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Trends in stomach cancer mortality in relation to living conditions in childhood. A study among cohorts born between 1860 and 1939 in seven European countries

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ABSTRACT

Aim: To assess whether secular trends in stomach cancer mortality were correlated with trends in infant mortality rate (IMR) or gross domestic product (GDP).

Methods: Data from seven European countries were analyzed. We used Poisson regression to describe mortality trends among birth cohorts of 1865–1939 and correlation coefficients to determine associations with IMR/GDP.

Results: Large differences were observed between birth cohorts in mortality from stomach cancer. In each country, these cohort differences were closely related to IMR/GDP levels at birth time. However, stronger associations were observed with measures of living conditions during later life. In comparisons between countries, stomach cancer mortality rates were not consistently related to national levels of IMR/GDP.

Conclusion: General living conditions in childhood do not seem to have had a predominant effect on secular trends in stomach cancer mortality. The mortality decline is likely to be related to more 1specific factors, such as declining *Helicobacter pylori* prevalence.

1. Introduction

In spite of declining incidence rates worldwide, stomach cancer is the second most important cause of death from cancer.[1] Previous studies confirm the importance of 'environment' in early life in determining the risk for stomach cancer.[1,2] Furthermore, a number of studies have shown a strong geographical correlation between mortality from stomach cancer in adulthood and infant mortality around the time of birth.[3,4] Also, mortality from stomach cancer showed consistent inverse socio-economic gradients and an association with socio-economic circumstances in childhood.[5]

Time trends of stomach cancer differ between populations and the role of living conditions on trends is not yet fully understood.[6] To our knowledge, no study on trends in stomach cancer focused on birth cohorts and looked at measures of their association with living conditions in early life.

To provide new evidence on the role of living conditions in early childhood on trends in stomach cancer mortality, we conducted a population-based time-series study. The main hypothesis of our study was that living conditions in childhood are associated with trends in stomach cancer mortality in national populations. We used data on stomach cancer mortality and population at risk for seven low-mortality European countries. Using these data, we tested four specific research hypotheses: (1) Trends in mortality from stomach cancer follow a cohort pattern, with lower mortality among younger cohorts. (2) Cohort trends in stomach cancer mortality correspond closely to cohort trends in living conditions in childhood. (3) For each cohort, differences between countries

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in stomach cancer mortality are closely correlated to differences in living conditions in childhood. (4) Stomach cancer mortality trends are associated with trends in living conditions in childhood rather than with trends in living conditions in adult life.

2. Materials and methods

We obtained data on stomach cancer mortality and population at risk, by year of death (1950–1999), sex, and five-year age groups for seven low-mortality European countries, i.e. Denmark, England and Wales, Finland, France, the Netherlands, Norway, and Sweden. For Denmark, Finland and Norway, data were available from 1951, and for Sweden from 1952. Data for France were available until 1997 and data for Denmark until 1998. The data were obtained from national statistical offices and related institutes. Compared to the mortality information available in the WHO Mortality Bank (http://www.euro.who.int/InformationSources/Data/20050117_1), our data went further back in time, and made a more detailed distinction among upper age groups, which is essential for the study of mortality by birth cohort. For stomach cancer, we included code 151 for revisions 6, 7, 8, and 9 of the International Classification of Diseases (ICD), and code C16 for ICD-10.[7]

Data on infant mortality rates (IMRs), defined as the number of deaths during the first year of life per 1000 live-born babies, for the period 1860–1969, were obtained from international compilations,[8] and for Finland from a national publication.[9] To reconstruct trends in real national gross domestic product (GDP), i.e. GDP expressed at constant 1995 prices in millions of national currency units, between 1865 and 1939, we used the historical national accounts data by Mitchell.[10] For the Netherlands, these historical data were available only from 1900 onwards, and for the earlier years, national accounts data from Statistics Netherlands were used (see Smits et al., 2000).[11] Further details on the reconstruction of the time series for GDP are given elsewhere.[12]

