

Educational inequalities in tuberculosis mortality in 16 European populations

Running title

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Abstract

Objective: We aim to describe the magnitude of socioeconomic inequalities in tuberculosis (TB) mortality by level of education in male, female, urban, and rural populations in several European countries.

Design: Data were obtained from the Eurothine project covering 16 populations between 1990 and 2003. Age- and sex-standardized mortality rates, the Relative Index of Inequality, and the slope index of inequality were used to assess educational inequalities.

Results: The number of TB deaths reported was 8530, with a death rate of 3 per 100 000 per year, of which 73% were males. Educational inequalities in TB mortality were present in all European populations. Inequalities in TB mortality were larger than in total mortality. Relative and absolute inequalities were large in Eastern Europe, and Baltic countries but relatively small in Southern countries and in Norway, Finland, and Sweden. Mortality inequalities were observed among both men and women, and in both rural and urban populations.

Conclusions: Socioeconomic inequalities in TB mortality exist in all European countries. Firm political commitment is required to reduce inequalities in the social determinants of TB incidence. Targeted public health measures are called for to improve vulnerable groups' access to treatment and thereby reduce TB mortality.

Introduction

Tuberculosis (TB) has deep social and economic roots:¹ it is widespread; currently one-third of the global population is infected;² and although treatment of TB is feasible and effective, active TB is lethal in more than 50% of cases when left untreated.³ In 2004, TB mortality accounted for 1.6 million deaths, mostly in developing countries.² Although the disease appeared to have been controlled by the 1980s, TB incidence started to increase again in industrialized countries around 1985.⁴ Several interrelated forces drove this resurgence, including increases in prison populations, homelessness, intravenous drug use, and immigration from countries where TB continued to be endemic. Above all, the decline in TB control activities and the human immunodeficiency virus (HIV) epidemic were two major factors that worked together to fuel the re-emergence of TB.⁵

Increasing TB incidence rates in the 1990s were reported in the former Soviet Union, former Yugoslavia, and some other countries in Eastern Europe. The lowest incidence in Europe is found in Southern countries and Scandinavia.⁶ Increased unemployment, homelessness, alcoholism, HIV transmission, and drug resistance, boost the incidence of TB.^{7,8}

Socioeconomic inequalities in mortality are omnipresent in Europe. People living in disadvantaged circumstances are known to have poorer health, more disability, and shorter lives than those who are more affluent.^{9,10} The association between economic deprivation and TB is well established and widespread.¹¹⁻¹³ In our study we chose education as the indicator of socioeconomic position because of data availability. The widening gap between the health of lower and higher socioeconomic groups has contributed to an increased awareness of health inequalities by governments and policymakers.¹⁴ Socioeconomic inequalities have widened in Eastern Europe in particular¹⁵.

The objective of this study was to estimate the magnitude of educational inequalities in TB mortality in different European countries with data from 1990 to 2003, and to investigate whether inequalities differ among urban and rural populations.

Material and methods

Data and population

This epidemiological study used the Eurothine project mortality data¹⁶ which is a collection of datasets with information on cause-specific mortality by socioeconomic position among people older than 30 years of age in several European countries. Mortality data from populations with information about TB and educational inequalities were obtained for this study (Table 1). All data covered entire national populations with the exceptions of Italy and Spain.

Information on mortality included a total of 3.5 million deaths among more than 51 million European citizens from 16 populations between 1990 and 2003. Mortality data came from cross-sectional unlinked mortality studies, in which information on socioeconomic data was derived separately from death certificates and census records or from longitudinal follow-up studies in which socioeconomic position, as determined during a census, has been linked to mortality. The analysis of data from longitudinal studies with about 10 years of follow-up was performed among people aged 30 to 74 years at baseline. Since the designs are different among countries, to approximate all populations in terms of average age at death, we performed our analysis on slightly older age groups (35-79 years) for all studies with cross-sectional design and for very short follow-up longitudinal studies; for longitudinal studies with a 5-year follow up period we chose people aged 30 to 79 years.

