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Original Research

Mortality and its predictive factors in participants with asthma: a 26-year follow-up

Marta A. Kisiel [a,*,1], Xingwu Zhou [b,1], Ida Fundberg [c], Amelie Barrling [c], Herman Sundqvist Lindelöf [d], Adriana-Maria Hiller [e], Christer Janson [f], Anna Rask-Andersen [a]

[a] Department of Medical Sciences, Occupational and Environmental Medicine, Uppsala University, Sweden
[b] Department of Medical Sciences: Clinical Physiology, Uppsala University, Uppsala, Sweden
[c] Department of Statistics, Uppsala University, Uppsala, Sweden
[d] Department of Medical Sciences, Uppsala University, Uppsala, Sweden
[e] Department of Clinical Sciences in Malmö, Lund University, Occupational and Environmental Medicine, Lund, Sweden
[f] Department of Medical Sciences: Respiratory, Allergy and Sleep Research, Uppsala University, Sweden

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ABSTRACT

Background: The long-term impact of asthma on mortality remains uncertain. This study aimed to assess mortality and its predictors over 26 years in asthmatic participants compared to those with or without other respiratory symptoms.
Methods: This longitudinal cohort study included participants recruited from the general Swedish population, followed from 1990 to 2016. The younger (30–39 years, n = 938) and older (60–69 years, at baseline, n = 1020) groups were divided into asthma, other and no respiratory symptoms. Baseline data included spirometry, allergy testing, smoking status, and quality of life. Survival analyses were conducted using Kaplan-Meier and Cox proportional hazards models.
Results: At 26-years follow-up the survival rates were 34 % and 95 % for asthmatics in the older and younger age groups, respectively. Asthma was not found to be a statistically significant independent predictor of mortality when compared to non-asthmatics in either age group (older group HR 95 % CI: 0.94 (0.77–1.15); younger group: 1.39 (0.63–3.09). Significant mortality predictors included increasing age ((1.13 (1.10–1.16)), male sex (1.73 (1.44–2.07), smoking (2.01 (1.65–2.44), lower forced expiratory volume in 1 s (FEV_1) (0.67 (0.60–0.76), and more symptoms (1.21 (1.01–1.45) in the older group, while age (1.14 (1.02–1.27) and other respiratory symptoms (2.44 (1.18–5.03) were predictors in the younger group. Risk factors significantly linked to mortality among older asthmatics included older age, male sex and current passive smoking, and only male sex in younger asthmatics.
Conclusion: Asthma was not a strong independent predictor of mortality in either age group, whereas age, male sex, other respiratory symptoms, smoking, and lower FEV_1, but not quality of life, were key risk factors. These findings highlight the importance of identifying high-risk individuals and addressing modifiable lifestyle factors such as smoking in mortality prevention strategies.

1. Introduction

Asthma is a common chronic respiratory disease characterised by airway inflammation, bronchial hyperresponsiveness, and variable airflow limitation. It affects individuals of all ages across different regions and socioeconomic backgrounds [1]. In addition to diagnosed asthma, respiratory symptoms are frequently observed in individuals without a formal asthma diagnosis, potentially indicating underlying respiratory diseases, airway inflammation, or environmental exposure [2]. Both asthma and respiratory symptoms pose significant public health concerns due to their impact on daily life and potential long-term complications [3].

* Corresponding author. Occupational and Environmental Medicine Akademiska university hospital, Dag Hammarsköjds väg 60, 751 85 Uppsala, Sweden.
E-mail address: marta.kisiel@medsci.uu.se (M.A. Kisiel).
[1] Authors contributed equally.

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A recent global burden of asthma report highlighted a decline in age-standardised asthma prevalence, mortality, and disability-adjusted life years (DALYs) over the past three decades, which may be attributed to advancements in disease management and treatment strategies [4]. However, despite these improvements, long-term studies on asthma mortality remain essential to identify high-risk individuals and to refine preventive and management strategies.

Few studies have examined the risk factors for asthma-related mortality with a long-term follow-up [5,6]. Our previous study assessed mortality in elderly asthmatic participants (60–69 years at baseline) over an 18-year follow-up [7]. We found no significant difference in mortality between asthmatic and non-asthmatic groups. However, a higher symptom score in the Gothenburg Quality of Life (GQL) instrument was strongly associated with increased all-cause mortality. Asthmatic participants reported lower quality of life as compared to non-asthmatics, emphasising the importance of quality-of-life assessments in clinical practice, a factor previously overlooked in asthma mortality studies. While asthma and respiratory symptoms are known to affect health-related quality of life [8], their direct impact on the long-term mortality remains less understood.

The present study extends our previous research by assessing mortality and its predictors at 26-years of follow-up. It further examines differences between asthmatics, participants with other respiratory symptoms, and those without any respiratory symptoms. To provide a broader perspective, we also evaluate mortality in younger participants with and without asthma at baseline, offering a comparative analysis between different age groups.

