Journal of Asthma and Allergy

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Level of Education Modifies Asthma Mortality in Norway and Sweden. The Nordic EpiLung Study

Helena Backman[1,*], Laxmi Bhatta[2,3,*], Linnea Hedman[1], Ben Brumpton[2], Iida Vähätalo[4,5], Paul G Lassmann-Klee[6], Bright I Nwaru[7], Linda Ekerljung[7], Steinar Krokstad[8,9], Sigrid Anna Aalberg Vikjord[2], Anne Lindberg[10], Hannu Kankaanranta[7], Eva Rönmark[1,*], Arnulf Langhammer[8,*]

[1]Section of Sustainable Health/ the OLIN Unit, Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden; [2]K.G. Jebsen Center for Genetic Epidemiology, Department of Public Health and Nursing, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology NTNU, Trondheim, Norway; [3]Division of Mental Health Care, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway; [4]Department of Respiratory Medicine, Seinäjoki Central Hospital, Seinäjoki, Finland; [5]Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland; [6]Clinical Physiology and Nuclear Medicine Unit, Helsinki University Hospital's Diagnostic Center and University of Helsinki, Helsinki, Finland; [7]Krefting Research Centre, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [8]HUNT Research Centre, Department of Public Health and Nursing, NTNU, Norwegian University of Science and Technology, Levanger, Norway; [9]Nord-Trøndelag Hospital Trust, Levanger Hospital, Levanger, Norway; [10]Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

*These authors contributed equally to this work

Correspondence: Helena Backman, Email helena.backman@norrbotten.se

Background and Aim: The relationship between socioeconomic status (SES), asthma and mortality is complex and multifaceted, and it is not established if educational level modifies the association between asthma and mortality. The aim was to study the association between asthma and mortality in Sweden and Norway and to what extent educational level modifies this association.

Participants and Methods: Within the Nordic EpiLung Study, >56,000 individuals aged 30–69 years participated in population-based surveys on asthma and associated risk factors in Sweden and Norway during 2005–2007. Data on educational level and 10-year all-cause mortality were linked by national authorities. The fraction of mortality risk attributable to asthma was calculated, and Cox regression was used to estimate hazard ratios (HR) and 95% confidence intervals (95% CI) for mortality related to asthma, stratified by educational level.

Results: In total, 5.5% of all deaths was attributed to asthma. When adjusted for potential confounders, the HR for mortality related to asthma was 1.71 (95% CI 1.52–1.93). Those with primary level of education had higher hazard of all-cause death related to asthma than those with tertiary level (HR 1.80, 95% CI 1.48–2.18, vs HR 1.39, 95% CI 0.99–1.95).

Conclusion: Asthma was associated with an overall 71% increased all-cause mortality and 5.5% of deaths can be attributed to asthma. Educational levels modified the risk of mortality associated with asthma, with the highest risk among those with primary education.

Keywords: epidemiology, cohort, prognosis

Introduction

Asthma is a common and disabling disease, with an estimated cumulative prevalence of 8–10% among adults in Western Europe, including the Nordic countries.[1,2] Along with increasing asthma prevalence, a surge in asthma mortality was seen between the 1960s and 1980s. The increased mortality from asthma could later at least partly be attributed to overuse of the β_2-agonist fenoterol. The mortality declined substantially following stricter regulations, less use,[3] and the introduction of the inhaled corticosteroid (ICS) based asthma treatment approach.[4]

Today, age-standardized mortality rates for asthma are low in most parts of Europe (0.7–0.9 per 100,000 in 2019 in the Nordic countries).[5] Causes of death may be misclassified or incomplete at higher ages,[6,7] especially when asthma is

Received: 16 November 2023
Accepted: 1 March 2024
Published: 18 March 2024

one component in a multi-morbid patient. Assessment of all-cause mortality is important to capture the entire burden of this common disease.

The Nordic countries are welfare states with high educational level. Despite similarities in legislation, culture and traditions, there are differences in mortality between and within these countries, partly related to socioeconomic factors.[8–10] Although respiratory disease[11] and low socioeconomic status (SES) both may be associated with mortality, it is unclear whether and to what extent education may modify mortality among individuals with asthma in these countries. Education by itself might improve health literacy[12] and asthma control[13] but it is also important to recognize other lifestyle factors that are related to both educational level and asthma control which can act as mediators between these two, such as obesity and smoking.

The Nordic EpiLung Study is a consortium with a remit to catalyze population-based surveys and Nordic registers to understand the contribution of SES to the burden of obstructive airway diseases across the Nordic countries. Within this framework, the large population-based Obstructive Lung Disease in Northern Sweden (OLIN) Studies, the West Sweden Asthma Study (WSAS), and the Trøndelag Health Study (HUNT) in mid-Norway collaborate. The aim here was to study 1) if asthma still is a risk factor for mortality and 2) how educational level influences asthma related mortality.

Materials and Methods

Study Populations

OLIN and WSAS in Sweden

In 2006, a postal questionnaire was sent to 7997 randomly sampled individuals aged 20–69 years residing in Norrbotten, the northernmost county of Sweden, within the framework of the OLIN studies, and n = 6165 (77% of invited) participated.[2] In 2008, the same questionnaire was sent to a random sample of n = 30,000 aged 17–74 years in the region of Västra Götaland within the WSAS, and n = 18,087 (60%) responded.[14] The questionnaire includes questions on asthma, respiratory symptoms including wheeze and attacks of shortness of breath, asthma medication use, and related factors such as smoking. The questionnaire has been used in several national and international surveys[2] and is validated.[15] In order to include a working-age sample, data from participants 30–69 years of age from OLIN (n=5224) and WSAS (n = 13,132) were pooled, resulting in a total sample size of 18,356.

