	0.40 (0.36–0.44)	0.41 (0.38–0.44)	0.28 (0.23–0.35)	0.26 (0.16–0.43)
Slovakia[b]	Eastern	0.64 (0.57-0.71)	0.59 (0.48–0.74)	0.58 (0.44–0.75)	0.75 (0.62–0.91)	0.83 (0.50–1.38)	0.71 (0.28–1.84)
Slovenia	Eastern	0.36 (0.29–0.45)	0.60 (0.38–0.95)	0.43 (0.26–0.73)	0.22 (0.15–0.34)	0.35 (0.13–0.90)	0.41 (0.09–1.89)
Ukraine	Eastern	0.67 (0.65–0.69)	0.36 (0.34–0.38)	0.47 (0.44–0.51)	0.51 (0.48–0.54)	0.35 (0.31–0.39)	1.10 (0.91–1.34)
	Eastern	0.44 (0.38–0.52)	0.43 (0.38–0.49)	0.48 (0.44–0.53)	0.42 (0.37–0.48)	0.47 (0.35–0.64)	0.64 (0.43–0.96)
Cyprus[c]	Southern	0.44 (0.27-0.74)	0.21 (0.07–0.60)	0.20 (0.07–0.61)	0.55 (0.16–1.90)	0.27 (0.02–3.57)	16.5 (0.1–19,872)
Greece	Southern	0.61 (0.56–0.67)	0.93 (0.77–1.13)	0.71 (0.58–0.89)	0.60 (0.52–0.70)	0.70 (0.49–1.01)	0.69 (0.40–1.19)
Italy	Southern	0.62 (0.60–0.65)	0.63 (0.57–0.69)	0.55 (0.50–0.61)	0.45 (0.42–0.49)	0.44 (0.35–0.55)	0.92 (0.62–1.34)
Malta	Southern	1.10 (0.77–1.55)	0.48 (0.21–1.14)	0.37 (0.10–1.45)	1.13 (0.65–1.95)	2.81 (0.29–27.2)	1.14 (0.06–23.1)
Portugal[b]	Southern	0.44 (0.40-0.48)	0.31 (0.25–0.37)	0.35 (0.28–0.44)	0.38 (0.31–0.47)	0.30 (0.18–0.49)	0.42 (0.19–0.93)
Spain	Southern	0.58 (0.56–0.61)	0.47 (0.43–0.52)	0.50 (0.45–0.56)	0.41 (0.38–0.45)	0.35 (0.28–0.45)	0.37 (0.26–0.54)
	Southern	0.59 (0.52–0.66)	0.51 (0.37–0.69)	0.5 (0.41–0.61)	0.49 (0.41–0.58)	0.44 (0.32–0.60)	0.59 (0.37–0.93)
Austria	Western	0.63 (0.57–0.69)	0.61 (0.49–0.76)	0.65 (0.50–0.85)	0.77 (0.64–0.92)	0.50 (0.32–0.80)	0.70 (0.36–1.36)
Belgium	Western	0.66 (0.61–0.72)	0.60 (0.51–0.71)	0.63 (0.51–0.78)	0.54 (0.46–0.63)	0.89 (0.55–1.45)	0.44 (0.18–1.09)
France[b]	Western	0.74 (0.71-0.77)	0.55 (0.51–0.60)	0.57 (0.52–0.63)	0.69 (0.64–0.75)	0.76 (0.60–0.96)	0.57 (0.38–0.85)
Germany	Western	0.71 (0.69–0.74)	0.59 (0.55–0.64)	0.63 (0.58–0.70)	0.74 (0.69–0.79)	0.69 (0.58–0.82)	0.93 (0.70–1.22)
Luxembourg	Western	0.44 (0.28–0.69)	0.31 (0.13–0.77)	0.69 (0.19–2.51)	0.77 (0.25–2.38)	1.87 (0.12–30.3)	0.13 (0.01–24.9)
Netherlands	Western	0.61 (0.57–0.65)	0.44 (0.38–0.50)	0.52 (0.44–0.63)	0.47 (0.42–0.52)	0.49 (0.33–0.72)	0.69 (0.36–1.31)
Switzerland[d]	Western	0.82 (0.74-0.90)	0.42 (0.34–0.53)	0.60 (0.46–0.80)	0.96 (0.81–1.14)	0.52 (0.29–0.94)	0.43 (0.18–1.05)
	Western	0.69 (0.64–0.74)	0.53 (0.48–0.59)	0.60 (0.57–0.64)	0.68 (0.57–0.80)	0.66 (0.57–0.77)	0.69 (0.55–0.88)
Denmark	Northern	0.72 (0.64–0.80)	0.45 (0.35–0.58)	0.48 (0.35–0.67)	0.33 (0.26–0.41)	0.30 (0.16–0.56)	0.46 (0.17–1.23)
Finland[a]	Northern	0.50 (0.44-0.58)	0.63 (0.48–0.83)	0.52 (0.38–0.70)	0.43 (0.34–0.55)	0.66 (0.34–1.29)	0.63 (0.24–1.61)