2. Materials and methods

2.1. Study design

This longitudinal cohort study was based on a Swedish population recruited in 1990. Baseline data for the study were collected through a survey and a physical examination, while mortality data were obtained in 2016 from the Swedish National Death Register, representing a 26-year follow-up. The study population was divided into two baseline age groups: a younger group (30–39 years) and an older group (60–69 years). Participants were further categorised into three subgroups within each age group: those with asthma, those with other respiratory symptoms, and those without any respiratory symptoms.

This study was approved by the Ethics Committees of Umeå University (§ 222, 1989-12-12) and Uppsala University (Dnr 01–313).

2.2. Study population

The study population has previously been described in detail [9]. The participants were recruited from the general populations of Jämtland and Gästrikland counties in central Sweden. At the time, Jämtland had 134,000 inhabitants, and Gästrikland had 147,000 inhabitants. The invited participants included all individuals born in 1974 (aged 16 years in 1990), randomly selected individuals born between 1951 and 1960 (aged 30–39 years in 1990), and randomly selected individuals born between 1921 and 1930 (aged 60–69 years in 1990).

In 1990, a postal survey was distributed to 12,732 of the above mentioned individuals, with a response rate of 89.3 % (n = 11,294). The survey comprised 22 questions addressing respiratory symptoms, including asthma diagnosis, asthma medication use, chronic bronchitis, emphysema, respiratory distress, shortness of breath, persistent cough with mucus, and wheezing.

A subset of the survey respondents reporting respiratory symptoms and those without respiratory symptoms were randomly selected and invited to undergo a physical examination. In total, 2548 participants completed the physical examination in 1990, including 1571 participants with respiratory symptoms and 977 participants without respiratory symptoms [10]. During the physical examination, the participants underwent lung function and allergy testing and completed a health-related quality-of-life questionnaire. The cohort included 616 participants meeting the criteria for asthma, 488 participants with respiratory symptoms not classified as asthma, and 347 participants without respiratory symptoms [11].

2.3. Study subgroups

2.3.1. The asthmatic group

Asthma diagnoses in 1990 were based on the clinical criteria at the time, including respiratory symptoms in the past year (e.g., breathlessness, wheezing, chest tightness, or dry cough) and reversibility in forced expiratory volume in 1 s (FEV_1). Reversibility was defined as an improvement in FEV_1 >15 % after inhalation of a β_2-agonist (salbutamol) [7].

2.3.2. Other respiratory symptoms group

Consisted of participants without a diagnosis of asthma but with respiratory symptoms. They did not fulfil the criteria for an asthma diagnosis during the examination in 1990. This group was also stratified into participants with FEV_1 % predicted <80 % and ≥80 %.

2.3.3. No respiratory symptoms group

Consisted of participants without respiratory symptoms during the physical examination in 1990.

2.4. Main outcome – mortality

At the 2016 follow-up, the causes of death were obtained from the National Board of Health and Welfare Mortality Database. The causes of death were classified according to the International Classification of Diseases, 9th Edition (ICD-9-CM) for the years 1990–1996, and the 10th Edition (ICD-10) for 1997 onwards. As in a previous study by Leander et al., [7] the causes of death were grouped into respiratory, cardiovascular, cancer-related and other conditions categories. The underlying cause of death was broadly categorised as death due to malignant neoplasms (C00–C97), diseases of the circulatory system (I00–I99), and diseases of the respiratory system (J00–J99).

2.5. Covariates

2.5.1. Quality of life

The quality of life at baseline was assessed using the **Gothenburg** Quality of Life (GQL) tool. The GQL assesses two parts: symptoms and well-being. Symptoms included dizziness, eye-problem, impaired hearing, headache, general fatigue, sleeping disturbance, nervousness, sweating, breathlessness, chest pain, coughing, irritability, exhaustion, impaired concentration, restlessness, depression, crying easily, difficulty relaxing, abdominal pain, nausea, diarrhea, constipation, loss of weight, overweight, feeling cold, pain in the joints, back pain, pain in the legs, difficulty in pressing urine). Well-being is further divided into physical, mental, and social well-being, with scores ranging from 1 (very bad) to 7 (excellent) [12]. Sub-dimensions include: Social Well-being: Assessed through variables such as family, home, work, economy, and spare time (score: 0–49); Mental Well-being: Includes mood, energy, self-confidence, patience, and sleep (score: 0–35); Physical Well-being: Includes health, memory, appetite, vision, and hearing (score: 0–42).

2.5.2. Lung function and allergy test

Spirometry (a lung function test) measured vital capacity (VC) and FEV_1 in liters before and after bronchodilator (salbutamol) administration. Reversibility (%) was calculated as the difference between pre-and post-bronchodilator FEV_1 values. [13] The results were compared to the Global Lung Function Initiative (GLI) reference scale, https://gli-calculator.ersnet.org/.