HUNT in Norway

During 2006–2008, all residents aged 20 years or older in northern Trøndelag county (located in central Norway) were invited to questionnaires, interview, and clinical examinations in the third survey of HUNT. Totally, 50,807 participated (54% of invited).[16] During the HUNT3 Survey, all participants were asked to provide information on having/ever had asthma or attacks of wheeze and/or shortness of breath. In the HUNT3 Lung Study, further detailed data on respiratory symptoms and asthma medication use was obtained. In total, 37,973 participants aged 30–69 years were included in the current study.

Ethical Approvals

All participants provided written informed consent, and the Swedish Ethical Review Authority (2023-00773-01) and The Regional Committee for Medical and Health Research Ethics in Norway (2017/2364/REK midt) approved the studies. The study complied with the declaration of Helsinki.

Asthma

Current asthma was defined as self- reported ever having had asthma in combination with at least one of the following during the last 12 months: a) any wheeze, b) shortness of breath or c) use of asthma medication.

Smoking and Educational Level

Smoking habits were categorized as non-smokers, ex-smokers (having quit more than one year earlier), or smokers. Smokers were further divided by the average number of cigarettes smoked daily into three groups: a) <5, b) 5–14, or c) >14 cigarettes/day. A dichotomized variable including ever smokers (current and ex-smokers) and never smokers was also created.

Educational level was linked from the national LISA database in Sweden and Statistics Norway in Norway as a proxy measure of SES and grouped into primary (<12 years), upper secondary (12–13 years), and tertiary (ie, university) education.

Mortality

Data on 10-year all-cause mortality was linked from the Swedish and Norwegian Cause of Death Registers. In WSAS, the number of person-years in the study was available as whole years only, in contrast to person-years with one decimal point in OLIN and HUNT.

Statistical Analysis

SPSS version 26 (IBM), Stata version 15.1 (StataCorp., College Station, Texas) and R 4.2.1 software (http://www.r-project.org) were used for statistical calculations. All statistics were calculated separately for Sweden and Norway. Chi-square tests were performed to compare proportions across groups, and *t*-test or ANOVA, as appropriate, to compare means. Mortality incidence curves were computed. P-values <0.05 were considered statistically significant.

Cox proportional hazards regression models were used to estimate hazard ratios (HR) with 95% confidence intervals (CI) for the association between current asthma and mortality. The regression analyses were performed crude and adjusted, with age, sex and smoking as covariates in the models. The smoking covariate included the following five categories: non-smokers, former smokers, and current smokers divided into three groups: a) <5, b) 5–14, or c) >14 cigarettes/day. The models based on Swedish data were additionally adjusted for cohort (WSAS/OLIN). These analyses were performed among all and also stratified by educational level, smoking habits and sex. Schoenfeld's global test to test the proportional hazards assumption in the Cox proportional hazards model was applied.

Meta-analysis with fixed effect was used to pool estimates from the regression models from both countries, using the *metafor* package in R. The proportion (%) of mortality risk attributable to current asthma, ie, the attributable risk, was calculated according to Levin's formula, as follows (based on crude HR): $P_a(HR - 1)/(P_a[HR - 1] + 1) * 100$, where P_a is the prevalence of asthma.

Supplementary Analysis

The regression analyses were also performed without smoking as covariate in the models, as smoking can be considered downstream in the causal pathway from educational level. As data on body mass index (BMI), physical activity and comorbidity (cardiovascular disease, blood pressure medication, diabetes, anxiety, and depression) were available in HUNT, we additionally adjusted for these variables in the Norwegian sample. As further supplementary materials, Cox proportional hazards regression models were used to estimate HR with 95% CI for the association between educational level (with tertiary education as reference category) and mortality among participants with and without current asthma. These models were performed crude, as well as adjusted for age, sex and smoking. The models based on Swedish data were additionally adjusted for cohort (WSAS/OLIN). The statistical interaction between current asthma and educational level was evaluated by including current asthma, educational level and an interaction term for these two variables as covariates in the Cox regression models among all participants described above.

Results

Characteristics at Baseline

In Sweden, the proportion of women was 53.1 and the mean age 49.9 years, with corresponding figures of 54.0% and 50.9 years in Norway. In Sweden, 16.7% were current smokers and 15.7% had primary educational level, compared to 27.6% and 21.0% in Norway. In Norway, the proportion with primary educational level was 20.6% in participants without current asthma and 26.1% in those with current asthma, while it was 15.7% regardless of having current asthma or not in Sweden (Table 1).

Table 1 Baseline Characteristics in Sweden and Norway, Among Participants with and without Asthma, and Among All

Characteristics		Sweden			Norway		
		Without Asthma N=16825	With Asthma N=1531	All N=18356	Without Asthma N=35108	With Asthma N=2865	All N=37973
Age	Mean (SD)	50.0 (11.3)	48.7 (11.2)	49.9 (11.3)	50.8 (10.5)	51.5 (10.9)	50.9 (10.6)
Sex	Women	52.5%	59.4%	53.1%	53.6%	58.3%	54.0%
Smoking	Non-smokers	58.6%	52.1%	58.1%	41.2%	31.2%	40.5%
	Ex-smokers	24.9%	28.9%	25.2%	31.6%	36.5%	31.9%
	Current smokers	16.4%	19.0%	16.7%	27.2%	32.3%	27.6%
Number of cigarettes/day Among current smokers	<5 cig/day	4.0%	4.7%	4.1%	1.2%	0.9%	1.2%
	5–14 cig/day	7.2%	8.5%	7.3%	13.2%	15.7%	13.3%
	>14 cig/day	4.2%	4.0%	4.2%	6.3%	10.0%	6.6%
	Missing	1.0%	1.8%	1.1%	6.5%	5.7%	6.5%
Educational level	Primary	15.7%	15.7%	15.7%	20.6%	26.1%	21.0%
	Upper secondary	52.4%	57.0%	52.8%	51.1%	51.5%	51.1%
	Tertiary	31.9%	27.3%	31.5%	28.3%	22.4%	27.9%

Notes: Characteristics are presented as column percent (%) except for age which is presented as mean (standard deviation).
Abbreviation: N, Number of individuals.