In order to describe mortality differences between birth cohorts, we analyzed the mortality data by means of a log-linear regression analysis (Poisson regression). The dependent variable was the number of deaths, with the person-years at risk as offset variable. As independent variables, we included age and cohort (one-year intervals in Table 1, and five-year intervals in Tables 2–4). In Tables 2–4, we expressed mortality

Table 1 – Annual change in mortality from stomach cancer in birth cohorts born between 1860 and 1939 in seven European countries, by country, 20-year cohort group and sex

Country	Cohort	Annual change in mortality (%)		
		Male	Female	Total
Denmark	1860–1879	−2.49*	−4.18*	−3.60*
	1880–1899	−3.90*	−5.64*	−4.85*
	1900–1919	−4.65*	−4.72*	−4.59*
	1920–1939	−2.83*	−1.92*	−2.51*
England and Wales	1860–1879	−0.16	−1.39*	−1.38*
	1880–1899	−1.11*	−2.73*	−1.94*
	1900–1919	−2.85*	−3.70*	−2.91*
	1920–1939	−4.71*	−4.39*	−4.59*
Finland	1860–1879	+0.88	−0.71	−0.43
	1880–1899	−3.75*	−5.00*	−4.70*
	1900–1919	−5.36*	−5.40*	−5.34*
	1920–1939	−4.98*	−3.86*	−4.36*
France	1860–1879	+1.10*	+0.67*	+0.46*
	1880–1899	−2.69*	−3.72*	−3.18*
	1900–1919	−4.08*	−5.28*	−4.33*
	1920–1939	−3.43*	−3.82*	−3.49*
Netherlands	1860–1879	−1.43*	−2.10*	−1.92*
	1880–1899	−1.74*	−3.33*	−2.72*
	1900–1919	−1.47*	−2.97*	−1.97*
	1920–1939	−1.89*	−1.39*	−1.55*
Norway	1860–1879	−2.46*	−4.15*	−3.56*
	1880–1899	−3.06*	−4.28*	−3.71*
	1900–1919	−3.77*	−4.11*	−3.84*
	1920–1939	−4.04*	−3.57*	−3.83*
Sweden	1860–1879	−0.90	−2.73*	−2.11*
	1880–1899	−3.59*	−4.98*	−4.31*
	1900–1919	−4.19*	−4.38*	−4.19*
	1920–1939	−4.12*	−3.08*	−3.76*

* Trends different from 0 with statistical significance ($p < 0.01$).

Table 2 – Correlation between stomach cancer mortality and indicators of living conditions at the time of birth, among 16 cohorts (born between 1860 and 1939 and followed for mortality in 1950–1999), per country and sex

