



<http://www.diva-portal.org>

This is the published version of a paper published in *Scientific Reports*.

Citation for the original published paper (version of record):

Stickley, A., Neligan, A., Baburin, A., Jasilionis, D., Krumins, J. et al. (2022)
Educational inequalities in epilepsy mortality in the Baltic countries and Finland in
2000-2015

Scientific Reports, 12(1): 4597

<https://doi.org/10.1038/s41598-022-08456-x>

Access to the published version may require subscription.

N.B. When citing this work, cite the original published paper.

To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>

Permanent link to this version:

<http://urn.kb.se/resolve?urn=urn:nbn:se:sh:diva-48677>



OPEN

Educational inequalities in epilepsy mortality in the Baltic countries and Finland in 2000–2015

Andrew Stickley^{1,2,3}, Aidan Neligan^{4,5}, Aleksei Baburin⁶, Domantas Jasilionis^{7,8}, Juris Kruminis⁹, Pekka Martikainen^{7,10,11}, Naoki Kondo², Tomiki Sumiyoshi³, Jae Il Shin¹², Hans Oh¹³, Kyle Waldman¹⁴ & Mall Leinsalu^{1,6}✉

Little is known about socioeconomic differences in epilepsy mortality. This study examined educational inequalities in epilepsy mortality in the general population in the Baltic countries and Finland in 2000–2015. Education-specific mortality estimates for individuals aged 30–74 in Estonia, Latvia and Lithuania were obtained from census-linked mortality datasets while data for Finland came from the register-based population and death data file of Statistics Finland. Trends and educational inequalities in epilepsy mortality were assessed using age-standardised mortality rates (ASMRs) per 100,000 person years and age-adjusted mortality rate ratios (RRs) calculated using Poisson regression. ASMRs were higher in men than women in all countries. ASMRs reduced in 2000–2015 among all men and women except for Finnish women. Among men, an inverse educational gradient in epilepsy mortality in 2000–2007 widened in 2008–2015 with ASMRs falling among high and mid educated men in all countries but increasing among low educated men in three countries. An inverse educational gradient in female mortality remained in all countries throughout 2000–2015. Although epilepsy mortality fell in the Baltic countries and Finland (men only) in 2000–2015, this masked a clear inverse educational gradient in mortality that became steeper across the period.

Epilepsy is a significant cause of mortality. In 2016, there were over 126,000 epilepsy-related deaths worldwide¹. Partly this reflects the fact that death rates are elevated in people with epilepsy (PWE). Specifically, a recent review of population-based studies in high-income countries by the International League Against Epilepsy (ILAE) Commission on Epidemiology found standardised mortality ratios (SMRs) ranging from 1.6 to 3.0 among PWE compared to the general population², while a corresponding study on low- and middle-income countries reported an even wider range of figures, from 1.3 to 7.2³. Despite an overall reduction in global epilepsy age-standardised mortality rates of almost 25% between 1990 and 2016, some countries nevertheless experienced large increases in their death rates during this period¹, while other research has also highlighted that epilepsy mortality rates can differ consistently between populations in different countries over time⁴. This supports the recent call for epilepsy-related mortality to be regarded as a public health priority⁵.

Despite the fact that epilepsy is seemingly linked to an increased mortality risk, many factors associated with this phenomenon remain under-researched. For example, as yet, there has been surprisingly little focus on socioeconomic variation in epilepsy deaths, even though low socioeconomic status has been linked to risk

¹Stockholm Centre for Health and Social Change, Södertörn University, 141 89 Huddinge, Sweden. ²Department of Social Epidemiology, Graduate School of Medicine and School of Public Health, Kyoto University, Kyoto, Japan. ³Department of Preventive Intervention for Psychiatric Disorders, National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo, Japan. ⁴Homerton University Hospital NHS Foundation Trust, Homerton Row, London E9 6SR, UK. ⁵DCEE, UCL Queen Square Institute of Neurology, Queen Square, London WC1N 3BG, UK. ⁶Department of Epidemiology and Biostatistics, National Institute for Health Development, Tallinn, Estonia. ⁷Max Planck Institute for Demographic Research, Rostock, Germany. ⁸Demographic Research Centre, Vytautas Magnus University, Kaunas, Lithuania. ⁹Demography Unit, Faculty of Business, Management and Economics, University of Latvia, Riga, Latvia. ¹⁰Population Research Unit, University of Helsinki, Helsinki, Finland. ¹¹Department of Public Health Sciences, Stockholm University, Stockholm, Sweden. ¹²Department of Pediatrics, Yonsei University College of Medicine, Yonsei-ro 50, Seodaemun-gu, Seoul, Korea. ¹³Suzanne Dworak-Peck School of Social Work, University of Southern California, 1149 South Hill Street suite 1422, Los Angeles, CA 90015, USA. ¹⁴Department of Sociology, Harvard University, Cambridge, MA, USA. ✉email: mall.leinsalu@sh.se

factors for epilepsy (e.g. head trauma, brain neoplasms) that might also result in higher mortality in PWE⁶. Importantly, there is some evidence that epilepsy mortality is associated with economic disadvantage and that a socioeconomic gradient might exist in epilepsy deaths. A retrospective cohort study of PWE in South Carolina showed that living in areas with low median household income was associated with an increased mortality risk in 2000–2013⁷. A recent review study on epilepsy deaths has also underlined the potential for socioeconomic variation in epilepsy mortality by noting that there was a nearly threefold difference in age-standardised epilepsy mortality rates between the most and least deprived neighbourhood deciles in England (13.1 vs. 5.1 per 100,000)⁸.