Low Educational Level as Risk Factor for Mortality

Persons with primary compared to tertiary education had higher mortality in both countries independent of having asthma or not (Table 2, Supplemental Table 1), also when stratified for smoking (Supplemental Tables 2 and 3).

Asthma as Risk Factor for Mortality

Current asthma was significantly associated with higher all-cause 10-year mortality in both countries (Figure 1), in Sweden with 6.7 vs 5.0 deaths/1000 person-years in individuals with vs without asthma, and with corresponding figures of 7.6 vs 3.8 in Norway (Table 2). When pooled, 5.5% of deaths were attributable to current asthma. The hazard ratios (HR) for current asthma were 1.58 (95% CI 1.28–1.95) in Sweden, 1.78 (1.54–2.06) in Norway, and a pooled adjusted estimate of 1.71 (1.52–1.93) when adjusted for age, sex and smoking (Figure 2). The association between current asthma and mortality was slightly stronger in women than men with HR 1.84 (95% CI 1.56–2.19) in women and 1.61 (1.36–1.90) in men, and in ever-smokers compared to non-smokers (HR 1.79 (1.56–2.05) vs 1.48 (95% CI 1.14–1.92)) (Figure 3).

Table 2 10-Year Mortality and Attributable Mortality Risk Due to Asthma, Stratified by Educational Level and Among All

Educational Level	Sweden				Norway				All
	Without Asthma N (per 1000 PY)	With Asthma N (per 1000 PY)	All N (Per 1000 PY)	Proportion (%) of Mortality Risk Attributable to Asthma	Without Asthma N (per 1000 PY)	With Asthma N (per 1000 PY)	All N (Per 1000 PY)	Proportion (%) of Mortality Risk Attributable to Asthma	Proportion (%) of Mortality Risk Attributable to Asthma
Primary	272 (10.9)	33 (14.7)	305 (11.2)	2.8%	420 (6.0)	91 (12.9)	511 (6.6)	10.0%	7.6%
Upper secondary	397 (4.6)	53 (6.3)	450 (4.8)	3.3%	668 (3.8)	97 (6.8)	765 (4.0)	5.7%	4.8%
Tertiary	148 (2.8)	13 (3.2)	161 (2.8)	0.9%	240 (2.4)	24 (3.8)	264 (2.5)	3.2%	2.4%
Total	817 (5.0)	99 (6.7)	916 (5.1)	2.8%	1328 (3.8)	212 (7.6)	1540 (4.1)	7.0%	5.5%

Notes: The proportion of mortality risk attributable to asthma was calculated using Levin's formula (please see methods section for details).
Abbreviation: N=Number of individuals, PY=Person-years.