Country	Sex	Pearson correlation coefficient (95% CI)	
		With IMR	With GDP
Denmark	Total	0.74 (0.39, 0.91)	−0.83 (−0.94, −0.58)
	Male	0.81 (0.53, 0.93)	−0.88 (−0.96, −0.68)
	Female	0.70 (0.32, 0.89)	−0.80 (−0.93, −0.51)
England and Wales	Total	0.89 (0.71, 0.96)	−0.97 (−0.99, −0.90)
	Male	0.96 (0.88, 0.99)	−0.99 (−1.00, −0.84)
	Female	0.86 (0.63, 0.95)	−0.94 (−0.98, −0.84)
Finland	Total	0.81 (0.51, 0.94)	−0.98 (−0.99, −0.94)
	Male	0.77 (0.44, 0.92)	−0.97 (−0.99, −0.92)
	Female	0.83 (0.56, 0.94)	−0.98 (−0.99, −0.93)
France	Total	0.92 (0.79, 0.97)	−0.93 (−0.97, −0.80)
	Male	0.93 (0.81, 0.98)	−0.94 (−0.98, −0.83)
	Female	0.91 (0.77, 0.97)	−0.92 (−0.97, −0.77)
Netherlands	Total	0.91 (0.74, 0.97)	−0.86 (−0.95, −0.62)
	Male	0.94 (0.82, 0.98)	−0.90 (−0.96, −0.73)
	Female	0.89 (0.71, 0.96)	−0.84 (−0.94, −0.58)
Norway	Total	0.87 (0.66, 0.95)	−0.84 (−0.94, −0.58)
	Male	0.90 (0.74, 0.97)	−0.88 (−0.96, −0.68)
	Female	0.85 (0.62, 0.95)	−0.81 (−0.93, −0.52)
Sweden	Total	0.96 (0.90, 0.99)	−0.90 (−0.96, −0.73)
	Male	0.98 (0.94, 0.99)	−0.94 (−0.98, −0.82)
	Female	0.94 (0.84, 0.98)	−0.87 (−0.95, −0.65)
All countries	Total	0.71 (0.34, 0.89)	−0.63 (−0.86, −0.20)
	Male	0.74 (0.38, 0.90)	−0.65 (−0.87, −0.23)
	Female	0.70 (0.32, 0.89)	−0.62 (−0.85, −0.18)

CI, confidence interval.

Table 3 – Correlation between stomach cancer mortality and indicators of living conditions at the time of birth, among seven European countries, per birth cohort (followed for mortality in 1950–1999), men and women combined

Birth cohort	Pearson correlation coefficient (95% CI)	
	With IMR	With GDP
1860–1864	−0.55 (−0.82, −0.08)	[a]
1865–1869	−0.46 (−0.78, 0.05)	−0.26 (−0.67, 0.27)
1870–1874	−0.29 (−0.70, 0.24)	−0.02 (−0.53, 0.48)
1875–1879	0.04 (−0.47, 0.52)	−0.23 (−0.65, 0.30)
1880–1884	0.53 (0.04, 0.81)	−0.44 (−0.77, 0.07)
1885–1889	0.40 (−0.11, 0.75)	−0.40 (−0.75, 0.12)
1890–1894	0.39 (−0.13, 0.74)	−0.31 (−0.70, 0.22)
1895–1899	0.35 (−0.18, 0.72)	−0.33 (−0.71, 0.19)
1900–1904	0.49 (−0.01, 0.79)	−0.17 (−0.62, 0.35)
1905–1909	0.46 (−0.04, 0.78)	−0.17 (−0.62, 0.35)
1910–1914	0.55 (0.08, 0.82)	−0.17 (−0.61, 0.36)
1915–1919	0.54 (0.06, 0.82)	0.06 (−0.45, 0.54)
1920–1924	0.40 (−0.12, 0.75)	−0.29 (−0.69, 0.24)
1925–1929	0.36 (−0.17, 0.72)	−0.29 (−0.68, 0.24)
1930–1934	0.35 (−0.18, 0.72)	−0.33 (−0.71, 0.19)
1935–1939	0.53 (0.04, 0.81)	−0.34 (−0.72, 0.19)

CI, confidence interval.
a Data for GDP were not available for all countries.

rates of each five-year birth cohort relative to the mortality rates of the birth cohort 1900–1904, thus enabling comparisons of the mortality rates between different cohorts. These relative cohort mortality measures were derived from the parameter estimates of the cohort variable in the regression analysis.

In these cohort analyses, control was made for age only. In additional analyses, we checked whether similar patterns would be observed when also controlling for the ‘drift’, the common linear trend, and non-linear period effects.[13,14] These additional analyses showed basically the same patterns of cohort differences in mortality as those shown below.