Against this backdrop, the current study will examine if there were socioeconomic differences, as assessed by differences in educational attainment, in epilepsy mortality among the general adult population in the Baltic countries (Estonia, Latvia, Lithuania) and Finland in 2000–2015. The Baltic countries have somewhat differing healthcare systems. Estonia and Lithuania have social health insurance systems underpinned by employment-based contributions with government funding for other non-employed groups, while in Latvia there is a national healthcare system funded through income tax and general revenues^{9,10}. Although these systems provide extensive medical coverage (from over 90% of the population in Estonia and Lithuania to universal coverage in Latvia), high user charges (in Latvia) and substantial out-of-pocket payments can limit access to healthcare services, especially in disadvantaged groups^{9,11}. Comparatively little is known about the epidemiology of epilepsy in the Baltic countries¹². However, there is some indirect indication that socioeconomic differences might be important for epilepsy mortality in these countries. Research from Estonia has shown, for example, that in a setting where epilepsy may be undertreated¹³, the level of education is linked to employment status among PWE, which in turn (i.e. underemployment/unemployment) may be associated with epilepsy severity¹⁴. This may be of relevance as other research has linked more seizures to an increased risk for sudden unexpected death in epilepsy (SUDEP)¹⁵. The results will be compared to Finland, a neighbouring Nordic welfare state, that has three times higher per capita health care spending and a much lower share of out-of-pocket payments¹¹.

Thus, building on and extending several recent studies that have examined epilepsy mortality in the general population (i.e. among all individuals irrespective of diagnostic status)^{4,16,17} this study has two main aims: (i) to examine changes in epilepsy mortality in the general population in the Baltic countries and Finland in 2000–2015; (ii) to determine if there are educational inequalities in epilepsy mortality in these countries and if there are, whether there have been any changes in them across the study period. Establishing whether there are educational inequalities in epilepsy mortality in these countries may be important for future attempts to reduce these deaths.

Methods

Mortality data. Data for Estonia, Latvia and Lithuania were obtained from census-linked mortality datasets based on the linkages between the population censuses in 2000 (2001 in Lithuania) and 2011 and death records involving all permanent residents. The censuses in the Baltic countries combined traditional survey-based enumeration (the share of coverage ranged from 91% in Latvia to 98% in Estonia) and register-based enumeration¹⁸. The register-based data did not include information about socioeconomic status (educational attainment) and were therefore excluded from the analysis. All individuals were followed from the census date until the date of death or emigration, or until the end of the follow-up period. The date and cause of death were linked from national mortality registries. All data linkages were performed by National Statistical Offices. Corresponding data for Finland were obtained from the register-based education-specific population and death data file of Statistics Finland covering the permanent total population. Data were originally organised into four sub-periods: 2000–2003, 2004–2007, 2008–2011 and 2012–2015. To ensure that a complete educational history was obtained and to achieve optimal accuracy of cause of death ascertainment, this study focuses on those aged 30–74 years. Population exposures were estimated by adding up the number of person years lived by individuals within each 5-year interval age group in a given period. Deaths were allocated to age intervals using the age at death. Data were anonymised and aggregated into multidimensional frequency tables combining deaths and population exposures split by study periods and sociodemographic variables before they were delivered for research purposes. As this study used secondary anonymised data ethical permission was not required.

Measures. Following the lead of earlier studies in the general population^{4,19}, all deaths where the underlying cause was classified as G40 (Epilepsy) or G41 (Status epilepticus) using the 10th revision of the International Classification of Diseases (ICD-10)²⁰ were considered as deaths from epilepsy (Appendix 1). Sociodemographic data are census-based and were coded by the statistical offices following a common study protocol. Socioeconomic status was assessed using data on educational level, which was categorised using the International Standard Classification of Education (ISCED) 2011²¹. *Low* education refers to primary and lower secondary education (ISCED categories 0–2), *middle (mid)* education includes upper secondary and post-secondary non-tertiary education (categories 3–4), and *high* education covers tertiary education (categories 5–8). The percentage of missing values for education was low (0–0.7%) and these cases were additionally excluded from the analysis (Table 1).

Statistical analysis. To increase the statistical power we combined data into two sub-periods: 2000–2007 and 2008–2015. This cutoff point coincided with the end of a period of strong economic growth that was followed by a sharp, although relatively short-term recession after 2008²². Age-standardised mortality rates (ASMRs) per 100,000 person years were calculated using the European Standard Population²³. Statistical testing of the change in the ASMRs between study periods was performed and exact p-values were included in the tables; the level of statistical significance was set at $p < 0.05$. Educational inequalities in epilepsy mortality were assessed by age-adjusted mortality rate ratios (RR) calculated using Poisson regression. ASMRs and RRs are presented together with 95% confidence intervals (CI). To assess the magnitude and direction of the potential bias related to the