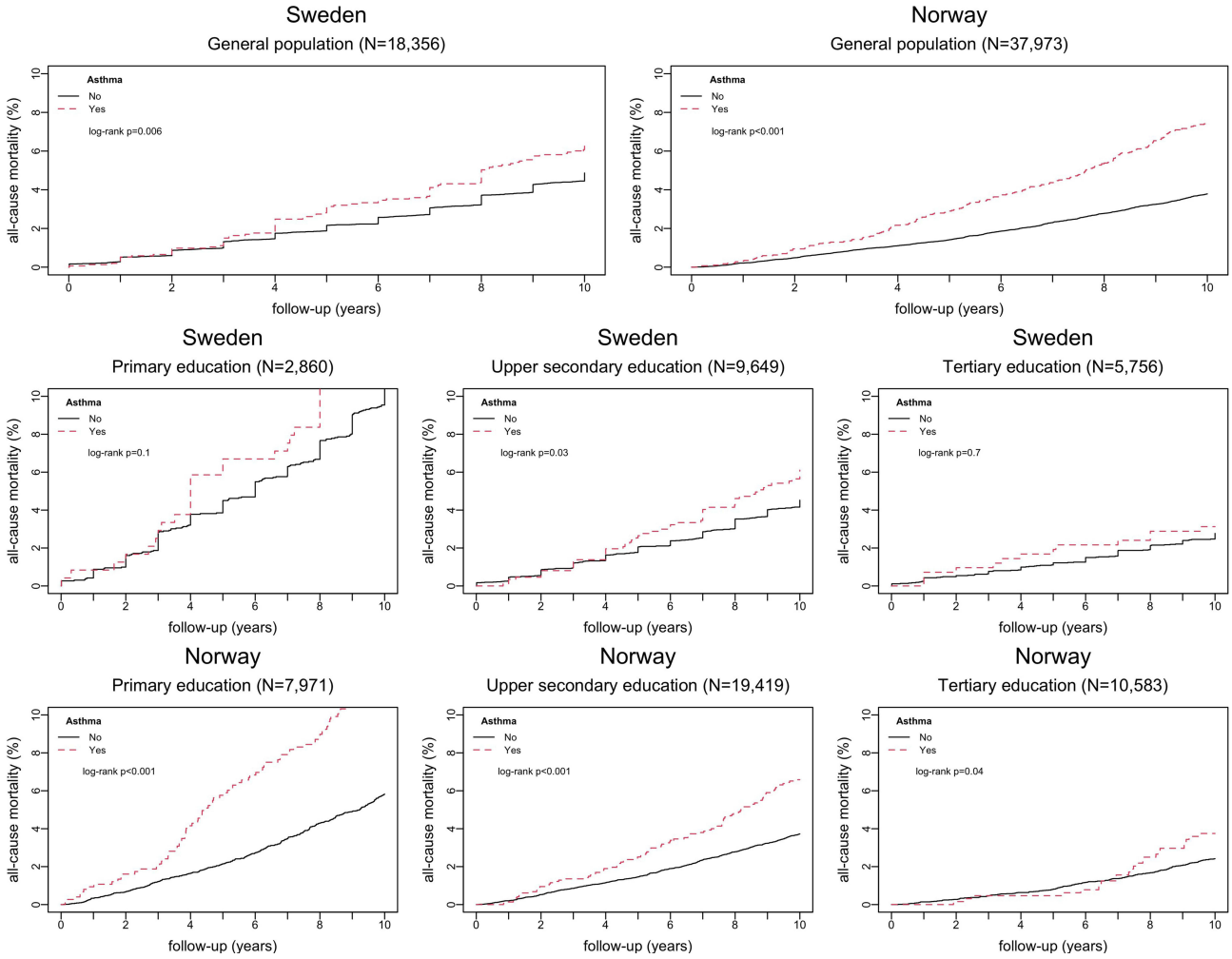

Figure 1 Mortality incidence curves among adults with asthma (red) compared to without asthma (black) and stratified by education.

Influence of Educational Level on Mortality Associated to Asthma

Stratification by level of education showed higher hazard for death related to current asthma by lower education with pooled adjusted HR 1.80 (1.48–2.18), HR 1.70 (1.43–2.02) and HR 1.39 (0.99–1.95) in those with primary school, upper secondary and tertiary education, respectively. This gradient was slightly clearer in Norway than in Sweden, but in both countries, the risk was lowest in those with tertiary education (Figure 2). The analysis on interaction between asthma and educational level yielded a pooled crude HR of 1.16 (95% CI 0.97–1.39) and adjusted HR of 1.12 (95% CI 0.94–1.34). Similar estimates were found in both sexes and in both countries (Figure 3), and inclusion of BMI, physical activity and comorbidity as covariates in the Norwegian data did not alter the results (Supplemental Table 4). Further, adjusting for age and sex only and not for smoking or BMI also yielded similar findings (Supplemental Table 5). Stratifying for smoking yielded wider confidence intervals and slightly less clear associations in non-smokers than in ever-smokers, but the association between current asthma and mortality was consistently weakest among those with tertiary education, regardless of smoking habits (Figure 3).

Discussion

In summary, this study of >56,000 working-age adults from two affluent Nordic countries showed that current asthma was associated with about 71% increased risk for all-cause mortality, and that 5.5% of all deaths could be attributed to asthma. Asthma was associated with increased all-cause mortality in both sexes and in ever-smokers as well as in non-smokers.