Cause of death was classified using the International Classification of Diseases. Most countries used the 9th version until 1996 and used the 10th version thereafter; exceptions are the following; Slovenia used the 9th version until 1997; the Spanish regions until 1999; Turin until 2001; and Switzerland, which used the 8th version until 1995 and the 10th version thereafter. All deaths reported as TB from any location (ICD 8 CM 10-18; ICD 9 CM 010-018, 137; ICD 10 CM A15-19, B90) in this database were obtained.

We used the highest acquired educational level as a measure of socioeconomic position. Education was categorized into four classes corresponding to the International

Standard Classification of Education (ISCED):¹⁷ (1) no education or primary education, (2) lower secondary education, (3) upper secondary education, and (4) post-secondary and tertiary education. Information on education was missing for 1.2% of the population, on average; these subjects were excluded from the analysis.

The place of residence measures the degree of urbanization of the residence area of the study population. It is based on country-specific measures of urbanization, such as the population size or the population density of the municipality where persons live. Information for this variable was only available for seven countries.

The linkage between census data and mortality registries was achieved for more than 96% of all deceased persons in all populations except Madrid (70%), the Basque Country (93%), and Barcelona (94.5%). Evaluations in Madrid and Barcelona observed no variation in this percentage according to age, sex, or educational position. Therefore, estimates of relative inequalities in mortality are not likely to be biased to a significant extent. In addition, we adjusted the estimates of absolute mortality rates by increasing these with correction factors (1/0.70, 1/0.93, and 1/0.945 respectively).

Data Analysis

We calculated absolute and relative levels of educational inequality using age- and sex-standardized mortality rates (ASMR) and the relative index of inequality (RII), respectively. We computed ASMR using the direct method with 5 years age groups, using the total population from all countries as a standard. The two lowest and two highest categories were combined together, respectively, into two broad groups to obtain stable ASMR estimates.

To estimate the extent of inequalities separately across all four educational levels, we computed the RII, a regression-based measure that takes into account the relative position of each educational group within the hierarchy of all educational groups before it is related to health indicators by means of regression. The RII results in a ratio that can be described as mortality at the very bottom of the educational hierarchy compared to the very top of the hierarchy. A high score on the RII implies large inequalities in mortality across the educational hierarchy. One advantage of this index is

that it can be applied comparably to all countries, provided that the educational classification is strictly hierarchical. For this paper, the RII was estimated using log linear regression with control for 5-year age group and gender. The regression model had a log link function and assumed a Poisson error distribution.

In addition to the relative measure of RII, we computed the SII (slope index of inequality), which is a measure of absolute difference between the predicted mortality rates at the lower end of the hierarchy and at the higher end of the hierarchy. The SII was derived from the RII and the mortality rate (MR) by the following formula:¹⁸

$$SII = 2 \times MR \times \frac{RII - 1}{RII + 1}$$

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS for Windows, version 16.0; Chicago, Illinois, USA). In all tests, the significance level used was $p < 0.05$.

Results

The mean average age of all people in our study was 51 years and 47% (24 million) of the people in our study were male. A total of 8530 deaths due to TB were reported, resulting in a global rate of 3 deaths per 100,000 annually (Table 1). The average age of TB death was 61 years (SD 17.6). The TB death rate increased with age for every country (Figure 1), ranging from 0.2 deaths due to TB per 100,000 in the population between 30 and 34 years of age to 10.9 deaths per 100,000 in the population between 75 and 79 years of age. However, in Estonia and Lithuania rates were generally higher in all age groups, with no clear age-related pattern. In total, 73% of all TB deaths occurred in males.