Pearson correlation coefficients were calculated in order to quantify associations between cohort-specific mortality rates and the level of infant mortality rate or GDP of each birth cohort. These correlations were estimated by comparing cohorts within countries. In addition, a pooled analysis was carried out by combining together all birth cohorts for all countries. We restricted all analyses to cohorts born between 1860 and 1939, thus excluding birth cohorts with too few deaths during the observation period. Additional analyses, with further restriction to birth cohorts born between 1865 and 1924 showed similar results as those reported below. We used SPSS for Windows (10.1) package, Excel for Windows, and SAS 8.0.

3. Results

Mortality of stomach cancer decreased over the successive cohorts from 1860 to 1939 (Table 1 and Fig. 1). For Finnish men, and in France, however, the decline started later, i.e. from birth cohorts 1880 onwards. The decline in stomach cancer over successive cohorts is generally stronger among women than among men.

Table 4 – Correlation between stomach cancer mortality and indicators of living conditions at different ages, among seven countries and 16 cohorts (born between 1860 and 1939 and followed for mortality in 1950–1999), per sex

Age[a]	Sex	Pearson correlation coefficient (95% CI)	
		With IMR	With GDP
0–4	Total	0.71 (0.34, 0.89)	−0.63 (−0.86, −0.20)
	Male	0.74 (0.38, 0.90)	−0.65 (−0.87, −0.23)
	Female	0.70 (0.32, 0.89)	−0.62 (−0.85, −0.18)
5–14	Total	0.77 (0.44, 0.92)	−0.66 (−0.87, −0.24)
	Male	0.79 (0.48, 0.92)	−0.68 (−0.88, −0.28)
	Female	0.76 (0.42, 0.91)	−0.64 (−0.86, −0.22)
15–24	Total	0.81 (0.53, 0.93)	−0.73 (−0.90, −0.36)
	Male	0.82 (0.54, 0.93)	−0.75 (−0.91, −0.41)
	Female	0.81 (0.52, 0.93)	−0.71 (−0.89, −0.32)
25–34	Total	0.84 (0.59, 0.94)	−0.76 (−0.91, −0.43)
	Male	0.84 (0.58, 0.94)	−0.79 (−0.93, −0.49)
	Female	0.84 (0.59, 0.94)	−0.74 (−0.90, −0.39)
35–44	Total	0.85 (0.62, 0.95)	−0.77 (−0.91, −0.44)
	Male	0.84 (0.59, 0.94)	−0.80 (−0.93, −0.51)
	Female	0.85 (0.62, 0.95)	−0.74 (−0.90, −0.39)
45–54	Total	0.85 (0.61, 0.95)	−0.81 (−0.93, −0.52)
	Male	0.83 (0.58, 0.94)	−0.85 (−0.95, −0.60)
	Female	0.85 (0.61, 0.95)	−0.78 (−0.92, −0.47)
55–64	Total	0.83 (0.56, 0.94)	−0.86 (−0.95, −0.63)
	Male	0.81 (0.52, 0.93)	−0.89 (−0.96, −0.71)
	Female	0.84 (0.58, 0.94)	−0.83 (−0.94, −0.58)
65+	Total	0.81 (0.53, 0.93)	−0.90 (−0.96, −0.72)
	Male	0.78 (0.46, 0.92)	−0.92 (−0.97, −0.79)
	Female	0.83 (0.56, 0.94)	−0.88 (−0.96, −0.68)

CI, confidence interval.
a The age group for which the living conditions of a cohort were measured. E.g. for age group 0–4 years, we measured the IMR and GDP of the period that the majority of the birth cohort was 0–4 years old.

Fig. 2 shows the trends in infant mortality (IMR) by five-year periods. The patterns were varied until about 1895. From 1895 onwards, a general decline in IMR emerged. In comparison with the mortality trends for stomach cancer, the declining trends in IMR are sharper and more stable.

Fig. 3 presents the trends in GDP at birth by five-year periods. An overall increase in GDP at birth can be observed for all countries. During 1915–1919, a decline in GDP at birth occurred, except for England and Wales. The increasing trends for GDP at birth were, however, not simultaneous to the declining mortality trends for stomach cancer. Moreover, irregularities in trends in GDP and stomach cancer mortality did not coincide.