TABLE 2 (Continued)

Country	Region	All-cause mortality: Relative odds (95% CI)			Congenital anomaly mortality: Relative odds (95% CI)		
		Under 1	Age 1–4	Age 5–9	Under 1	Age 1–4	Age 5–9
Ireland[b,e]	Northern	0.44 (0.39-0.50)	0.45 (0.34–0.59)	0.57 (0.40–0.81)	0.53 (0.44–0.64)	0.81 (0.43–1.53)	1.52 (0.54–4.29)
Norway	Northern	0.56 (0.49-0.63)	0.39 (0.30–0.50)	0.42 (0.31–0.58)	0.46 (0.36–0.58)	0.40 (0.22–0.72)	0.45 (0.16–1.31)
Sweden	Northern	0.63 (0.57-0.70)	0.61 (0.50–0.76)	0.65 (0.51–0.84)	0.39 (0.32–0.47)	0.52 (0.30–0.91)	0.55 (0.26–1.17)
United Kingdom[f]	Northern	0.63 (0.61-0.66)	0.58 (0.54–0.62)	0.64 (0.58–0.71)	0.78 (0.73–0.84)	0.50 (0.41–0.62)	0.99 (0.72–1.37)
	Northern	0.58 (0.51-0.65)	0.52 (0.45–0.60)	0.56 (0.49–0.65)	0.47 (0.34–0.66)	0.50 (0.41–0.62)	0.76 (0.54–1.08)
All regions		0.54 (0.50-0.59)	0.48 (0.44–0.53)	0.53 (0.49–0.56)	0.49 (0.44–0.55)	0.51 (0.44–0.60)	0.65 (0.53–0.80)

Note: The bold entries were to emphasize that these were summary rows eg Northern = summary of Denmark, Finland, Ireland, Norway, Sweden and UK.

[a] 2015 population data replaced with 2014.

[b] 2015 data missing (2011 too for Slovakia).

[c] 2000, 2001, 2002, 2003 data missing.

[d] 2014 and 2015 population data replaced with 2013.

[e] 2014 population data replaced with 2013.

[f] 2000 data missing.