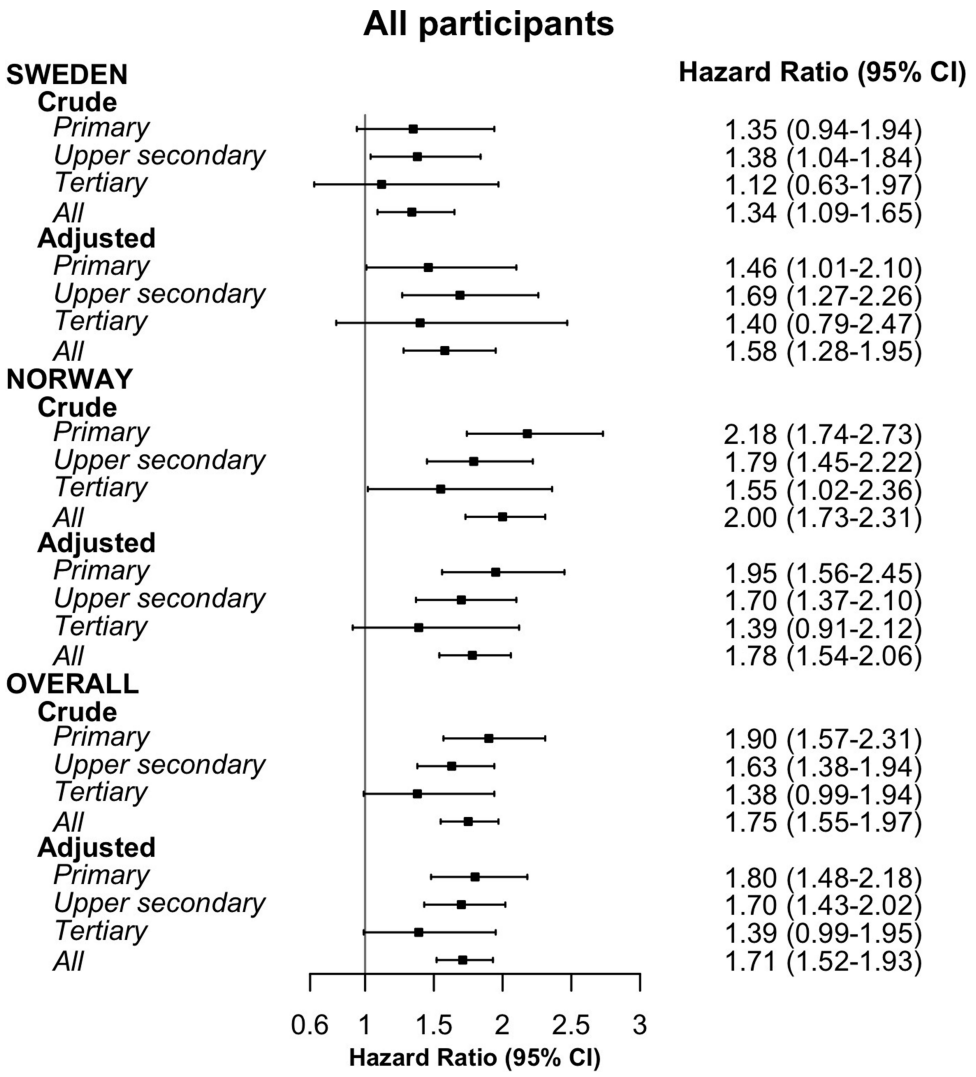

Figure 2 Asthma as a risk factor for 10-year mortality, among all participants and stratified by educational levels. Results are expressed as Hazard ratios with 95% Confidence intervals (CI) from crude Cox proportional hazard models, and from models adjusted for age, sex and smoking.

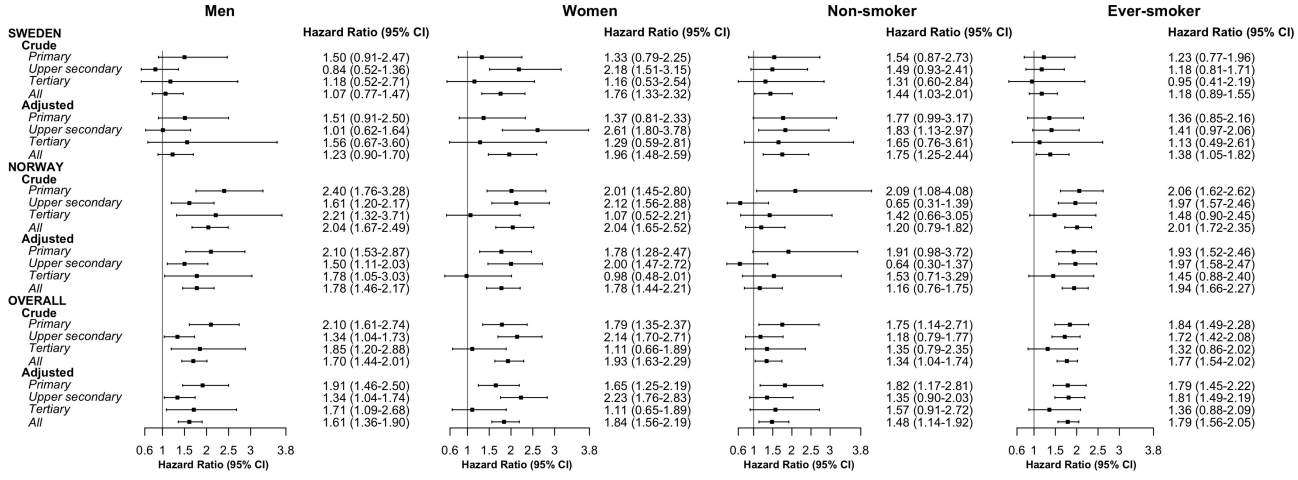

Figure 3 Asthma as a risk factor for 10-year mortality, among men, women, non-smokers, and ever-smokers, in all and stratified by educational levels. Results are expressed as Hazard ratios with 95% Confidence intervals (CI) from crude Cox proportional hazard models, and from models adjusted for age, sex and smoking.

When comparing the hazard of all-cause mortality related to current asthma by level of education, the risk was most increased in individuals with primary educational level and lowest in individuals with tertiary educational level.

We found a substantially increased mortality related to asthma. Ours is one of the first population-based studies reporting an increased all-cause mortality among adults with asthma vs those without asthma in the high income countries Norway and Sweden. In line with our findings of a substantially increased mortality, one Swedish register-based study on children and young adults found an increase in all-cause mortality related to asthma,[17] and population-based studies from the 1990s on adults in the neighboring Finland[18,19] and Denmark[20–22] have yielded similar results. There is also one Finnish study with data from early 2000s,[23] and results from both the US[11] and other European countries[24,25] that support an increased risk for all-cause mortality related to having asthma in adulthood, although there are also a few studies showing no such increased risk.[25,26]

In low-income countries, overuse of short-acting beta$_2$-agonists is a potential explanation for increased mortality in individuals with asthma as patients cannot afford to buy costly asthma medication such as ICS. In Norway and Sweden, such treatment is reimbursed, and costs should have less influence on purchased treatment.[10] However, lack of adherence is a problem in all countries. New guidelines[27] recommend use of ICS whenever the patient uses SABA, and specifically ICS-formoterol both as maintenance and reliever medication. This reduces the risk of severe exacerbations and hospitalizations[28] and could be expected to decrease mortality[29] when this change is implemented in health care. This treatment approach is recommended in Norway from 2022 and in Sweden from 2023.