Table 2 shows the correlation coefficients comparing the levels of IMR and GDP at birth with mortality from stomach cancer at adult age for the same cohorts. There was a significant strong positive association (correlation coefficients ranging from 0.70 to 0.98) between stomach cancer and IMR in all countries. The association between stomach cancer mortality and GDP at birth was strongly negative, with correlation coefficients ranging from −0.98 to −0.80. When the

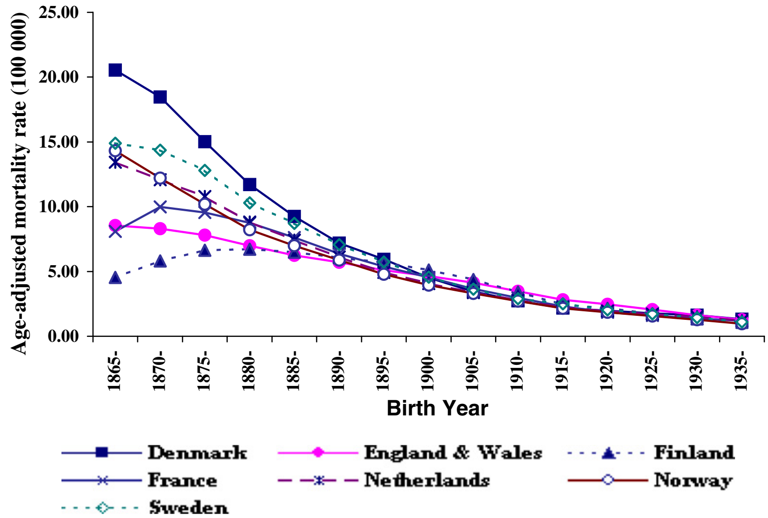

Fig. 1 – Trends in stomach cancer mortality for five-year cohorts born between 1865 and 1939 followed for mortality in 1950–1999 in seven European countries.

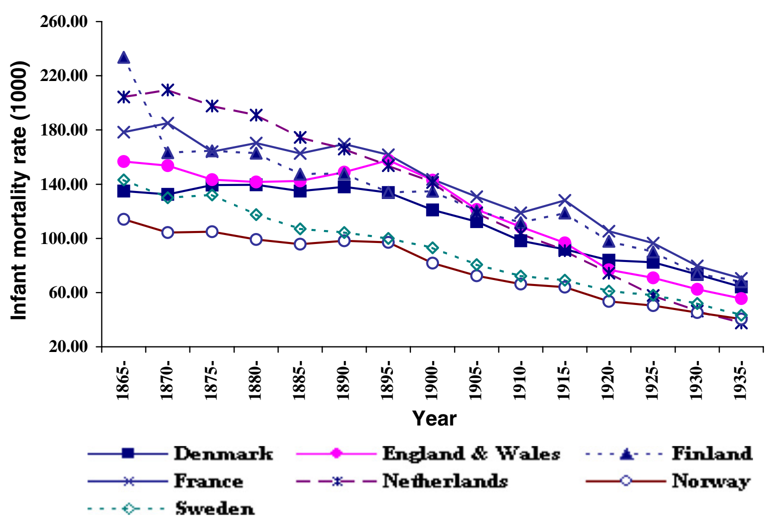

Fig. 2 – Trends in infant mortality rate between 1865 and 1939 in seven European countries.

different countries are pooled, the overall correlation was positive for IMR (0.71) and negative for GDP at birth (−0.63). The correlation coefficients were generally higher among men than among women.

In Table 3, correlations across countries between stomach cancer mortality and IMR and GDP at birth are calculated for each five-year birth cohort separately. The relationship between stomach cancer mortality and IMR was positive for cohorts born after 1875 (correlation coefficients ranging from 0.04 to 0.55), and negative for cohorts born before (correlation coefficients ranging from −0.55 to −0.29). The association between stomach cancer mortality and GDP at birth was in general negative but variable for the different birth cohorts (correlation coefficients ranging from −0.44 to 0.06).