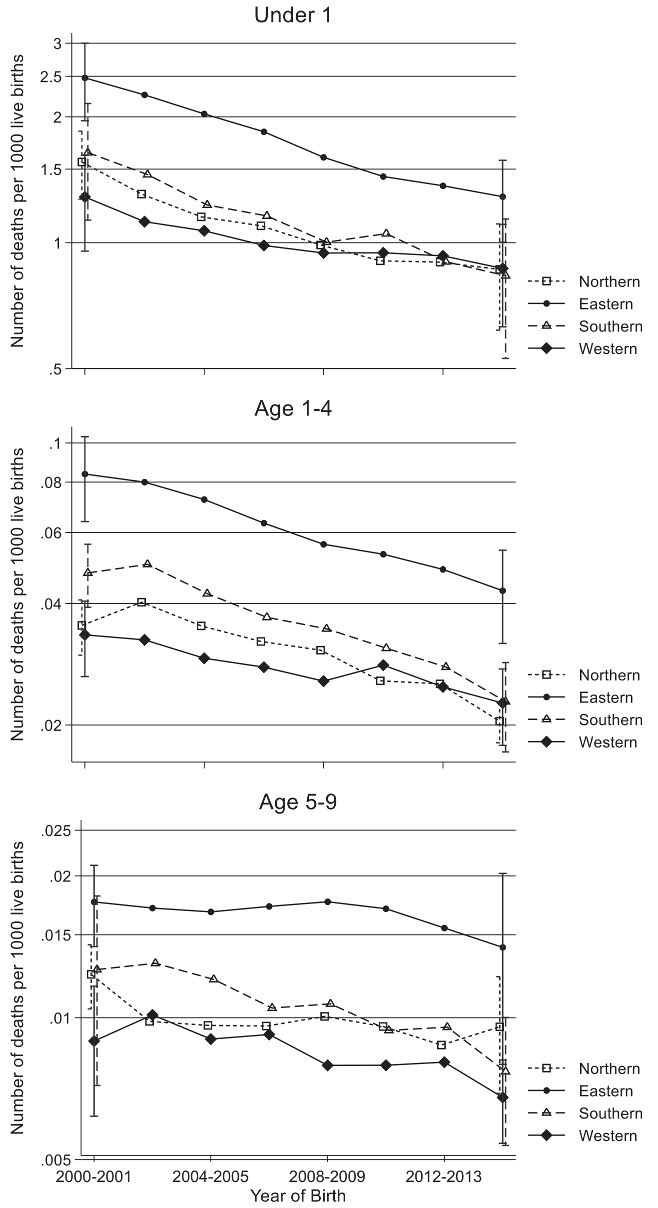

FIGURE 2 Congenital anomaly mortality in four regions of Europe (95%CI): 2000–2015 for ages under 1 year, 1–4 years, and 5–9 years

anomalies decreased. On average Southern Europe had the highest proportion of deaths due to congenital anomalies in infants, and Western the lowest. However, there was a large amount of variation between countries. Ireland, Greece, and Malta had the highest proportions of infants (37.9–40.8%), with Greece the highest for ages 1–4 as well. For ages 5–9 Malta, Austria and Greece had the highest proportions (18.5, 15.6, 15.3%, respectively). The countries with the smallest proportions of deaths include Luxembourg (15.4%), Cyprus (16.5%), and Bulgaria (19.9%) for infants, Luxembourg (10%), France (10.3%), and Belgium (11.2%) for ages 1–4 and Cyprus (2.8%), Romania (4.3%) and Belgium (5.6%) for ages 5–9.