Some individuals with asthma develop chronic airway obstruction and COPD, mainly due to tobacco smoking but also due to more severe disease with ongoing inflammation. For some years the co-existence of asthma and COPD has been labelled Asthma COPD Overlap (ACO), and it has been shown that these patients have more respiratory symptoms, more exacerbations, poor quality of life, more rapid decline in lung function, higher mortality than patients with asthma or COPD alone.[30,31] In contrast to our findings, a large population-based Danish study found an increased asthma-related risk for all-cause mortality among smokers but not among never-smokers.[32] We found associations between asthma and mortality both in non-smokers and in ever-smokers, even though the risk was slightly more increased in ever-smokers, indicating an independent association.

Level of education influenced mortality related to asthma in our study, as we found the highest risk in those with primary education, while the risk was lowest in those with tertiary education, although no significant statistical interaction was found. Several studies have found that individuals with lower levels of education are more likely to have asthma than those with higher levels of education,[33,34] and there are several potential explanations for this relationship. Individuals with lower levels of education may, eg, be more likely to work in jobs that expose them to environmental triggers for asthma, such as air pollution or irritants in the workplace.[27,35] They may also have less access to healthcare and be less likely to afford or seek medical treatment for their symptoms, which could lead to worse asthma control and clinical outcomes.[13]

Additionally, low educational level increases the risk for life style factors related to poorer health outcomes,[9] such as smoking, less healthy diet or lack of exercise, which can contribute to the development of asthma.[34] Low education can also relate to low asthma control,[13] level of health literacy[12] and less knowledge and understanding about asthma and how to effectively manage the disease, including adherence to medications and improper inhaler technique.[36] Further, individuals with lower levels of education may be more likely to experience anxiety, which can worsen asthma symptoms.[37] Additionally, they may not have access to resources to manage their stress or mental health, which potentially can further exacerbate their asthma.

It is important to note that the relationship between SES and asthma is complex and likely influenced by multiple factors. As these are mainly downstream from educational level in the pathway to asthma, they should not be adjusted for when analyzing relationships with SES, but are certainly of utmost importance for enabling preventive measures. Nevertheless, to enable comparisons with another studies, we performed our analyses crude and also adjusted for smoking and BMI which are risk factors for a plethora of adverse health outcomes. However, adjustment meant only minor changes of our estimates. however. More research is needed to fully understand the mechanisms mediating this relationship and to develop effective interventions to reduce the burden of asthma in individuals with low educational attainment. Addressing educational disparities and increasing access to healthcare and resources has the potential to reduce asthma disparities and improve health on a population level.

Regarding limitations of the current study, we cannot exclude residual confounding, eg, by tobacco smoking. In attempt to investigate this, we stratified the analyses for sex and smoking habits and found associations between asthma and mortality in both men and women and never- and ever smokers, which is supportive of our findings of increased all-cause mortality

among individuals with asthma. Another limitation in the stratified analyses was that we combined current and former smokers into one ever smoker category, which was necessary to keep statistical power. Current asthma was further defined by self-report instead of clinical examinations including spirometry, and thus the validity could be questioned. In Sweden, clinical validation studies on the survey question about physician-diagnosed asthma in adults with incident asthma have, however, shown a positive predictive value of >90%.[38] Those with well-controlled asthma may not be included in our definition of current asthma, and one could speculate that misclassification of these people may have attenuated the results. Regarding strengths, large population samples from two countries were included, yielding a total sample size of >56,000. Valid data on educational level and all-cause mortality were linked from national registries in Sweden and Norway and none or only limited selection bias has been found in the epidemiological surveys.[14,16,39]

Conclusion

In conclusion, asthma associated with a 71% increased risk for all-cause mortality and about 5.5% of deaths from all causes can be attributed to asthma. Educational level modified the risk of mortality associated with asthma, as the risk was highest in individuals with primary educational level and lowest in individuals with tertiary educational level.

Abbreviations

ATS, American Thoracic Society; BMI, Body Mass Index; COPD, Chronic Obstructive Pulmonary Disease; CI, Confidence Interval; ERS, European Respiratory Society; HR, Hazard Ratio; HUNT, Trøndelag Health Study; SES, Socioeconomic status; ICS, Inhaled Corticosteroids; OLIN, Obstructive Lung Disease in Northern Sweden; WSAS, West Sweden Asthma Study.

Acknowledgments

Helena Backman and Laxmi Bhatta are co-first authors of this study. Eva Rönmark and Arnulf Langhammer are co-senior authors of this study. We would especially like to acknowledge the participants in the OLIN, WSAS and HUNT studies. Also, the late Bo Lundbäck, founder of the OLIN and WSAS studies, and the research staff is acknowledged for their excellent work.

The Trøndelag Health Study (HUNT) is a collaboration between HUNT Research Centre (Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology NTNU), Trøndelag County Council, Central Norway Regional Health Authority, and the Norwegian Institute of Public Health.

Funding

Financial support was provided by the Nordic Council, the Swedish Research Council for Health, Working Life and Welfare (FORTE, Dnr 2022-00381), the Swedish Research Council, the Swedish Heart-Lung foundation, Northern County Councils' Regional Federation, a regional agreement between Umeå University and Västerbotten County Council (ALF), Region Norrbotten, the VBG Group Herman Krefting Foundation for Asthma and Allergy Research, Sweden, the Swedish Asthma and Allergy Foundation, and ALF agreement (Grants from the Swedish state under the agreement between the Swedish Government and the county councils). LB and BB received support from the K.G. Jebsen Center for Genetic Epidemiology funded by Stiftelsen Kristian Gerhard Jebsen; Faculty of Medicine and Health Sciences, NTNU; The Liaison Committee for education, research and innovation in Central Norway; and the Joint Research Committee between St Olavs Hospital and the Faculty of Medicine and Health Sciences, NTNU.

