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ORIGINAL ARTICLE

School life expectancy and risk for tuberculosis in Europe

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Abstract
Objective This study aims to investigate the effect of country-level school life expectancy on Tuberculosis (TB) incidence to gain further understanding of substantial variation in TB incidence across Europe.
Methods An ecological study examined the prospective association between baseline country-level education in 2000 measured by school life expectancy and TB incidence in 2000–2010 in 40 countries of the WHO European region using quantile regression. Subsequently, to validate the ecological associations between education and TB incidence, an individual-level analysis was performed using case-based data in 29 EU/EEA countries from the European Surveillance System (TESSy) and simulating a theoretical control group.
Results The ecological analysis showed that baseline school life expectancy had a negative prospective association with TB incidence. We observed consistent negative effects of school life expectancy on individuals' TB infections prospectively.
Conclusions These findings suggests that country-level education is an important determinant of individual-level TB infection in the region, and in the absence of a social determinants indicator that is routinely collected for reportable infectious diseases, the adoption of country-level education for reportable infectious diseases would significantly advance the field.

Keywords Tuberculosis · Education · Social determinants of health · Epidemiology · Europe

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Introduction

Inequalities in health among different socio-economic groups represent a persistent challenge in global health. Among the social determinants of health, a consistent association between education and health is well documented and poor health status is not limited only to groups without formal education. Rather, there are social gradients of health status by level of education, (Adler and Ostrove 1999; Marmot 2006) with higher education leading to better wellbeing and health. Mortality and morbidity differ systematically by level of educational attainment, even in a high-income country, such as Sweden (Erikson 2001). Education plays a role as an agent which reproduces socio-economic position across generations, by influencing characteristics and behaviours of individuals.

It is suggested that years of formal education completed is one of the most important determinants of health (Cutler and Lleras-Muney 2006; Grossman 2005). The mechanism that underlies the association between education and health is often explained with three pathways (World Health Organization 2007): materialist factors, behavioural or lifestyle factors, and psychosocial factors. Education increases individuals' income and therefore their chances for a better living environment and access to health services, but also provides access to information on healthy behaviour. Moreover, education also enhances self-efficacy and self-esteem (Lundborg 2008; Subramanian et al. 2010). The schooling system is the primary agent of socialization in societies, provides equitable opportunity and can therefore promote societal cohesion (Putnam 1993). Studies that investigate the impacts of income inequality consistently report that education is a protective factor (Feinstein et al. 2006) and this pattern is also observed in countries with universal health care systems (Daniels et al. 2000). A meta-analysis of the effect of education on mortality revealed a causal association even after controlling for the effect of other socio-economic factors (Baker et al. 2011), and a recent study showed a negative association between an individual's education and mortality from TB (Álvarez et al. 2011). But it is unclear to what extent education is associated with the incidence of infectious diseases. Provision of high-quality equitable education could reduce inequities in other socio-economic factors and education is less politically contentious than other measures, such as redistribution of income.

While the contribution of infectious diseases to overall mortality is smaller than that of non-communicable diseases, (World Health Organization 2011) a systematic review on infectious diseases and socio-economic factors found health disparities in infectious diseases in every European state (Semenza and Giesecke 2008). TB is concentrated in the socially and economically disadvantaged population since its incidence is exacerbated by interrupted or incomplete treatment practices, socio-economic factors and immigration from countries where the disease is endemic (Álvarez et al. 2011; Drobniewski et al. 1997; Semenza and Giesecke 2008). Not only individual socio-economic factors but also macro-level factors may have an impact on risk of TB infection, as abundant evidence from the studies in other health outcomes suggested. The study from Brazil identified independent effects of socio-economic factors at individual and area levels on risk of TB (de Alencar Ximenes et al. 2009). Moreover, country-level differentials in TB incidence by level and distribution of GDP have been reported (Ploubidis et al. 2012; Suk et al. 2009). An increase in TB incidence rates in the former Soviet Union and some other Eastern European countries led to an increase in TB incidence in the WHO European Region between the early 1990s and the early 2000s. In the UK, the incidence has still been on increase, and London has the highest rate of TB among western European capitals (Zenner et al. 2013). Although the incidence has declined since 2000, the level is still higher than that in 1994, (ECDC/WHO Regional Office for Europe 2013) reducing inequalities in TB incidence needs to be addressed in Europe as in the rest of the world.