Relative educational inequalities in TB mortality were present in all European populations included in this study. In all populations, inequalities in TB mortality were larger than in total mortality, although they were not statistically significant in some Nordic and Southern countries (Table 2). The largest relative inequalities were observed

in Eastern European populations, Baltic countries, and Denmark. The smallest differences were found in Nordic countries and in Belgium. In all cases, people with higher levels of education had lower mortality rates. The absolute size of educational inequalities in all TB mortality, as expressed by the SII, was highest in Lithuania (35.8 deaths per 100,000 person-years), followed by Estonia and Hungary (Figure 2). Whereas Denmark had large inequalities in relative sense, absolute differences in this country were small.

Since TB mortality in Baltic countries is greater for younger ages, we analyzed whether the large inequalities in TB mortality in these countries could be observed for both the older and the younger ages: for the youngest (35-49 years old), mortality rates in Estonia and Lithuania were much higher in the low educational level (44 and 73 deaths per 100,000, respectively) than in the high educational level (10 and 9 deaths per 100,000); this difference was smaller in the eldest Estonian and Lithuanian populations (65-79 years old): low educational level, 16 and 22 deaths per 100,000; and high educational level, 10 and 11 deaths per 100,000, respectively.

Some gender differences can be seen when the populations are stratified by gender, except in Hungary and the Czech Republic (Table 3). Overall TB mortality rates were much lower in women. Inequalities shown by the RII were generally higher in men (but not in all countries), although not statistically significant. Actually, mortality among highly educated men is similar to that observed among lower educated women.

In our study, 66% of the people were living in urban areas overall; the proportion of urban-dwelling participants ranged from 72% in Norway to 49% in Slovenia. There were no important differences regarding absolute level of mortality (Table 4). The global ASMR rates were similar between rural and urban populations. Large inequalities according to educational level existed in both in rural and urban areas. We found higher RII in all urban populations except those in Hungary and Slovenia; however, the differences in RII between urban and rural populations were not statistically significant.

Discussion

In total, 8530 TB deaths were reported, with a death rate of 3 per 100,000 per year, of which 73% of decedents were male. Educational inequalities in TB mortality were present in all European populations. Relative and absolute educational inequalities in TB mortality were large in Eastern Europe and Baltic countries but relatively small in Southern countries and in Norway, Finland, and Sweden. The mortality rates were similar in rural and urban populations.

Our study included a broad geographical scope with countries from both Eastern and Western Europe. Although we optimized the comparability of the data from different countries, this comparability might be compromised in several ways. Some data had a cross-sectional unlinked design, while other consisted of census-linked mortality follow-up studies. It has been demonstrated that mortality inequalities based on unlinked mortality data are prone to the numerator-denominator bias. This bias relates to the fact that deaths (the numerator) are classified according to educational information on the death certificates, whereas the population (the denominator) is classified using the educational information from the population census. The educational levels could be reported differently in these two sources.¹⁹ An important mechanism might be ‘promoting the dead’, where surviving relatives describe the educational level of deceased relatives higher than is true.^{20 21} We combined the two lowest educational levels, where this bias is more likely to occur, thereby minimizing possible overestimation of mortality inequalities in Central Eastern and Baltic countries. Although residual bias might have remained, it is unlikely to explain the large inequalities that were consistently observed in most Central Eastern and Baltic countries.

Socioeconomic position, the relative position of a person in society, is determined by the educational level that one has attained usually completed in early adulthood, by the occupation that one holds across adult life, by the income that one earns, and by the wealth that is accumulated over life.²² In this study, we used education as the indicator of socioeconomic position. Information on mortality in relationship to level of education is available for most European countries; which is not the case for other socioeconomic variables. The experience of previous studies suggests that similar

international patterns are likely to be observed when using occupational class. We observed large differences between countries in the distribution of the population by education. These differences may be partly due to real variation in educational attainment in different countries. However, these variations might also be the result of international differences in educational systems, consequently compromising the comparability of educational inequalities between countries. We used the RII as a measure to handle this problem. The RII estimates can be compared across countries, provided that a hierarchical classification of educational levels is available in each country. This problem is therefore partially solved, but does not completely disappear.