Disclosure

HB reports personal fees from AstraZeneca, Boehringer Ingelheim and GSK, outside the submitted work. SAAV reports personal fees from AstraZeneca, outside the submitted work. ALi reports personal fees from AstraZeneca, Boehringer Ingelheim, GSK and Novartis, outside the submitted work. HK reports personal fees from GSK, Boehringer Ingelheim, AstraZeneca, MSD, Novartis, Orion Pharma and SanofiGenzyme, outside the submitted work. ALa reports personal fees from SanofiGenzyme, outside the submitted work. The authors report no other conflicts of interest in this work.

References

1. Langhammer A, Johnsen R, Gulsvik A, Holmen TL, Bjermer L. Sex differences in lung vulnerability to tobacco smoking. *Eur Respir J*. 2003;21(6):1017–1023. doi:10.1183/09031936.03.00053202
2. Backman H, Raisanen P, Hedman L, et al. Increased prevalence of allergic asthma from 1996 to 2006 and further to 2016-results from three population surveys. *Clin Exp Allergy*. 2017;47(11):1426–1435. doi:10.1111/cea.12963
3. Pearce N, Beasley R, Crane J, Burgess C, Jackson R. End of the New Zealand asthma mortality epidemic. *Lancet*. 1995;345(8941):41–44. doi:10.1016/S0140-6736(95)91159-6
4. Ebmeier S, Thayabaran D, Braithwaite I, Benamara C, Weatherall M, Beasley R. Trends in international asthma mortality: analysis of data from the WHO mortality database from 46 countries (1993-2012). *Lancet*. 2017;390(10098):935–945. doi:10.1016/S0140-6736(17)31448-4
5. International Respiratory Coalition, European Respiratory Society. Lung Facts, Asthma, based on the Global Burden of Disease Database; 2023. Available from: https://international-respiratory-coalition.org/diseases/asthma/. Accessed October 16, 2023.
6. Reid DW, Hendrick VJ, Aitken TC, Berrill WT, Stenton SC, Hendrick DJ. Age-dependent inaccuracy of asthma death certification in Northern England, 1991-1992. *Eur Respir J*. 1998;12(5):1079–1083. doi:10.1183/09031936.98.12051079
7. Johansson LA, Bjorkenstam C, Westerling R. Unexplained differences between hospital and mortality data indicated mistakes in death certification: an investigation of 1,094 deaths in Sweden during 1995. *J Clin Epidemiol*. 2009;62(11):1202–1209. doi:10.1016/j.jclinepi.2009.01.010
8. Mackenbach JP. Health inequalities in Europe. how does Norway compare? *Scand J Public Health*. 2019;47(6):666–671. doi:10.1177/1403494819857036
9. Mackenbach JP, Stirbu I, Roskam AJ, et al. Socioeconomic inequalities in health in 22 European countries. *N Engl J Med*. 2008;358(23):2468–2481. doi:10.1056/NEJMsa0707519
10. Vinjerui KH, Bjorngaard JH, Krokstad S, Douglas KA, Sund ER. Socioeconomic position, multimorbidity and mortality in a population cohort: the HUNT study. *J Clin Med*. 2020;9(9):2759. doi:10.3390/jcm9092759
11. He X, Cheng G, He L, et al. Adults with current asthma but not former asthma have higher all-cause and cardiovascular mortality: a population-based prospective cohort study. *Sci Rep*. 2021;11(1):1329. doi:10.1038/s41598-020-79264-4
12. van der Heide I, Rademakers J, Schipper M, Droomers M, Sorensen K, Uiters E. Health literacy of Dutch adults: a cross sectional survey. *BMC Public Health*. 2013;13(1):179. doi:10.1186/1471-2458-13-179
13. Ilmarinen P, Stridsman C, Bashir M, et al. Level of education and asthma control in adult-onset asthma. *J Asthma*. 2021;26:1–13.
14. Nwaru BI, Ekerljung L, Radinger M, et al. Cohort profile: the West Sweden Asthma Study (WSAS): a multidisciplinary population-based longitudinal study of asthma, allergy and respiratory conditions in adults. *BMJ Open*. 2019;9(6):e027808–e027808. doi:10.1136/bmjopen-2018-027808
15. Ekerljung L, Ronmark E, Lotvall J, Wennergren G, Toren K, Lundback B. Questionnaire layout and wording influence prevalence and risk estimates of respiratory symptoms in a population cohort. *Clin Respir J*. 2013;7(1):53–63. doi:10.1111/j.1752-699X.2012.00281.x
16. Krokstad S, Langhammer A, Hveem K, et al. Cohort profile: the HUNT study, Norway. *Int J Epidemiol*. 2013;42(4):968–977. doi:10.1093/ije/dys095
17. Caffrey Osvald E, Bower H, Lundholm C, Larsson H, Brew BK, Almqvist C. Asthma and all-cause mortality in children and young adults: a population-based study. *Thorax*. 2020;75(12):1040–1046. doi:10.1136/thoraxjnl-2020-214655
18. Huovinen E, Kaprio J, Vesterinen E, Koskenvuo M. Mortality of adults with asthma: a prospective cohort study. *Thorax*. 1997;52(1):49–54. doi:10.1136/thx.52.1.49
19. Lemmetyinen RE, Karjalainen JV, But A, et al. Higher mortality of adults with asthma: a 15-year follow-up of a population-based cohort. *Allergy*. 2018;73(7):1479–1488. doi:10.1111/all.13431
20. Lange P, Ulrik CS, Vestbo J, Vestbo J. Mortality in adults with self-reported asthma. Copenhagen city heart study group. *Lancet*. 1996;347(9011):1285–1289. doi:10.1016/S0140-6736(96)90937-X
21. Ali Z, Dirks CG, Ulrik CS. Long-term mortality among adults with asthma: a 25-year follow-up of 1,075 outpatients with asthma. *Chest*. 2013;143(6):1649–1655. doi:10.1378/chest.12-2289
22. Lange P, Colak Y, Ingebrigtsen TS, Vestbo J, Marott JL. Long-term prognosis of asthma, chronic obstructive pulmonary disease, and asthma-chronic obstructive pulmonary disease overlap in the Copenhagen City heart study: a prospective population-based analysis. *Lancet Respir Med*. 2016;4(6):454–462. doi:10.1016/S2213-2600(16)00098-9
23. Mattila T, Vasankari T, Kauppi P, Mazur W, Harkanen T, Heliovaara M. Mortality of asthma, COPD, and asthma-COPD overlap during an 18-year follow up. *Respir Med*. 2023;207:107112. doi:10.1016/j.rmed.2022.107112
24. Huang S, Vasquez MM, Halonen M, Martinez FD, Guerra S. Asthma, airflow limitation and mortality risk in the general population. *Eur Respir J*. 2015;45(2):338–346. doi:10.1183/09031936.00108514
25. Dantzer C, Tessier JF, Nejjari C, Barberger-Gateau P, Dartigues JF. Mortality of elderly subjects with self-reported asthma in a French cohort, 1991-1996. *Eur J Epidemiol*. 2001;17(1):57–63. doi:10.1023/A:1010996718008
26. Bellia V, Pedone C, Catalano F, et al. Asthma in the elderly: mortality rate and associated risk factors for mortality. *Chest*. 2007;132(4):1175–1182. doi:10.1378/chest.06-2824
27. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2023. Updated July 2023. Available from: https://www.ginasthma.org. Accessed 15 March 2024.
28. Sobieraj DM, Weeda ER, Nguyen E, et al. Association of inhaled corticosteroids and long-acting beta-agonists as controller and quick relief therapy with exacerbations and symptom control in persistent asthma: a systematic review and meta-analysis. *JAMA*. 2018;319(14):1485–1496. doi:10.1001/jama.2018.2769
29. Nwaru BI, Ekstrom M, Hasvold P, Wiklund F, Telg G, Janson C. Overuse of short-acting β 2 -agonists in asthma is associated with increased risk of exacerbation and mortality: a nationwide cohort study of the global SABINA programme. *Eur Respir J*. 2020;55(4):1901872. doi:10.1183/13993003.01872-2019
30. Backman H, Jansson SA, Stridsman C, et al. Chronic airway obstruction in a population-based adult asthma cohort: prevalence, incidence and prognostic factors. *Respir Med*. 2018;138:115–122. doi:10.1016/j.rmed.2018.03.036