Our study aims to investigate the effect of country-level education on TB incidence by applying ecological as well as individual-level analyses. While attribution of socio-economic factors at individual and country level as well as level of individual education to TB infection has been studied, there are few studies which investigate country-level educational differentials on TB incidence. We first examine the concurrent and prospective effect of country-level education on the incidence of TB in 2000–2010 in countries in the WHO European Region. Secondly, we aim to validate the observed effects of country-level education using individual TB case data derived from the European Surveillance System (TESSy). Prior to this study, the rich infectious disease case data have not been used for macro-level analysis to examine health inequalities in the WHO European region. Our individual-level analysis using TB cases allows us to reduce the major bias of ecological analysis, i.e. ecological fallacy, and propose a new method for studies of inequalities on the prevalence and incidence of infectious diseases.

Methods

Ecological analysis

Data

In the ecological analysis, TB incidence in 40 countries of the WHO European Region between 2000 and 2010 was used as the dependent variables. With respect to the explanatory variables, we selected expected years of schooling, or school life expectancy in 2000 as baseline to assess the prospective effect of educational policy over 11 years, based on the hypothesis that the effect of country-level education may have latency period until making an impact on TB. School life expectancy refers to the expected total number of years which a child at the age of entry in primary education can expect to attend in the future, assuming that the probability of his or her being enrolled in school at any age is equal to the current enrolment ratio for that age based on the UNESCO definition. While only limited countries have data on average year of schooling, the school life expectancy data are available in most of the countries in the world. Therefore, the measure was selected as a proxy for the overall level of national educational system. Due to the wide coverage of the indicator, the measure has been used in previous studies, and the new measure of Human Development Index (HDI) has employed school life expectancy since 2010. The data were downloaded in December 2011 from the website of the UNESCO Institute for Statistics. In order to have enough countries in the two analyses and as school life expectancy is not normally distributed, we categorized the school life expectancy variable into three by dividing the 29 countries with the TESSy data into tertiles based on the school life expectancy. For the ecological analysis, we used the same categories. The estimates in 2000 were used because school life expectancy is fairly stable over years and in order to assess prospective effects over a long time period.

In order to reliably estimate the effect of education on TB rates, we controlled for net migration rates. Migration is one of the key factors related to TB outcomes in Europe. Immigration from TB epidemic countries may increase TB incidence and prevalence in recipient countries. In the WHO European Region, 8.7 per cent of notified TB cases were foreign-born in 2010, and only six countries observed a decrease in TB notifications among the foreign-born between 2001 and 2010 (ECDC/WHO Regional Office for Europe 2013). For instance, large numbers of foreign-born nationals from high TB epidemic countries may contribute to the higher incidence of TB in the UK than in other European countries (Gilbert et al. 2009). The data on net migration in 2000 were extracted from the World Bank's World Development Indicators in March 2012.

We did not employ Gross Domestic Product (GDP) per capita into the final model because the association between the level of GDP and education is highly co-linear (Kawachi and Blakely 2001) and arguably can be thought of as bidirectional. A preliminary analysis showed that the correlation between school life expectancy and GDP in our sample was very high (Spearman's rank correlation coefficient 0.82). Level and distribution of wealth, often measured by GDP per capita and the Gini coefficient, have been consistently linked with population health, including TB rates (Beckfield 2004; Ploubidis et al. 2012). Countries with higher GDP per capita and lower Gini coefficient generally have better population health. High level of education increases individual income as well as leads to economic growth by producing more productive population (Schultz 1961). It is suggested that labour income growth among tertiary-educated individuals contributed to more than half of the GDP growth in OECD countries over the last decade (OECD 2012). In turn, countries with high level of GDP per capita are able to spend more on education, but an economic return from education at individual and national level is substantial (Lutz et al. 2008). This causality and reverse causality imply bidirectional relationship between education and GDP. Thus, GDP or Gini was not included in the analysis.