Although all data came from populations with reliable cause-of-death registries, causes of death could be coded differently between countries due to variations in national diagnosing practices. This problem would only bias our estimates when coding practices differ between the educational levels of the deceased. There is no evidence to support this possibility, but we cannot completely rule out such a bias. There is a general awareness of underreporting of TB deaths, but it is still necessary to investigate whether these problems are related to the educational level of the deceased.

The high age- and sex-standardized mortality rates and large inequalities in mortality in Estonia and Lithuania could be explained partially by the higher incidence of TB in these countries,^{7,28} which to some extent may be attributed to HIV deaths reported as TB deaths, especially in the younger age groups. There were a large number of TB deaths in the younger age groups of these countries (Figure 1), and the large inequalities are mainly in the younger ages, and not so much in the older age groups. Because the HIV epidemic is a relatively new phenomenon and will only affect the youngest age groups in our study, there may be other explanations affecting inequalities in mortality in Baltic countries, such as alcohol consumption, prevalence of multidrug-resistant TB, and homelessness (extreme poverty). These factors may play a role in other European countries as well, although HIV is likely to be the most important confounder.^{15, 29-31} The relatively large inequalities observed in males in Barcelona could also be due to higher HIV mortality, since the data from Barcelona start in the early 1990s, before antiretroviral therapy was introduced. Multidrug resistance TB is potentially another important confounding factor, but multidrug resistance could well be in the mediation pathway between education and TB mortality since the level of

education can affect, for example, the adherence to medication.³² Unfortunately we do not have information to perform further analysis with confounders.

Despite some limitations, our results show that educational inequalities in TB mortality are present in all European countries. The magnitude of inequality in TB mortality is clearly higher than that reported for other diseases.²³ Inequality in TB mortality is produced by inequalities in both incidence and case fatality. Inequalities in incidence are largely due to differences in nutritional and living conditions (e.g., housing, homelessness, imprisonment, sanitation, poor ventilation and household crowding). Inequalities in case fatality are more dependent on social inequalities in access to health care, treatment, and co-morbidity (e.g., due to HIV, intravenous drug use, and alcohol consumption).²⁴ Although inequalities in incidence may be more fundamental, death from TB can be prevented; anti-TB treatment is both effective and cost-effective. Limited access to health care will lead to delays in initiating anti-TB treatment, as has been observed in health services in several countries, and is amenable to targeted public health policies.²⁵⁻²⁷

Conclusions

We provide evidence of tuberculosis inequalities, and our analysis may be regarded as a first step to lead public health policy makers to those target populations that are vulnerable and help tailor social and health services to these groups. This implies 1) better monitoring of TB inequalities by implementing adequate surveillance systems of socioeconomic indicators, possible confounders and regional differences; 2) better targeting of effective interventions such as Directly Observed Treatment, Short-course (DOTS) to the most vulnerable populations; and 3) engaging more effectively with non-governmental organisations and civic society to better reach disadvantaged populations. Fighting TB is essentially fighting unacceptable socioeconomic inequalities underlying the disease. Cross-sectoral partnerships are essential to reduce health inequalities; a biomedical approach alone will not suffice to deal with this problem. We conclude that socioeconomic inequalities in TB mortality exist in all European countries. Firm political commitment is required to reduce inequalities in the social determinants of incidence of TB, such as poverty and education. Targeted public

health measures are called for to improve the access of vulnerable groups to treatment, thereby reducing TB mortality.

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Ethics and transparency statement

Ethical approval was not required for the study and the authors state that they have no conflict of interest

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Table1: Countries included in the analysis and sources of data.