31. Jalasto J, Kauppi P, Luukkonen R, et al. Self-reported physician diagnosed asthma with COPD is associated with higher mortality than self-reported asthma or COPD alone. a Prospective 24-year study in the population of Helsinki, Finland. *COPD*. 2022;19(1):226–235. doi:10.1080/15412555.2022.2061935
32. Colak Y, Afzal S, Nordestgaard BG, Lange P. Characteristics and prognosis of never-smokers and smokers with asthma in the Copenhagen general population study. A prospective cohort study. *Am J Respir Crit Care Med*. 2015;192(2):172–181. doi:10.1164/rccm.201502-0302OC
33. Hedlund U, Eriksson K, Ronmark E. Socio-economic status is related to incidence of asthma and respiratory symptoms in adults. *Eur Respir J*. 2006;28(2):303–310. doi:10.1183/09031936.06.00108105
34. Schyllert C, Lindberg A, Hedman L, et al. Low socioeconomic status relates to asthma and wheeze, especially in women. *ERJ Open Res*. 2020;6(3):00258–2019. doi:10.1183/23120541.00258-2019
35. Schyllert C, Ronmark E, Andersson M, et al. Occupational exposure to chemicals drives the increased risk of asthma and rhinitis observed for exposure to vapours, gas, dust and fumes: a cross-sectional population-based study. *Occup Environ Med*. 2016;73(10):663–669. doi:10.1136/oemed-2016-103595
36. Williams MV, Baker DW, Honig EG, Lee TM, Nowlan A. Inadequate literacy is a barrier to asthma knowledge and self-care. *Chest*. 1998;114(4):1008–1015. doi:10.1378/chest.114.4.1008
37. Leander M, Lampa E, Rask-Andersen A, et al. Impact of anxiety and depression on respiratory symptoms. *Respir Med*. 2014;108(11):1594–1600. doi:10.1016/j.rmed.2014.09.007
38. Lundback B, Ronmark E, Jonsson E, Larsson K, Sandstrom T. Incidence of physician-diagnosed asthma in adults--a real incidence or a result of increased awareness? Report from the obstructive lung disease in Northern Sweden studies. *Respir Med*. 2001;95(8):685–692. doi:10.1053/rmed.2001.1126
39. Raisanen P, Hedman L, Andersson M, et al. Non-response did not affect prevalence estimates of asthma and respiratory symptoms - results from a postal questionnaire survey of the general population. *Respir Med*. 2020;173:106017. doi:10.1016/j.rmed.2020.106017