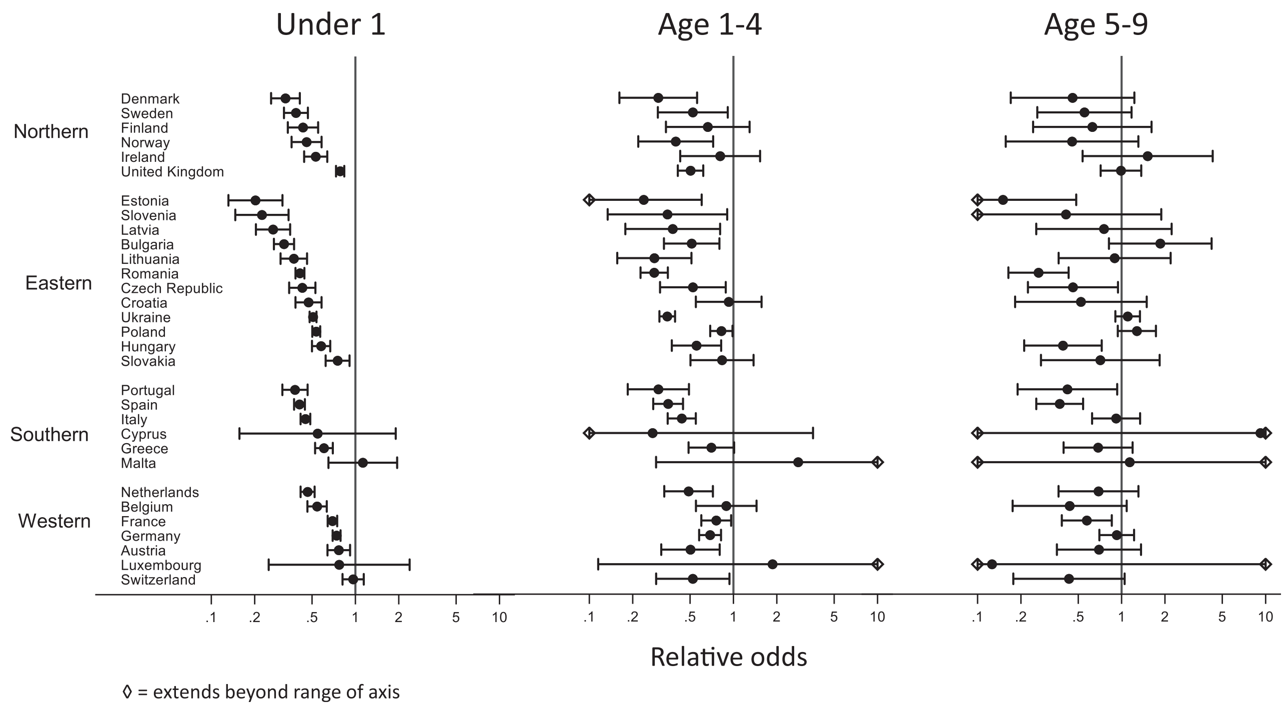

FIGURE 3 Relative odds of congenital anomaly death in 2015 compared with 2000 (95% CI) for ages under 1 year, 1–4 years, and 5–9 years

4 | DISCUSSION

This study shows that from 2000 to 2015 in Europe there was a decrease in all-cause mortality in infants and children up to age 9 by an average of 46% (95% CI: 41–50%), 52% (95% CI: 47–56%), and 47% (95% CI: 44–51%) for under 1, age 1–4 and age 5–9, respectively. Furthermore, deaths from congenital anomalies also significantly decreased by similar amounts; an average of 51% (95% CI: 45–56%), 49% (95% CI: 40–56%), and 35% (95% CI: 20–47%) for under 1, age 1–4 and age 5–9, respectively. The proportion of deaths due to a congenital anomaly, therefore, remained relatively constant over the time period at around 28% of infant deaths due to congenital anomalies, 17% of deaths ages 1–4 and 10% of deaths for children aged 5–9. However, there was significant heterogeneity in mortality rates across Europe, where countries from Eastern Europe had the highest mortality rates, but also experienced the greatest both absolute and proportional reductions in mortality.

Our findings of a 46% (95% CI: 41–50%) decrease in infant mortality over 16 years (2000–2015) is in line with Onambele et al. (2019) findings of a − 3.8% annual change in infant mortality in the EU from 1994 to 2015, using data from the Eurostat database, furthermore supported by their findings of higher mortality rates in Eastern Europe and lower in Scandinavian countries (Onambele et al., 2019).

There are many possible reasons for the decline in all-cause mortality, many linked to increases in socio-economic status (Sartorius & Sartorius, 2014) as it can be seen that where income is lower, infant health is lower and mortality is higher (Spencer, 2004). A measure of income can be disposable income; Northern and Western Europe had more disposable income in 2016 compared with Eastern and Southern Europe (Eurostat, 2018) helping to explain the heterogeneity in mortality seen. Furthermore, there was great economic growth in the majority of Europe from 2003 to 2015 (Darvas, Mazza, & Midoes, 2019) which could partly explain the decrease in mortality rate. However, Greece suffered an economic crisis which caused them to decrease their public health spending to less than any other pre-2004 EU member (Kentikelenis, Karanikolos, Reeves, McKee, & Stuckler, 2014), which many have contributed to increasing mortality and might explain their insignificant decrease in death rate for age 1–4. Another factor in reducing infant and childhood mortality is vaccines where a complete set of vaccines can reduce relative risk of mortality by 27% in children (McGovern & Canning, 2015). This combined with Eastern Europe having lower vaccination rates with the lowest vaccine coverage rate in Europe of 89.1% for infant DTP in Romania compared with Northern Europe where Finland and Sweden had the highest rate of 98.2% (Sheikh et al., 2018) would explain the heterogeneity in mortality.