Region	Area	Type of study	Years Covered	Person-years of follow-up	No. of total deaths	No. of TB deaths	Educational level (% of population in Low Educational group)
Southern	BAR	Longitudinal	1992-2001	8151810	81588	280	73.4
	MDR	Longitudinal	1996-1997	3663333	32269	70	67.0
	BSQ	Longitudinal	1996-2001	6098458	44960	93	72.2
	TUR	Longitudinal	1991-2001	4873109	50621	72	73.5
Nordic	DNK	Longitudinal	1996-2000	14619327	183284	154	51.3
	NRW	Longitudinal	1990-2000	19956767	213022	349	37.0
	FIN	Longitudinal	1990-2000	25874201	270232	746	53.3
	SWE	Longitudinal	1991-2000	43042216	393038	508	41.1
Central Western	SWZ	Longitudinal	1990-2000	27910587	255275	253	29.7
	BEL	Longitudinal	1991-1995	24861015	283349	379	65.9
Central Eastern	HUN	CS unlinked	1999-2002	21031348	368029	1262	64.3
	POL	CS unlinked	2001-2003	54883245	717743	2373	56.9
	SLO	Longitudinal	1991-2000	9647452	101557	215	49.8
	CZR	CS unlinked	1999-2003	25761450	344973	385	63.5
Baltic	EST	CS unlinked	1998-2002	3435255	60873	458	30.1
	LIT	CS unlinked	2000-2002	5156703	78399	933	30.7

^aCS Cross-sectional

Table 2: Age- and sex-standardized mortality rates (deaths per 100 000) and relative index of inequality.

Region	Area	All-cause mortality					Tuberculosis						
		ASMR	ASMR		RII	95% Confidence	ASMR	ASMR		RII	95% Confidence		
		Total	Low education	High education	Interval	Total	Low education	High education	Interval				
Southern	BAR	1011.4	1071.2	840.2	1.61	1.56	1.66	3.8	4.5	2.1	5.23	2.95	9.25
	MDR	868.1	909.9	746.0	1.46	1.39	1.53	1.9	2.1	0.8	3.50	0.99	12.39
	BSQ	742.8	760.6	677.8	1.46	1.38	1.56	1.6	1.7	0.6	5.62	0.90	35.09
	TUR	1110.2	1163.8	928.3	1.50	1.45	1.55	1.5	1.7	0.6	3.69	1.33	10.26
Nordic	DNK	1324.8	1461.9	1111.6	2.14	2.08	2.19	1.1	1.5	0.6	11.26	3.59	35.34
	NRW	1144.1	1348.1	991.4	2.04	2.01	2.08	1.8	2.2	1.5	2.36	1.45	3.82
	FIN	1301.6	1429.4	1058.4	2.08	2.04	2.11	3.7	3.9	3.2	2.08	1.47	2.95
	SWE	939.5	1057.3	809.6	1.61	1.59	1.63	1.2	1.3	1.1	1.37	1.01	1.86
Central	SWZ	1010.4	1242.8	900.2	1.91	1.87	1.94	1.0	1.5	0.8	3.42	2.08	5.63
Western	BEL	1175.3	1250.5	931.6	1.83	1.80	1.86	1.6	1.7	1.2	2.40	1.50	3.82
Central	HUN	1605.5	1874.3	1009.5	3.76	3.70	3.82	5.8	7.6	2.5	16.40	12.10	22.20
Eastern	POL	1289.8	1531.1	843.2	2.52	2.50	2.55	4.3	6.2	1.2	19.14	15.61	23.45
	SLO	1382.6	1605.5	1158.7	2.03	1.98	2.08	2.7	4.4	1.5	7.66	4.40	13.34
	CZR	1243.5	1456.6	805.3	3.90	3.84	3.95	1.4	1.8	0.6	20.11	12.53	32.30
Baltic	EST	1715.4	2202.7	1472.5	2.19	2.13	2.26	14.2	31.5	10.0	9.91	6.55	15.00
	LIT	1490.6	2150.3	1158.1	2.08	1.69	2.56	19.1	54.4	10.2	30.33	21.43	42.95

^a ASMR: Age and sex standardized mortality rates

^b RII: Relative Index of Inequality

Table 3: Age-standardized mortality rates (deaths per 100 000) and relative index of inequality, with stratification by gender.