Sex	Country	Period	Deaths N	Person Years N	Educational level				ASMR (95% CI)	Change	
					High %	Middle %	Low %	Missing %		2008–2015 vs. 2000–2007	p-value
Men	Finland	2000–2007	407	11,597,283	26.8	39.3	33.9	0.0	3.4 (3.1–3.8)		
		2008–2015	351	11,963,418	28.7	44.5	26.9	0.0	2.8 (2.5–3.1)		
										–0.6	0.008
	Estonia	2000–2007	234	2,540,646	25.4	48.7	25.2	0.7	9.4 (8.2–10.6)		
		2008–2015	197	2,634,549	27.6	51.2	20.7	0.5	7.5 (6.5–8.6)		
										–1.9	0.023
	Latvia	2000–2007	323	3,989,498	15.3	58.2	25.9	0.6	8.2 (7.3–9.1)		
		2008–2015	200	3,927,536	18.3	62.4	19.1	0.3	5.1 (4.4–5.8)		
										–3.1	<0.001
	Lithuania	2001–2007	418	5,836,369	16.3	59.8	23.3	0.5	7.2 (6.5–7.9)		
		2008–2015	386	6,463,171	19.3	61.0	19.4	0.3	5.9 (5.3–6.5)		
										–1.3	0.006
Women	Finland	2000–2007	181	11,834,081	31.3	36.2	32.5	0.0	1.5 (1.3–1.7)		
		2008–2015	190	12,111,012	36.5	40.1	23.4	0.0	1.5 (1.3–1.7)		
										0.0	0.944
	Estonia	2000–2007	62	3,138,593	34.7	44.9	19.9	0.5	2.0 (1.5–2.5)		
		2008–2015	39	3,132,532	40.0	46.2	13.4	0.3	1.3 (0.9–1.7)		
										–0.7	0.029
	Latvia	2000–2007	57	5,073,222	19.0	58.7	21.9	0.4	1.2 (0.9–1.5)		
		2008–2015	47	4,854,352	26.1	60.0	13.7	0.2	1.0 (0.7–1.2)		
										–0.2	0.234
	Lithuania	2001–2007	89	7,018,533	19.0	59.3	21.2	0.5	1.3 (1.0–1.6)		
		2008–2015	94	7,677,380	24.7	60.4	14.6	0.3	1.2 (0.9–1.4)		
										–0.1	0.549

Table 1. Characteristics of the study populations and age-standardised mortality rates per 100,000 person years for epilepsy in 2000–2015 in the 30–74 age group. The follow-up in the 1st period started from the census date in the Baltic countries, i.e. 31.03.2000 in Estonia, 1.03.2000 in Latvia, and 6.04.2001 in Lithuania; in 2008 the follow-up started on January 1; the follow-up ended on December 31 in the respective periods. ASMR age-standardised mortality rate per 100,000 person years, CI confidence interval.

exclusion of register-based data from census records in the Baltic countries we performed a sensitivity analysis for Latvia comparing ASMRs for epilepsy mortality while excluding and including register-based data. Statistical analyses were performed using SPSS Statistics for Windows, version 26.0 (IBM Corp. 2019) and STATA 14.2 (Stata Corp., College Station, Texas, USA).

Results

There were 3275 epilepsy deaths in the four countries in 2000–2015 and approximately 103.8 million person years of follow-up. Among men, ASMRs were much higher in the Baltic countries than in Finland in 2000–2007 ranging from 7.2 (95% CI: 6.5–7.9) (Lithuania) to 9.4 (95% CI: 8.2–10.6) (Estonia) per 100,000. Male epilepsy deaths decreased in all countries from 2000–2007 to 2008–2015 with the reduction in ASMRs ranging from -0.6 per 100,000 in Finland to -3.1 in Latvia (Table 1). In all countries the reduction in male ASMRs was statistically significant. Among women ASMRs were lower than for men and similar across the four countries, ranging from 1.2 (95% CI: 0.9–1.5) (Latvia) to 2.0 (95% CI: 1.5–2.5) (Estonia) per 100,000 in 2000–2007. A reduction occurred in female epilepsy ASMRs in all countries except Finland across the study period ranging from -0.1 (Lithuania) to -0.7 (Estonia) per 100,000 but was only statistically significant in Estonia.

Among men a clear educational gradient was observed in epilepsy mortality in all of the countries in 2000–2007 (Table 2). Among the high educated, epilepsy ASMRs ranged from 1.5 (95% CI: 1.0–1.9) (Finland) to 5.1 (95% CI: 3.4–6.9) (Estonia) per 100,000, while the corresponding figures for the mid educated were 3.4 (95% CI: 2.8–3.9) (Finland) to 8.2 (95% CI: 6.5–9.9) (Estonia), and for the low educated ASMRs ranged from 5.7 (95% CI: 4.9–6.5) (Finland) to 18.5 (95% CI: 15.2–21.7) (Latvia) per 100,000. Compared to the high educated, those with mid education had mortality rate ratios ranging from 1.6 (95% CI: 1.1–2.4) (Estonia) to 3.1 (95% CI: 1.8–5.4) (Latvia), while the corresponding figures for the low educated were 3.3 (95% CI: 2.2–4.9) (Estonia) to 8.3 (95% CI: 4.7–14.7) (Latvia). From 2000–2007 to 2008–2015 a reduction was observed in epilepsy ASMRs among all groups except for in three of the low educated groups where there was an increase of 0.4 (Finland) to 1.1 (Lithuania) per 100,000. The reduction was significant for the high educated in Finland and Estonia, for the mid educated in all countries but Estonia, and for the low educated in Latvia. In all other groups the changes were not statistically significant. These changes resulted in the educational gradient widening among all groups