In the ecological models, we included the countries of the WHO European Region which covers all European countries as well as Central Asian countries. The region includes 53 countries, but 13 countries, such as Liechtenstein, San Marino, Monaco and Kosovo, do not have data on school life expectancy or other variables. Therefore, complete information on all predictors were only available for 40 countries.

Statistical modelling

We performed multivariable quantile regression models, adjusting for net migration and country. Country-level aggregated TB data follow a skewed distribution, so the distributional assumptions of linear regression are invalid. Quantile regression relaxes this assumption, and no parametric distributional form is assumed for the error. Thus, it can be used for skewed distributions since the median or quantiles of the dependent variable are modelled instead of the mean.

Individual-level analysis

Data

Since 2008, the surveillance activities in the WHO European Region and Liechtenstein have been jointly coordinated by the European Centre for Disease Prevention and Control (ECDC) and the WHO Regional Office for Europe. Designated national disease surveillance institutions are responsible for reporting the data to the European level through a joint data collection entry point. For the 27 European Union (EU) Member States and 3 European Economic Area (EEA) countries, case-based data are submitted, processed and validated through TESSy database hosted by ECDC (ECDC/WHO Regional Office for Europe 2013). Case-based TB surveillance data submitted until 2 February 2012 for the years 2000–2010 were extracted from TESSy.

10-year age group and sex of each case were controlled for each model. Older individuals are susceptible to reactivation of latent TB because of immune dysregulation, and the TB incidence in the population over 60 years old in high-income countries is higher (Dolin et al. 1994). Considering also the difference in age structure in the countries studied, any country-level analysis needs to be adjusted for age (World Health Organization 2011). There is also consistent evidence that males are more likely to be infected with TB (World Health Organization 2011). For this analysis, 895, 109 TB cases with age and sex data collected between 2000 and 2010 in the 29 countries were used. Liechtenstein was excluded for this analysis since the country had only 5 cases in 2007. In addition, 2893 cases were excluded because either their age or sex data were missing.

The TESSy data have only cases, that is, no control group. We thus considered control populations which were defined based on the mid-year population in 2000 for all the countries, available at Eurostat. The data are aggregated by sex and 5-year age group. After combining the data into 10-year age groups, a 'theoretical' control group was obtained by subtracting the number of TB cases in each sex–age stratum from the population figure for the corresponding sex–age stratum within each country.

Statistical modelling

Logit model was performed by adjusting for age group and sex as well as country-level net migration, and country. The analysis allowed us to examine the effects of country-level school life expectancy on individual-level likelihood of having TB. All models were estimated with Stata 12.

Results

Online Resource Tables 1 and 2 present descriptive statistics of the TB incidence in the 40 countries for the ecological analysis. There is considerable country-level variation with respect to TB incidence (4.3–167.0 per 100,000 population in 2000) in Europe (Online Resource Table 1). The median TB incidence across the 40 countries decreased from 21.5 per 100,000 in 2000 to 12.5 per 100,000 in 2010 (Online Resource Table 2).

Online Resource Table 3 provides descriptive statistics from the TESSy data for the individual-level analysis. Several countries joined TESSy after 2000, and thus, there were fewer than 29 countries before 2007.

Table 1 presents 75th quantile regression parameter estimates, their respective confidence intervals, and p-values derived from bootstrapped standard errors (1000 replications). We modelled quantile regression at 25th and 50th quantiles (results not shown), but the associations with education were weak. This implies that the effect of country-level school life expectancy on TB is stronger in the countries with high TB incidence, while the association is weaker in the countries with low TB incidence. In other words, the educational indicator has larger negative impact on the countries at the 75th quantile, i.e. Ukraine, Lithuania, Latvia, Georgia, Azerbaijan, Tajikistan, Uzbekistan, Moldova, Kyrgyzstan and Romania. Low country-level school life expectancy measured at baseline (2000) was, relative to high country-level school life expectancy, negatively associated with the national incidence of TB prospectively in 2002–2006 at the 5 per cent significance level. The estimated coefficients were very similar for all years between 2001 and 2010. The strongest effect was observed in 2005 where low relative to high country-level school life expectancy was associated with a difference in incidence at the 75th percentile of 91 (95 % CI: 11.9, 170.1) per 100,000.