Table 4 shows the correlation coefficients between stomach cancer and IMR and GDP at birth from the pooled analysis. In this table, IMR and GDP are not only measured for the time of birth of each cohort, but also for older ages of the cohorts. There was a significant strong positive association between stomach cancer and infant mortality rate as measured for different ages of the cohorts (correlation coefficients ranging from 0.70 to 0.85). The associations were stronger with the IMR that applied to the time that a cohort was relatively old. There was a strong negative association between stomach cancer mortality and GDP at different ages of the cohort (correlation coefficients ranging from −0.92 to −0.62). The associations were stronger for GDP measured at the older ages.

4. Discussion

In this study, the well-known cohort-wise decline in stomach cancer in seven European countries has been confirmed. For each sex and country, we observed large differences between cohorts in mortality rates from stomach cancer. These differences were closely related to levels of IMR and GDP at the time

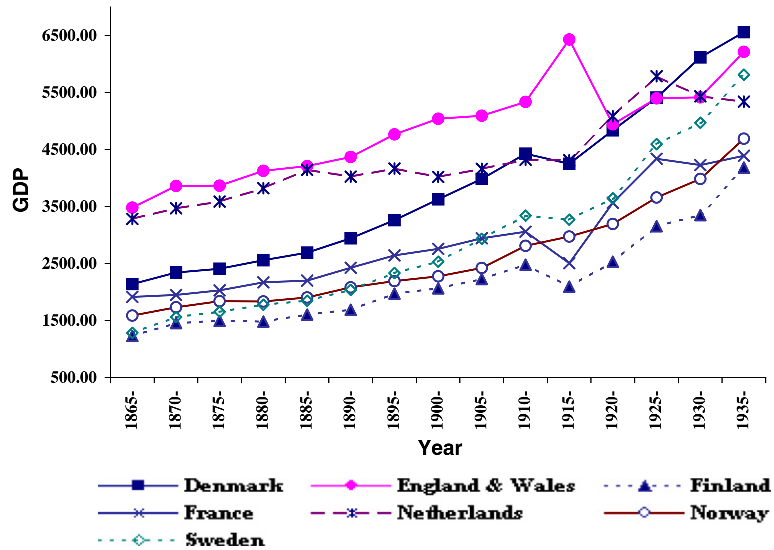

Fig. 3 – Trends in real GDP per capita at 1995 US Dollars (adjusted by means of the purchasing power parities of 1995) between 1865 and 1939 in seven European countries.

of birth. Strong correlations between mortality trends and IMR and GDP were observed for each sex and country.

However, part of our additional findings do not support our basic hypothesis that improvements in general living conditions in childhood had driven the secular decline in stomach cancer mortality in western European countries. First, stronger associations were observed with measures of living conditions during later phases of life instead of early life. Second, past irregularities in trends in living conditions (which reflect important historical phenomena such as deep economic crises) were not associated with similar irregularities in trends in stomach cancer mortality in later life. Finally, in comparisons between countries (instead of between birth cohorts), we did not observe a consistent association between stomach cancer mortality rates and national levels of IMR or GDP.

4.1. *Evaluation of data and methods*

The mortality and population data used in this study come from data sources that are known to have good quality.[15–17] Any problems with the coverage or completeness of death registries or population registries are likely to have no or minimal effects on our results.

We should stress that our objectives, empirical analyses, and inferences all refer to the same level of analyses, i.e. national populations. In this type of analysis, there is a risk of ecological fallacy[18] but this fallacy will only be committed if inferences towards the individual level would be made. We refrain from making such inferences and we warn that trends in stomach cancer mortality at the national level may strongly be influenced by factors that are not necessarily the most important determinants of stomach cancer at the individual level.