Country	Educational level	ASMR (95% CI)		Change 2008–2015 vs. 2000–2007	<i>p</i> – value	Rate ratio (95% CI)	
		2000–2007	2008–2015			2000–2007	2008–2015
Finland	High	1.5 (1.0–1.9)	0.8 (0.5–1.0)	–0.7	0.007	1	1
	Mid	3.4 (2.8–3.9)	2.5 (2.1–2.9)	–0.9	0.012	2.4 (1.7–3.4)	3.0 (2.0–4.5)
	Low	5.7 (4.9–6.5)	6.1 (5.1–7.1)	0.4	0.542	3.8 (2.7–5.2)	7.1 (4.8–10.5)
Estonia	High	5.1 (3.4–6.9)	3.0 (1.8–4.2)	–2.1	0.046	1	1
	Mid	8.2 (6.5–9.9)	6.7 (5.3–8.1)	–1.5	0.171	1.6 (1.1–2.4)	2.1 (1.4–3.4)
	Low	17.0 (13.3–20.7)	17.8 (13.6–22.0)	0.8	0.779	3.3 (2.2–4.9)	5.5 (3.5–8.7)
Latvia	High	2.0 (0.9–3.1)	1.1 (0.3–1.9)	–0.9	0.194	1	1
	Mid	6.7 (5.6–7.8)	4.8 (3.9–5.6)	–1.9	0.006	3.1 (1.8–5.4)	4.3 (2.1–8.8)
	Low	18.5 (15.2–21.7)	11.3 (8.4–14.2)	–7.2	0.026	8.3 (4.7–14.7)	10.1 (4.8–21.0)
Lithuania	High	2.6 (1.5–3.6)	1.6 (0.9–2.3)	–1.0	0.124	1	1
	Mid	6.9 (6.0–7.8)	5.3 (4.5–6.0)	–1.6	0.007	2.6 (1.7–4.0)	3.2 (2.0–5.1)
	Low	14.6 (11.9–17.3)	15.7 (12.9–18.5)	1.1	0.582	5.5 (3.6–8.4)	9.0 (5.6–14.5)

Table 2. Age-standardised mortality rates per 100,000 person years and mortality rate ratios by educational level for epilepsy in 2000–2015 among men in the 30–74 age group. ASMR age-standardised mortality rate per 100,000 person years, CI confidence interval.

Country	Educational level	ASMR (95% CI)		Change 2008–2015 vs. 2000–2007	<i>p</i> – value	Rate ratio (95% CI)	
		2000–2007	2008–2015			2000–2007	2008–2015
Finland	High	0.4 (0.2–0.7)	0.5 (0.3–0.7)	0.1	0.803	1	1
	Mid	1.0 (0.7–1.3)	1.3 (1.0–1.6)	0.3	0.234	2.5 (1.4–4.4)	2.7 (1.7–4.5)
	Low	3.4 (2.6–4.1)	3.9 (3.0–4.8)	0.5	0.424	8.2 (4.8–14.1)	8.1 (5.0–13.2)
Estonia	High	1.5 (0.8–2.2)	0.4 (0.0–0.7)	–1.1	0.007	1	1
	Mid	1.5 (0.9–2.1)	0.9 (0.4–1.5)	–0.6	0.191	1.0 (0.5–2.0)	2.5 (0.9–7.0)
	Low	7.1 (3.8–10.4)	8.4 (4.2–12.6)	1.3	0.646	3.3 (1.7–6.5)	16.2 (5.9–44.4)
Latvia	High	0.2 (0.0–0.4)	0.2 (0.0–0.5)	0.0	0.803	1	1
	Mid	0.8 (0.5–1.2)	0.8 (0.5–1.1)	0.0	0.826	4.0 (1.0–17.0)	3.3 (1.0–11.1)
	Low	5.3 (3.1–7.5)	4.1 (1.9–6.4)	–1.2	0.465	25.4 (6.0–107.8)	19.2 (5.6–66.0)
Lithuania	High	0.6 (0.2–1.0)	0.5 (0.2–0.9)	–0.1	0.857	1	1
	Mid	1.1 (0.8–1.4)	0.8 (0.5–1.0)	–0.3	0.097	1.8 (0.9–3.9)	1.5 (0.7–3.0)
	Low	5.7 (3.3–8.2)	6.1 (3.8–8.3)	0.4	0.826	7.2 (3.2–16.2)	11.7 (5.8–23.9)

Table 3. Age-standardised mortality rates per 100,000 person years and mortality rate ratios by educational level for epilepsy in 2000–2015 among women in the 30–74 age group. ASMR age-standardised mortality rate per 100,000 person years, CI confidence interval.

in all countries. Thus, compared to high educated individuals, those with mid education had rate ratios ranging from 2.1 (95% CI: 1.4–3.4) (Estonia) to 4.3 (95% CI: 2.1–8.8) (Latvia), while for the low educated, the figures were 5.5 (95% CI: 3.5–8.7) (Estonia) to 10.1 (95% CI: 4.8–21.0) (Latvia).