Table 2 shows the results derived from the individual-level analysis. Strong associations between country-level school life expectancy at baseline and individuals' odds of having TB were observed between 2000 and 2010. People living in countries with a low level of school life expectancy (<14.0 years) had 3.40 (95 % CI: 3.02–5.73) times the odds of being notified as a TB case in 2000, compared with people in countries with a high level of school life expectancy (≥16.0 years). This OR increased to a maximum of 3.56 (95 % CI: 1.99–6.39) in 2002 before decreasing to 2.13 (95 % CI: 1.09–4.16) in 2010.

Discussion

Our results derived from two methodological approaches suggest that school life expectancy is negatively associated with the incidence of TB. Both the ecological and individual-level analyses showed higher levels of country-level school life expectancy to be associated with lower TB incidence. The impact of school life expectancy in 2000 increases for the first few years and gradually diminishes over time, while the timing of the peak in the two models differed. This may be interpreted as a lagged effect of school life expectancy on TB rates, since the school life expectancy measured at baseline had a prospective negative association with TB. One possible explanation for the effect of school life expectancy is that it is mediated by individual educational level. As a country has longer school life expectancy, more educated individuals follow a healthy lifestyle, purchase more nutritious food, live in more hygienic housing and safer environments, and have better access to health services (Lynch et al. 2000) compared to individuals in countries with lower school life expectancy. The far-reaching impacts of education on TB notification in Europe have direct policy implications. Educational attainment is an important health determinant in need of strengthening, even in Europe.

We found that the effect of education peaked in 2002 and diminished over time in the individual-level analysis among the countries with TESSy data, while the peak was in 2005 in the ecological analyses among 40 countries. This suggests that the baseline country-level education in 2000 had prospective latency effects on TB incidence. The decline of effect was also found even when stratifying the countries by eastern and western/southern regions (results are not presented here, available from corresponding author). However, this finding does not necessarily suggest that health differentials due to education disappeared over time. While the effect of the baseline education disappears, it is possible that data relating to more recent education might become a more important predictor of TB in later periods. It is also possible that school life expectancy has a

Table 1 Educational attainment and risk of TB in the European Union and European Economic Area; 75th quantile regression

	2000		2001		2002	
	Coeff.	95 % CI	Coeff.	95 % CI	Coeff.	95 % CI
School life expectancy[a]						
Low	45	[−8.7 98.7]	57	[−3.6 117.6]	71	[3.7 138.3]*
Medium	9	[−9.9 27.9]	7	[−12.2 26.2]	8	[−9.3 25.3]
High	ref.		ref.		ref.	
Net migration rate						
<0 %	71	[22.4 119.6]**	72	[15.5 128.5]*	68.1	[6.1 130.1]*
0–3 %	ref.		ref.		ref.	
≥3 %	1	[−14.9 14.9]	1	[−16.2 18.2]	2.1	[−12.9 17.1]
N (countries)	40		40		40	
Pseudo R2	0.5823		0.5825		0.5779	

	2003		2004		2005	
	Coeff.	95 % CI	Coeff.	95 % CI	Coeff.	95 % CI
School life expectancy[a]						
Low	81.3	[8.0 154.6]*	85	[8.0 162.0]*	91	[11.9 170.1]*
Medium	7.3	[−8.2 22.8]	3	[−13.3 19.3]	7	[−7.4 21.4]
High	ref.		ref.		ref.	
Net migration rate						
<0 %	65	[−3.3 133.3]	64.2	[−8.5 136.9]	59	[−16.8 134.8]
0–3 %	ref.		ref.		ref.	
≥3 %	4	[−8.2 16.2]	4.2	[−10.6 19.0]	4	[−9.4 17.4]
N (countries)	40		40		40	
Pseudo R2	0.5797		0.5776		0.579	