The outcome measures in our study were rates of stomach cancer according to birth cohort and country. Differences in mortality rates by place and over time are the result of a complex interplay of many factors. In our analysis of associations with IMR and GDP, we were not able to control for potential confounders. For example, the inverse (instead of positive) correlations of stomach cancer mortality with IMR and GDP in the cross-national analyses might have been confounded by cross-national differences in factors such as modern diet and health care services. Given this potential for confounding, the correlations observed in this study should be regarded with caution.

In our analysis, the IMR and GDP were used as indicators of general conditions of living in different periods. These two indicators were used because of the availability and comparability of data for seven European countries over a long period of time. For a possible alternative indicator, body length, continuous historical time series were only available for four countries.[19] It should be acknowledged that both IMR and GDP are only approximate indicators of the concept of ‘general living conditions’. None the less, the IMR is one of the most important indicators of social development. Reidpath concluded that the IMR is an important indicator of health for whole populations, as structural factors affecting the health of entire populations also have an impact on the mortality rate of infants.[20] The correspondence between the findings for IMR and those for GDP lends support to our general conclusion that improvements in general living conditions in childhood are not strongly related to the secular decline in stomach cancer mortality in western European countries.

4.2. *Interpretation*

Our findings of declining patterns of stomach cancer correspond well with the results of previous studies.[1–4,21] Differences between birth cohorts in rates of mortality from stomach cancer were also observed in studies that controlled for period effects.[7,22]

The relation between adverse childhood social circumstances and higher adulthood mortality risk has been demonstrated in several studies.[2,21,23] Individual-level studies showed that childhood socioeconomic position influences stomach cancer mortality in later life.[24] The association between childhood social circumstances and mortality probably comes about through a variety of processes.[25] Migrant studies also suggest the importance of environment in early life in determining the risk of stomach cancer.[1]

The etiology of stomach cancer is linked to environmental factors, including nutrition in childhood (e.g. salt consumption, vitamin C intake),[26] *Helicobacter pylori* infection,[1,27] and interaction between these factors.[28] Infection with *H. pylori* during infancy and childhood offers a plausible mechanism to explain the association between poor childhood circumstances and stomach cancer.[29] Favourable developments in childhood nutrition might have contributed to the secular decline in stomach cancer mortality.

It is important to recognize that our measures of general living conditions in childhood (IMR and GDP) cannot measure in detail all specific elements that may be relevant for stomach cancer. In case of *H. pylori*, we would need to acquire data on the prevalence of *H. pylori* infection in childhood in the different birth cohorts. These data were not available for any of the countries considered. Accepting that past trends in stomach cancer mortality may be strongly determined by past trends in the incidence of *H. pylori* infection, our results suggest that the latter trends are not closely correlated with past trends in IMR and GDP.

Some of our results suggest that secular trends in stomach cancer are largely determined by changes in adult socioeconomic circumstances and lifestyles, rather than childhood.[30] For example, the marked cohort pattern of stomach cancer mortality, which peaked among birth cohorts born around 1875, might be determined by cohort-specific trends in smoking, alcohol consumption and other factors related to later phases of the life course. Similarly, improvements during the 20th century in the environment and nutrition may have resulted in a gradually lower incidence of stomach cancer, while more accessible and effective facilities for cancer therapy may have helped to reduce its case fatality.[30]

As a conclusion, our results do not provide sufficient support for our main hypothesis that living conditions in childhood have a predominant effect on secular trends in stomach cancer mortality in national populations. Trends in stomach cancer mortality follow a cohort pattern, but this pattern is not consistently related to indicators of general living conditions in childhood. Trends in stomach cancer mortality seem to be determined by a set of more specific determinants that might operate in adult life as well as early life. Future studies should determine the contribution of more specific factors, such as *H. pylori* infection, instead of general living conditions in early life.

Conflict of interest statement

None declared.

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