Among women the results were more variable (Table 3). In 2000–2007, low educated women had higher epilepsy ASMRs compared with the high educated in all countries. Among the high educated, ASMRs ranged from 0.2 (95% CI: 0.0–0.4) (Latvia) to 1.5 (95% CI: 0.8–2.2) (Estonia) per 100,000, for the mid educated from 0.8 (95% CI: 0.5–1.2) (Latvia) to 1.5 (95% CI: 0.9–2.1) (Estonia) and for the low educated from 3.4 (95% CI: 2.6–4.1) (Finland) to 7.1 (95% CI: 3.8–10.4) (Estonia) per 100,000. Rate ratios for the low educated ranged from 3.3 (95% CI: 1.7–6.5) (Estonia) to 25.4 (95% CI: 6.0–107.8) (Latvia) compared to the high educated, while the corresponding figures for the mid educated varied from 1.0 (95% CI: 0.5–2.0) (Estonia) to 4.0 (95% CI: 1.0–17.0) (Latvia). In Finland there was an increase in ASMRs across all educational groups in 2008–2015 compared to 2000–2007 although there was little change in the mortality rate ratios in this period. In contrast, the results varied for women by educational group in the Baltic countries where ASMRs decreased or remained the same among the high and mid educated (in Latvia also among the low educated) but increased among the low educated in Estonia and Lithuania. Except for high educated Estonian women, the changes in ASMRs were not statistically significant. These changes resulted in epilepsy mortality rate ratios rising in the mid and low educated in Estonia and falling in these groups in Latvia; in Lithuania the rate ratio increased for the low educated but decreased for the mid educated. Noticeably, in 2008–2015 the mortality rate ratios of low educated women in the Baltic countries were especially elevated ranging from 11.7 (95% CI: 5.8–23.9) in Lithuania to 19.2 (95% CI: 5.6–66.0) in Latvia.

Results from the sensitivity analysis showed that excluding register-based records had no effect on female epilepsy mortality in 2000–2015 (Appendix 2). For men, the impact varied by period with a small reduction (–2.4%) observed in mortality in 2000–2007 while a small increase (+1.9%) was seen for the 2008–2015 period.

Discussion

This study examined educational differences in epilepsy mortality in the Baltic countries and Finland in 2000–2015. Across the period, ASMRs were much higher among men in the Baltic countries compared to those in Finland, whereas for women, ASMRs were similar across the countries. With the exception of women in Finland, there was a reduction in epilepsy ASMRs among both sexes in all countries during the study period. However, this overall reduction masked differences between men and women across the countries according to their level of education. Specifically, there were reductions in epilepsy mortality among high and mid educated men in all of the countries whereas epilepsy mortality increased among low educated men in three of the four countries. This meant that by the end of the study period the educational gradient that was observed in epilepsy mortality rate ratios in 2000–2007 had become more pronounced and ranged between 5 and 10 for low educated men compared to high educated men in all countries. ASMRs were lower for women and there was more variation in the changes that occurred in epilepsy mortality across country educational groups in 2000–2015. Nevertheless, the inverse educational gradient in epilepsy mortality seen in the earlier period still remained in 2008–2015 in all countries but was especially elevated among low educated women in the Baltic countries where epilepsy mortality rate ratios ranged between 11 and 19.

Comparing our findings with those from other studies in the general population is complicated by a range of issues such as differences in the way epilepsy mortality has been classified¹⁶, the (non-)stratification of the population by sex²⁴, as well as the use of data from different time periods²⁵. However, there is some indication that epilepsy ASMRs may be elevated among men in the Baltic countries compared to some other countries¹⁹. The reduction we observed in epilepsy mortality in nearly every male and female country group across the study period accords with the finding from the Global Burden of Disease Study where overall epilepsy ASMRs across 195 countries and territories fell by 24.5% during the 1990–2016 period. The authors of that study suggested that the reduction might be due to improved access to treatment¹. It can be speculated that this might have also been a factor in the reduction that we observed. However, previous research from Estonia has also shown that not taking anti-seizure medication (ASM) is common¹³ and is linked to an increased mortality risk among individuals with chronic epilepsy²⁶. In Estonia and Latvia most/all of the licensed ASMs are fully reimbursed¹², thus possibly indicating non-adherence to ASMs which may explain the still very high level of epilepsy mortality among men in the Baltic countries.

There was an inverse association between educational level and epilepsy mortality with higher ASMRs in the mid and especially the low educated as compared to the high educated. Although there has been comparatively little research on socioeconomic inequalities in epilepsy mortality to date, our findings are in line with those from previous studies in England and the United States that have linked socioeconomic disadvantage with higher epilepsy mortality^{7,8}. It is possible that various factors might play a role in the increased prevalence of epilepsy mortality among low educated individuals. For example, lower education has been associated with more severe epilepsy as measured by hospitalisation/the frequency of hospitalisations^{27,28}, while other research has linked lower area socioeconomic status (SES) to emergency medical service assignments for seizures²⁹ and individual socioeconomic disadvantage to poor seizure control³⁰. This might be important as seizure frequency and severity have been linked to an increased risk for mortality³¹, specifically, SUDEP³². In turn, greater seizure frequency and severity might stem from ASM non-compliance, which is higher in the low educated³³, and which has also been identified as a separate risk factor for SUDEP³⁴, although this finding remains contested³². Future research should be undertaken in our study countries to determine the role of SES in ASM non-compliance, and whether lower ASM use is linked to mortality, especially as an earlier study from Estonia showed that a large proportion of PWE (22%) were not taking ASMs, indicating a high treatment gap³⁵.