	2006		2007		2008	
	Coeff.	95 % CI	Coeff.	95 % CI	Coeff.	95 % CI
School life expectancy[a]						
Low	86.8	[7.0 166.6]*	78.2	[−2.9 159.3]	68.1	[−14.3 150.5]
Medium	4.8	[−6.4 16.0]	5.2	[−5.9 16.3]	5.1	[−3.9 14.1]
High	ref.		ref.		ref.	
Net migration rate						
< 0 %	61	[−18.1 140.1]	60	[−15.0 135.0]	59	[−22.0 140.0]
0–3 %	ref.		ref.		ref.	
≥3 %	3.8	[−5.5 13.1]	4.2	[−6.3 14.7]	2.7	[−4.9 10.3]
N (countries)	40		40		40	
Pseudo R2	0.5797		0.5776		0.579	

	2009		2010	
	Coeff.	95 % CI	Coeff.	95 % CI
School life expectancy[a]				
Low	61.8	[−20.5 144.1]	63.3	[−20.6 147.2]
Medium	3.8	[−8.5 16.1]	4.3	[−8.1 16.7]
High	ref.		ref.	

Table 1 continued

	2009		2010	
	Coeff.	95 % CI	Coeff.	95 % CI
Net migration rate				
<0 %	59	[−23.3 141.3]	58	[−24.0 140.0]
0–3 %	ref.		ref.	
≥3 %	1.6	[−7.6 10.8]	2	[−8.7 12.7]
N (countries)	40		40	
Pseudo R2	0.5519		0.5429	

* $0.01 \le p < 0.05$, ** $0.001 \le p < 0.01$, *** $p < 0.001$

[a] School life expectancy: Low (<14.0 years), Medium (14.0–15.9 years), High (≥16.0 years)

Table 2 Individual-level analysis: logistic regression of TB and school life expectancy, European Union and European Economic Area, 2000–2010

	2000		2001		2002		2003	
	Adjusted OR[b]	[95 % CI]	Adjusted OR[b]	[96 % CI]	Adjusted OR[b]	[97 % CI]	Adjusted OR[b]	[97 % CI]
School life expectancy[a]								
Low	3.40	[2.02 5.73]***	3.43	[1.96 6.02]***	3.56	[1.99 6.39]***	3.24	[1.82 5.79]***
Medium	1.16	[0.70 1.92]	1.06	[0.70 1.58]	0.99	[0.64 1.53]	0.99	[0.66 1.48]
High	1.00		1.00		1.00		1.00	
Age group								
0–9	0.22	[0.16 0.29]***	0.24	[0.19 0.30]***	0.22	[0.18 0.28]***	0.21	[0.16 0.27]***
10–19	0.37	[0.31 0.43]***	0.38	[0.32 0.46]***	0.36	[0.30 0.43]***	0.36	[0.29 0.45]***
20–29	1.00		1.00		1.00		1.00	
30–39	1.14	[0.98 1.34]	1.16	[1.00 1.35]*	1.16	[0.99 1.36]	1.14	[0.96 1.35]
40–49	1.29	[0.97 1.71]	1.30	[1.00 1.69]*	1.30	[0.95 1.78]	1.25	[0.94 1.66]
50–59	1.16	[0.83 1.61]	1.18	[0.87 1.61]	1.23	[0.85 1.77]	1.21	[0.84 1.74]
60–69	1.16	[0.78 1.74]	1.11	[0.82 1.51]	1.05	[0.77 1.43]	1.01	[0.74 1.38]
70+	1.50	[0.84 2.70]	1.48	[0.91 2.42]	1.45	[0.88 2.37]	1.41	[0.88 2.27]
Gender								
Female	1.00		1.00		1.00		1.00	
Male	2.04	[1.80 2.31]***	2.00	[1.76 2.27]***	2.06	[1.78 2.39]***	2.02	[1.80 2.28]***
Net migration rate								
<0 %	3.55	[1.61 7.84]**	4.31	[2.62 7.07]***	4.70	[2.84 7.79]***	5.01	[3.03 8.28]***
0–3 %	1.00		1.00		1.00		1.00	
≥3 %	1.13	[0.48 2.63]	1.28	[0.76 2.16]	1.37	[0.80 2.34]	1.39	[0.86 2.25]
N (countries)	22		24		26		27	
N (cases and controls)	338,985,551		423,867,445		435,213,993		438,126,931	