Region	Area	Tuberculosis Male						Tuberculosis Female					
		AMR	ASMR		RII	95% Confidence		ASMR	AMR		RII	95% Confidence	
		Total	Low education	High education		Interval		Total	Low education	High education		Interval	
Southern	BAR	6.4	7.6	3.8	4.67	2.54	8.58	1.5	1.7	0.5	11.40	2.02	64.26
	MDR	2.5	2.6	1.7	1.73	0.45	6.69	1.4	1.7	0.0	n.a.	n.a.	n.a.
	BSQ	2.4	2.5	1.2	3.61	0.58	22.53	1.0	1.0	0.0	n.a.	n.a.	n.a.
Nordic	TUR	1.8	2.1	0.9	7.41	1.86	29.55	1.2	1.3	0.4	1.32	0.29	6.07
	DNK	1.5	2.1	0.8	10.53	2.84	39.06	0.8	0.9	0.4	13.80	1.25	151.87
	NRW	2.2	2.6	1.9	1.80	0.97	3.32	1.5	1.9	1.2	3.68	1.66	8.19
	FIN	4.4	4.8	4.2	1.95	1.26	3.02	3.0	3.1	2.3	2.24	1.25	4.03
Central	SWE	1.2	1.3	1.2	1.10	0.74	1.65	1.2	1.3	1.0	1.81	1.13	2.89
Central	SWZ	1.4	2.2	1.1	3.75	2.09	6.73	0.7	0.8	0.6	2.80	1.09	7.19
Western	BEL	2.4	2.6	1.8	2.36	1.40	3.99	0.8	0.9	0.6	2.55	0.94	6.96
Central	HUN	9.7	12.8	3.8	20.47	14.50	28.88	2.4	3.1	1.3	7.18	3.76	13.71
Eastern	POL	7.5	10.8	1.9	20.47	16.36	25.64	1.5	2.1	0.5	13.56	8.31	22.11
	SLO	4.1	7.1	2.1	10.03	5.31	18.93	1.5	1.9	1.0	2.90	0.94	9.00*
	CZR	2.2	3.0	0.8	31.37	18.05	54.60	0.7	0.8	0.3	4.35	1.77	10.69
Baltic	EST	25.8	51.3	18.1	9.25	5.91	14.50	3.9	13.9	2.8	15.56	5.15	47.04
	LIT	34.3	93.8	17.8	33.55	22.92	49.11	5.6	19.4	3.5	17.17	7.32	40.25

^a AMR: Age standardized mortality rates

^b RII: Relative Index of Inequality

^c n.a.: not applicable

Table 4: Age- and sex-standardized tuberculosis mortality rates for rural and urban populations.

Region	Country	Tuberculosis Rural					Tuberculosis Urban						
		ASMR	ASMR		RII	95% Confidence	ASMR	ASMR		RII	95%		
		Total	Low education	High education		Interval	Total	Low education	High education		Confidence Interval		
Nordic	NRW	1.6	1.8	1.3	2.00	0.69	5.73	2.0	2.5	1.6	2.88	1.66	5.00
	FIN	3.8	3.9	3.0	2.03	0.89	4.63	3.6	4.1	3.1	2.38	1.55	3.66
Central	HUN	6.5	7.6	2.0	26.76	9.60	51.83	5.4	7.7	2.6	14.92	10.54	21.14
Eastern	POL	4.5	5.3	0.9	16.18	10.40	25.15	4.1	7.1	1.2	28.53	22.42	36.27
	SLO	2.1	3.8	1.5	7.39	3.20	17.06	3.3	4.6	1.3	6.33	2.83	14.17
Baltic	EST	12.2	20.4	7.4	7.31	3.19	16.78	15.5	70.3	11.5	25.15	12.15	54.11
	LIT	23.5	48.8	12.8	19.39	10.78	34.85	16.7	60.6	9.4	40.41	25.76	60.64

^a ASMR: Age and sex standardized mortality rates

^b RII: Relative Index of Inequality

Figure 2. Absolute educational differences in tuberculosis mortality rates, expressed as the slope index of inequality (SII).