The inverse educational gradient observed in 2000–2007 widened in 2008–2015 with epilepsy mortality increasing among low educated men and women in all countries except Latvia, while it either fell or remained the same for the mid and high educated in all of the countries except among Finnish women. These changes coincided with the onset of the Great Recession in 2008–2009. At that time there was a sharp rise in overall unemployment (especially in the Baltic countries)²², although there is some indication that the low educated may have been disproportionately affected across time³⁶. In addition, for those who remained in work government austerity measures in response to the economic crisis resulted in reduced social benefits as well as wage cuts for public sector workers³⁷. In this context, perceived financial distress might have been important for mortality as it has been linked to ASM non-compliance in other research³⁸. It is also possible that educational differences with respect to access to specialist epilepsy care that have been observed in other settings^{27,39} might have been exacerbated in this period although we observed a sharp fall in epilepsy ASMRs among the low educated in Latvia, where there is some evidence that unmet medical need grew sharply in 2010–2012 due to an inability to afford medical care⁴⁰.

This study has a number of strengths including being able to use across-time population-based register data for four countries to undertake one of the first examinations of the role of socioeconomic differences in epilepsy mortality in the general population. However, the study also has several limitations. First, it should be noted that although we focused on epilepsy as an underlying cause of death, these deaths constitute only a minority of all deaths among PWE. An earlier study that reported on epilepsy mortality in England in 2001–2006 found that epilepsy was recorded as the underlying cause of death on only 48% of the death certificates where epilepsy was mentioned¹⁹. Another study in a well-defined cohort of PWE indicated that even fewer deaths may be recorded as only 7% of death certificates mentioned epilepsy⁴¹. Indeed, a major issue for using death certificates to identify

SUDEP is that it is not a recognised category in ICD-10⁴². Thus, studies that rely on epilepsy as an underlying cause of death will inevitably underestimate epilepsy mortality; however, we do not have any evidence that underestimation is related to specific educational groups. Second, we were not able to control for the potentially confounding effects of early-onset epilepsy and/or epilepsy severity in this study that may have impacted educational attainment. Third, it is possible that other measures of SES besides education, such as wealth/poverty, may have also been important for the observed associations but we lacked the data to examine the independent effects of these factors. Fourth, the small number of epilepsy deaths, especially among the high educated and among women, resulted in large confidence intervals for some of the estimates, and may partly explain the sometimes very large rate ratios measuring educational inequalities. Fifth, although a sensitivity analysis using Latvian data showed that excluding register-only-based records had little impact on overall epilepsy mortality, we cannot discount the possibility that the effect of excluding these data might have varied between different educational groups, which could have affected our results. Finally, given the comparative lack of epidemiological data on epilepsy in the Baltic countries¹², it was not possible to examine our results in terms of factors such as ASM access across the period or the incidence of epilepsy²⁴ that might have helped us to better contextualise our findings. This highlights the urgent need for more epilepsy-related research to be undertaken in the Baltic countries, especially among those with low SES.

In conclusion, this study shows that there are differences in epilepsy mortality in the Baltic countries and Finland by education level and that ASMRs are elevated among men in the Baltic countries compared to their counterparts in Finland. Importantly, inequalities in epilepsy mortality grew among men and women (except among Latvian females) in all of the countries across the study period, highlighting the need for action to reduce the comparatively high epilepsy mortality rates amongst lower educated individuals.

Data availability

The data that support the findings of this study are available from National Statistical Offices, i.e. Statistics Estonia, Statistics Lithuania, Central Statistical Bureau of Latvia and Statistics Finland but restrictions apply on the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with the permission of the data providers.