	2004		2005		2006		2007	
	Adjusted OR[b]	[97 % CI]	Adjusted OR[b]	[97 % CI]	Adjusted OR[b]	[97 % CI]	Adjusted OR[b]	[97 % CI]
School life expectancy[a]								
Low	3.06	[1.70 5.52]***	2.79	[1.57 4.96]***	2.78	[1.58 4.90]***	2.59	[1.33 5.05]**
Medium	0.89	[0.59 1.33]	0.81	[0.55 1.21]	0.82	[0.56 1.21]	0.94	[0.64 1.38]
High	1.00		1.00		1.00		1.00	

Table 2 continued

	2004		2005		2006		2007	
	Adjusted OR[b]	[97 % CI]	Adjusted OR[b]	[97 % CI]	Adjusted OR[b]	[97 % CI]	Adjusted OR[b]	[97 % CI]
Age group								
0–9	0.23	[0.19 0.27]***	0.21	[0.17 0.25]***	0.21	[0.16 0.27]***	0.24	[0.19 0.29]***
10–19	0.35	[0.28 0.44]***	0.37	[0.28 0.48]***	0.40	[0.29 0.55]***	0.37	[0.27 0.52]***
20–29	1.00		1.00		1.00		1.00	
30–39	1.18	[0.97 1.43]	1.20	[0.95 1.52]	1.23	[0.96 1.57]	1.17	[0.91 1.50]
40–49	1.23	[0.93 1.63]	1.21	[0.89 1.64]	1.18	[0.88 1.59]	1.12	[0.85 1.50]
50–59	1.26	[0.85 1.86]	1.29	[0.84 1.97]	1.33	[0.85 2.07]	1.29	[0.80 2.08]
60–69	0.98	[0.72 1.35]	0.95	[0.69 1.32]	0.93	[0.66 1.29]	0.90	[0.65 1.24]
70+	1.40	[0.89 2.19]	1.39	[0.88 2.20]	1.40	[0.91 2.17]	1.32	[0.92 1.89]
Gender								
Female	1.00		1.00		1.00		1.00	
Male	2.01	[1.75 2.31]***	2.01	[1.70 2.37]***	1.94	[1.65 2.28]***	1.97	[1.70 2.28]***
Net migration rate								
<0 %	5.36	[3.20 8.97]***	5.60	[3.43 9.13]***	5.64	[3.48 9.12]***	5.29	[3.33 8.41]***
0–3 %	1.00		1.00		1.00		1.00	
≥3 %	1.48	[0.91 2.40]	1.57	[1.00 2.46]*	1.72	[1.12 2.64]*	1.97	[1.29 2.99]**
N (countries)	27		27		27		27	
N (cases and controls)	438,211,838		437,851,917		437,927,335		486,173,248	

	2008		2009		2010	
	Adjusted OR[b]	[97 % CI]	Adjusted OR[b]	[97 % CI]	Adjusted OR[b]	[97 % CI]
School life expectancy[a]						
Low	2.70	[1.38 5.28]**	2.25	[1.16 4.34]*	2.13	[1.09 4.16]*
Medium	0.93	[0.61 1.39]	0.82	[0.55 1.22]	0.79	[0.52 1.19]
High	1.00		1.00		1.00	
Age group						
0–9	0.25	[0.19 0.32]***	0.24	[0.18 0.32]***	0.23	[0.17 0.32]***
10–19	0.38	[0.29 0.49]***	0.36	[0.28 0.45]***	0.35	[0.27 0.44]***
20–29	1.00		1.00		1.00	
30–39	1.19	[0.96 1.48]	1.12	[0.91 1.39]	1.16	[0.96 1.40]
40–49	1.18	[0.88 1.59]	1.13	[0.84 1.51]	1.11	[0.83 1.48]
50–59	1.34	[0.82 2.22]	1.33	[0.80 2.22]	1.32	[0.82 2.12]
60–69	0.91	[0.65 1.28]	0.92	[0.65 1.29]	0.95	[0.66 1.35]
70+	1.37	[0.94 1.99]	1.36	[0.93 1.98]	1.36	[0.95 1.94]
Gender						
Female	1.00		1.00		1.00	
Male	1.99	[1.69 2.36]***	1.96	[1.64 2.33]***	1.99	[1.71 2.33]***
Net migration rate						
<0 %	5.33	[3.33 8.52]***	5.60	[3.57 8.77]***	5.23	[3.23 8.48]***
0–3 %	1.00		1.00		1.00	
≥3 %	2.15	[1.38 3.36]**	2.10	[1.38 3.20]**	1.96	[1.22 3.13]**
N (countries)	27		27		27	