It has been shown that a lower perinatal mortality rate in children with congenital anomalies is associated with higher levels of TOPFA (termination of pregnancy for fetal anomalies) (Best et al., 2020). This may explain the much higher percentages of deaths from congenital anomalies, over 40% for infants, in Ireland and Malta compared with other countries as TOPFA was illegal in these countries, whereas in all the other countries such terminations do occur (Boyle et al., 2018).

Almli et al. (2020) found a 10% decrease in infant deaths from congenital anomalies from 2003 to 2017 in the United States (Almli et al., 2020), compared with our observed decrease in Europe of 51% over a similar time frame. However, there is considerable heterogeneity between countries, with 10% not incomparable to some European countries. In earlier studies Powell-Griner(1990) found the infant mortality rate from congenital anomalies declined by 30% in the United States, 19% in Sweden, 37% in Scotland, and 34% in England and Wales from the years 1976 to 1985 (Powell-Griner & Woolbright, 1990). However, Dastgiri et al. (2003) found no significant difference in survival rates of those born with congenital anomalies over a slightly later time period from 1980 to 1997 (Dastgiri et al., 2003) in Glasgow, UK. Tennant et al. (2010) observed an annual 8% decrease in mortality from 1985 to 2003 in Northern England. However, once the occurrence of terminations for fetal anomalies was adjusted for, the decrease was reduced to 5% per annum. These decreases are of a similar magnitude to those observed here over a later time period.

Part of these decreases may be explained by the increasing prevalence of prenatal screening and the subsequent termination of pregnancies for fetal anomalies (Liu et al., 2002; Loane et al., 2013; Richmond & Atkins, 2005; Wyldes & Tonks, 2007) with many of those terminations occurring in fetuses with lethal anomalies. However, the birth prevalence of congenital anomalies has remained relatively stable (Loane et al., 2013; Taruscio et al., 2014) and in addition reductions in mortality have also been seen in countries in which terminations for fetal anomalies are illegal, such as Malta and Ireland. This suggests that TOPFA is not the only reason for the reduction in deaths from congenital anomalies.

The strength of this study is that the analysis is based upon a very large data set from WHO covering a large geographical region, derived from official death notifications. By comparing the WHO data set to EUROCAT data for similar regions, Boyle did find all-cause and congenital deaths of infant to be reasonably complete (Boyle et al., 2018) but there were countries (e.g., Finland) where data for congenital anomaly deaths from European Congenital Anomaly registries was 29% higher than the WHO estimates (Boyle et al., 2018). This is likely to occur when congenital anomalies had not been given as the primary cause of death on death certificates.

The weakness of this study is as mentioned above where the presence of a congenital anomaly could have contributed to the death but if they were not the underlying cause then the death would not have been counted as a congenital anomaly death. In addition, the data analyses all congenital anomalies and differences may occur over time in the classification and recording of minor anomalies. All the data analyzed is secondary data so data collection methods are unknown as well is their accuracy and there is a small amount of missing data for some countries. As the number of live births and stillbirths from congenital anomalies was not known, a full analysis of survival from congenital anomalies could not be completed and the effect of terminations could not be evaluated. It would have been informative to have been able to examine the mortality for specific congenital anomalies, as the anomalies are extremely heterogeneous. However, such data were not available.

This study has used routine data to demonstrate that the mortality from congenital anomalies decreased across Europe from 2000 to 2015 and that differences between countries (particularly those in Eastern Europe) decreased. The improvements in survival in children with congenital anomalies were very similar to those observed in all children, resulting in the proportions of deaths due to congenital anomalies to remain relatively constant.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the WHO database on cause of death (https://apps.who.int/healthinfo/statistics/mortality/causeofdeath_query/start.php).

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