Received: 21 June 2021; Accepted: 7 March 2022

Published online: 17 March 2022

References

1. GBD. Epilepsy collaborators. Global, regional, and national burden of epilepsy, 1990–2016: a systematic analysis for the global burden of disease study 2016. *Lancet Neurol.* **18**(357–375), 2019. [https://doi.org/10.1016/S1474-4422\(18\)30454-X](https://doi.org/10.1016/S1474-4422(18)30454-X) (2016).
2. Thurman, D. J. *et al.* The burden of premature mortality of epilepsy in high-income countries: a systematic review from the Mortality Task Force of the International League Against Epilepsy. *Epilepsia* **58**, 17–26. <https://doi.org/10.1111/epi.13604> (2017).
3. Levira, F. *et al.* Premature mortality of epilepsy in low- and middle-income countries: a systematic review from the Mortality Task Force of the International League Against Epilepsy. *Epilepsia* **58**, 6–16. <https://doi.org/10.1111/epi.13603> (2017).
4. Suarez-Medina, R. *et al.* Epilepsy mortality trends in Cuba compared with England and Wales: 1987–2010. *Epilepsy Behav.* **85**, 72–75. <https://doi.org/10.1016/j.yebeh.2018.04.031> (2018).
5. Devinsky, O., Spruill, T., Thurman, D. & Friedman, D. Recognizing and preventing epilepsy-related mortality: a call for action. *Neurology* **86**, 779–786. <https://doi.org/10.1212/WNL.0000000000002253> (2016).
6. Beghi, E. & Hesdorffer, D. Prevalence of epilepsy—an unknown quantity. *Epilepsia* **55**, 963–967. <https://doi.org/10.1111/epi.12579> (2014).
7. Wilson, D. A., Malek, A. M., Wagner, J. L., Wannamaker, B. B. & Selassie, A. W. Mortality in people with epilepsy: a statewide retrospective cohort study. *Epilepsy Res.* **122**, 7–14. <https://doi.org/10.1016/j.eplepsyres.2016.01.008> (2016).
8. Morrish, P., Duncan, S. & Cock, H. Epilepsy deaths: learning from health service delivery and trying to reduce risk. *Epilepsy Behav.* **103**, 106473. <https://doi.org/10.1016/j.yebeh.2019.106473> (2020).
9. Roots, A., Ainsaar, M. & Nahkur, O. Economic inequality in satisfaction with healthcare in the Baltic countries during and after the economic crisis (2008–2014). *J Balt Stud* **50**, 21–37 (2019).
10. Waters, H. R. *et al.* Health insurance coverage in Central and Eastern Europe: trends and challenges. *Health Aff.* **27**, 478–486. <https://doi.org/10.1377/hlthaff.27.2.478> (2008).
11. World Health Organisation. Global Health Expenditure Database (GHED). <https://apps.who.int/nha/database/Select/Indicators/en> (WHO, 2016) (Accessed 1 December 2021).
12. Jedrzejczak, J. *et al.* Current status of epilepsy health care for adult patients from central and eastern European Union countries—a survey of members of the Central Europe Epilepsy Experts Working Group. *Seizure* **22**, 452–456. <https://doi.org/10.1016/j.seizure.2013.03.001> (2013).
13. Oun, A., Haldre, S. & Magi, M. Use of antiepileptic drugs in Estonia: an epidemiologic study of adult epilepsy. *Eur. J. Neurol.* **13**, 465–470. <https://doi.org/10.1111/j.1468-1331.2006.01268.x> (2006).
14. Herodes, M., Oun, A., Haldre, S. & Kaasik, A. E. Epilepsy in Estonia: a quality-of-life study. *Epilepsia* **42**, 1061–1073. <https://doi.org/10.1046/j.1528-1157.2001.0420081061.x> (2001).
15. DeGiorgio, C. M., Markovic, D., Mazumder, R. & Moseley, B. D. Ranking the leading risk factors for sudden unexpected death in epilepsy. *Front. Neurol.* **8**, 473. <https://doi.org/10.3389/fneur.2017.00473> (2017).
16. Greenlund, S. F., Croft, J. B. & Kobau, R. Epilepsy by the numbers: epilepsy deaths by age, race/ethnicity, and gender in the United States significantly increased from 2005 to 2014. *Epilepsy Behav.* **69**, 28–30. <https://doi.org/10.1016/j.yebeh.2017.01.016> (2017).
17. Kinney, M. O., McCarron, M. O. & Craig, J. J. The reliable measurement of temporal trends in mortality attributed to epilepsy and status epilepticus in Northern Ireland between 2001–2015. *Seizure* **64**, 16–19. <https://doi.org/10.1016/j.seizure.2018.11.017> (2019).
18. Statistical Office of Estonia, Central Statistical Bureau of Latvia, Statistics Lithuania. 2011 Population and housing censuses in Estonia, Latvia and Lithuania. <https://osp.stat.gov.lt/services-portlet/pub-edition-file?id=19698/> (2015) (Accessed 23 October 2019).
19. Goldacre, M. J., Duncan, M., Griffith, M. & Turner, M. R. Trends in death certification for multiple sclerosis, motor neuron disease, Parkinson's disease and epilepsy in English populations 1979–2006. *J. Neurol.* **257**, 706–715. <https://doi.org/10.1007/s00415-009-5392-z> (2010).
20. World Health Organisation. *International Classification of Diseases and Related Health Problems (10th Revision, Volume 1) Tabular list. Fifth edition.* (WHO, 2016).