Table 2 continued

	2008		2009		2010	
	Adjusted OR[b]	[97 % CI]	Adjusted OR[b]	[97 % CI]	Adjusted OR[b]	[97 % CI]
N (cases and controls)	486,606,697		486,895,273		486,036,813	

Notes: The 29 countries included in this analysis were Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain Sweden and United Kingdom. Germany and Latvia have been included since 2001, Cyprus and Greece since 2002, Lithuania since 2003 and Bulgaria and Spain since 2007

* $0.01 \le p < 0.05$, ** $0.001 \le p < 0.01$, *** $p < 0.001$

[a] School life expectancy: Low (<14.0 years), Medium (14.0–15.9 years), High (≥16.0 years)

[b] The results were adjusted for net migration, age and sex, and country-level net migration rate

cross-sectional effect as observed in the results from the individual-level analyses, but this is likely to be confounded by previous years' school life expectancy. Nevertheless, our results consistently document level of education to be an important determinant of notified TB cases. These findings highlight the need for an individual-level indicator of social determinants that is routinely collected for reportable infectious diseases, along with date of diagnosis, age and sex. Thus, public health policy should consider adding level of education to the list of variables collected for notifiable infectious diseases. Such an indicator is essential for the assessment of social determinants of infectious diseases at the individual level. Moreover, a social determinant indicator can also help elucidate the causal pathways underlying the association we describe here between the level of education at individual and macro-level and disease notification.

It should also be noted while interpreting these results that TB case management has improved during this period in Europe in response to the TB control programme DOTS (directly observe treatment, short-course) launched by WHO in 1995. For instance, Romania, the country with the highest TB incidence in EU, started to implement the WHO-recommended DOTS strategy gradually since 1997 which was subsequently expanded to the entire country by 2005. The DOTS coverage increased from four percent in 2000 to 54 percent in 2003 (Marica et al. 2009). The case detection rate also improved from 46 per cent in 2002 to 75 percent in 2006. Incidence reached a peak of 175 cases per 100,000 population in 2002 and declined to 116 in 2010 (World Health Organization 2011). Similar trends were found in the other countries with the high TB incidence in EU, i.e. Baltic regions (ECDC/WHO Regional Office for Europe 2013). The improvement in TB case management also may have contributed to reduce the effect of the baseline school life expectancy over time.

It is also possible that the effect of country-level education is underestimated, particularly in the late 2000s, due to any degree of internal heterogeneity of individual educational attainment within countries. Migrants originating from lower school life expectancy countries may be likely to contribute to a good proportion of TB cases in countries with higher level of school life expectancy. For example, between 2001 and 2010, eleven EU Member States experienced rising trends of cases of foreign origin (ECDC/WHO Regional Office for Europe 2013). Such a trend could contribute to exposure misclassification and bias the results towards the Null.

There are also further potential confounders apart from age and sex which we were unable to take into account. In the individual-level analysis for instance, we could not control for immigration status because a substantial amount of the data were incomplete and so, this variable could not be included in the analysis.

Ecological analysis showed that the school life expectancy is negatively associated with TB rates in the WHO European region. This effect was confirmed by an individual-level study where individual TB cases were used and a theoretical control group constructed. Further research is needed not only to identify country-level predictors that account for the TB variance remaining unexplained by our models, but also to disentangle the relative contribution of school life expectancy on the individual-level pathways that lead to TB. Despite these limitations, this study introduced a new opportunity to utilize TB case-based data by creating theoretical control groups for study of health inequalities. Our findings suggest that assessment of the impact of country-level education could be used for more equitable health policy planning for TB control.

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