21. UNESCO. *International Standard Classification of Education ISCED 2011*. (UNESCO Institute of Statistics, 2012).
22. World Bank. World Bank Open Data. <http://data.worldbank.org> (2019) (Accessed 10 December 2019).
23. Waterhouse, J., Muir, C. S., Correa, P. & Powell, J. *Cancer Incidence in Five Continents*. (IARC, 1976).
24. Neligan, A. & Walker, M. C. Falling status epilepticus mortality rates in England and Wales: 2001–2013?. *Epilepsia* **57**, e121–124. <https://doi.org/10.1111/epi.13402> (2016).
25. Bruce, M., Griffiths, C., Brock, A. & Majeed, A. Trends in mortality and hospital admissions associated with epilepsy in England and Wales during the 1990s. *Health Stat. Q.* **21**, 23–29 (2004).
26. Rakitin, A., Liik, M., Oun, A. & Haldre, S. Mortality risk in adults with newly diagnosed and chronic epilepsy: a population-based study. *Eur. J. Neurol.* **18**, 465–470. <https://doi.org/10.1111/j.1468-1331.2010.03195.x> (2011).
27. Andersson, K. *et al.* Socioeconomic outcome and access to care in adults with epilepsy in Sweden: a nationwide cohort study. *Seizure* **74**, 71–76. <https://doi.org/10.1016/j.seizure.2019.12.001> (2020).
28. Li, X., Sundquist, J. & Sundquist, K. Socioeconomic and occupational risk factors for epilepsy: a nationwide epidemiological study in Sweden. *Seizure* **17**, 254–260. <https://doi.org/10.1016/j.seizure.2007.07.011> (2008).
29. Magnusson, C. & Zelano, J. High-resolution mapping of epilepsy prevalence, ambulance use, and socioeconomic deprivation in an urban area of Sweden. *Epilepsia* **60**, 2060–2067. <https://doi.org/10.1111/epi.16339> (2019).
30. Tian, N., Boring, M., Kobau, R., Zack, M. M. & Croft, J. B. Active epilepsy and seizure control in adults - United States, 2013 and 2015. *MMWR Morb. Mortal. Wkly. Rep.* **67**, 437–442. <https://doi.org/10.15585/mmwr.mm6715a1> (2018).
31. Forsgren, L. *et al.* Mortality of epilepsy in developed countries: a review. *Epilepsia* **46**(Suppl 11), 18–27. <https://doi.org/10.1111/j.1528-1167.2005.00403.x> (2005).
32. Watkins, L., Shankar, R. & Sander, J. W. Identifying and mitigating Sudden Unexpected Death in Epilepsy (SUDEP) risk factors. *Expert Rev. Neurother.* **18**, 265–274. <https://doi.org/10.1080/14737175.2018.1439738> (2018).
33. Malek, N., Heath, C. A. & Greene, J. A review of medication adherence in people with epilepsy. *Acta Neurol. Scand.* **135**, 507–515. <https://doi.org/10.1111/ane.12703> (2017).
34. Hughes, J. R. A review of sudden unexpected death in epilepsy: prediction of patients at risk. *Epilepsy Behav.* **14**, 280–287. <https://doi.org/10.1016/j.yebeh.2008.12.004> (2009).
35. Oun, A., Haldre, S. & Magi, M. Prevalence of adult epilepsy in Estonia. *Epilepsy Res.* **52**, 233–242. [https://doi.org/10.1016/s0920-1211\(02\)00234-6](https://doi.org/10.1016/s0920-1211(02)00234-6) (2003).
36. Brixiova, Z. & Egert, B. Labour market reforms and outcomes in Estonia. *Comp. Econ. Stud.* **54**, 103–120 (2012).
37. Kattel, R. & Raudla, R. The Baltic republics and the crisis of 2008–2011. *Eur. Asia Stud.* **65**, 426–449 (2013).
38. Burneo, J. G. *et al.* Disparities in epilepsy: report of a systematic review by the North American Commission of the International League Against Epilepsy. *Epilepsia* **50**, 2285–2295. <https://doi.org/10.1111/j.1528-1167.2009.02282.x> (2009).
39. Mattsson, P., Tomson, T., Eriksson, O., Brannstrom, L. & Weitoft, G. R. Sociodemographic differences in antiepileptic drug prescriptions to adult epilepsy patients. *Neurology* **74**, 295–301. <https://doi.org/10.1212/WNL.0b013e3181cbcd5c> (2010).
40. Karanikolos, M., Gordeev, V. S., Mackenbach, J. P. & McKee, M. Access to care in the Baltic States: did crisis have an impact?. *Eur. J. Public Health* **26**, 236–241. <https://doi.org/10.1093/eurpub/ckv205> (2016).
41. Bell, G. S., Gaitatzis, A., Johnson, A. L. & Sander, J. W. Predictive value of death certification in the case ascertainment of epilepsy. *J. Neurol. Neurosurg. Psychiatry* **75**, 1756–1758. <https://doi.org/10.1136/jnnp.2003.029918> (2004).
42. Neligan, A. & Walker, M. C. In response: comment on falling status epilepticus mortality rates in England and Wales: 2001–2013. *Epilepsia* **57**, 1732–1733. <https://doi.org/10.1111/epi.13554> (2016).

Author contributions

A.S. and M.L. conceptualised the study. M.L., D.J., J.K., P.M. oversaw data acquisition. M.L. analysed the data. A.S. and M.L. drafted and revised the manuscript. A.N., A.B., D.J., J.K., P.M., N.K., T.S., J.I.S., H.O., and K.W. contributed to interpreting the data and drafting and revising the manuscript. M.L. is the guarantor. All authors read and approved the submitted version of the manuscript.

Funding

Open access funding was provided by Södertörn University. The data collection for this study was financed by *Riksbankens Jubileumsfond* – The Swedish Foundation for Humanities and Social Sciences (grant P15-0520:1). The work by ML and AB was also supported by institutional funding to the National Institute for Health Development, Estonia. The work by DJ has been supported by the Max Planck Society within the framework of the project “On the edge of societies: New vulnerable populations, emerging challenges for social policies and future demands for social innovation. The experience of the Baltic Sea States” (2016–2021). PM was supported by the Academy of Finland (#308247, # 345219), the European Research Council under the European Union’s Horizon 2020 research and innovation programme (grant agreement No 101019329), and the NordForsk grant for the project WELLIFE (#83540). JK was supported by the Latvian National Research Project “DemoMig”.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1038/s41598-022-08456-x>.

Correspondence and requests for materials should be addressed to M.L.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher’s note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

© The Author(s) 2022