A skin prick test using Phazet lancets (Pharmacia Diagnostics) assessed 10 allergens. A wheal ≥3 mm in diameter was considered positive [14].

2.5.3. Other covariates

This study included the following variables collected via the survey: smoking status (current, ex- and never), snus (daily or never/occasional; is a moist, finely ground smokeless tobacco product that is typically placed under the upper lip), passive smoking in childhood (based on the question ''Did anyone smoke at home during your first 10 years of childhood?''; passive smoking current (based on the question: Are you currently experiencing passive smoking at home or at work daily?''). Sex and age were based on Swedish social security numbers.

2.6. Statistical analysis

Baseline characteristics (1990) were summarised using descriptive statistics: categorical variables as counts with percentages and continuous variables as means ± standard deviations (SD). Subgroup comparisons within the two age groups were performed using chi-squared tests for categorical data and one way ANOVA for continuous data.

The primary outcome was mortality at the 26-year follow-up, analysed using the Kaplan-Meier method to estimate survival probabilities. Survival distributions between three groups such as asthma (in two age groups), with and without respiratory symptoms were compared using the log-rank (Mantel-Cox) test. Additionally, Kaplan-Meier curve was performed with stratified group with respiratory symptoms into FEV_1 % predicted <80 % and ≥80 %.

Cox Proportional Hazards Models were applied to identify mortality predictors. Three models were developed: (1) Model 1: Replicated variables used by Leander 2010 et al. [7], including subgroup, sex, age, smoking status, skin prick test, and FEV_1; (2) Model 2: Adjusted for Model 1 variables and additional factors, such as quality of life; (3) Model 3: Used stepwise selection to identify significant predictors for asthmatic participants.

Model fit was assessed via the likelihood ratio test (chi-squared), and multicollinearity was evaluated using the Variance Inflation Factor (VIF), with a threshold of >5 indicating high correlation. Missing data were handled through multiple imputations. The number of missing data is presented in Supplementary Table 1. All analyses were conducted using R, with a statistical significance set at $p < 0.05$.

3. Results

3.1. The study participants' characteristics at baseline

At baseline, the older age group consisted of 1020 participants, of whom 24 % had asthma and 50 % had other respiratory symptoms. The younger age group comprised 938 participants, with 29 % in the asthma group and 29 % in the other respiratory symptom group. The distribution of participants is shown in Fig. 1.

Approximately 40 % of the participants in the asthmatic group in both age groups were males, as shown in Table 1. The prevalence of current and ex-smokers was higher among asthmatics in the younger age group as compared to the older age group. Additionally, passive smoking in childhood or currently, as well as the use of snus, was more frequent in younger asthmatic participants than in the older ones. In both age groups, passive smoking during childhood was significantly lower in the participants without respiratory symptoms as compared to those with asthma and other respiratory symptoms. The asthmatic subgroup in both age groups also had a significantly higher rate of positive skin prick tests. FEV_1 % predicted (mean), both before and after bronchodilator use, was significantly lower in the asthmatic participants, while reversibility was significantly higher compared to other subgroups in both age groups. On the other hand, significantly more participants with other respiratory symptoms had FEV_1 % predicted <80 %, in both age groups. These findings are consistent with an asthma diagnosis.

The number of symptoms in the GQL was significantly higher in the asthmatic subgroup (median of 9 and 7 symptoms in the older and the younger groups, respectively) as compared to the non-asthmatic subgroups in both age groups. In the older age group, asthmatics rated their physical and mental well-being significantly higher than those in the other two subgroups (Supplementary Table 2). In the younger age group, the no-symptom group reported significantly better social and physical well-being and lower symptom scores. For both physical and social domains, the younger asthmatic group's scores were intermediate, falling between those with respiratory symptoms and those without respiratory symptoms (Supplementary Table 2).

3.2. Cause of death at 26-years follow-up

At the 26-year follow-up, cardiovascular disease was the most common cause of death among asthmatic participants in the older age group, as shown in Table 2. This was also true for the two subgroups without asthma. In the younger age group, respiratory disease was the leading cause of death among asthmatic participants, followed by other causes and cardiovascular disease. This pattern was also observed in the subgroup with no symptoms.

3.3. Kaplan-Meier survival curves

All-cause mortality was highest in the older age group in the other respiratory symptoms group. There was no significant difference in mortality rates between asthmatics and the subgroup without respiratory symptoms in both age groups. However, there was a significant difference in the distribution of deaths between at all time points between three subgroups within both age groups. The survival rate in the older age group was 33.8 % for asthmatics, 34.3 % for those without respiratory symptoms, and 20.9 % for the other respiratory symptoms subgroup, as shown in Fig. 2A. In the younger age group, the survival rates were 95 % for asthmatics, 92 % for those with other respiratory symptoms, and 97 % for those without symptoms, as shown in Fig. 2B.

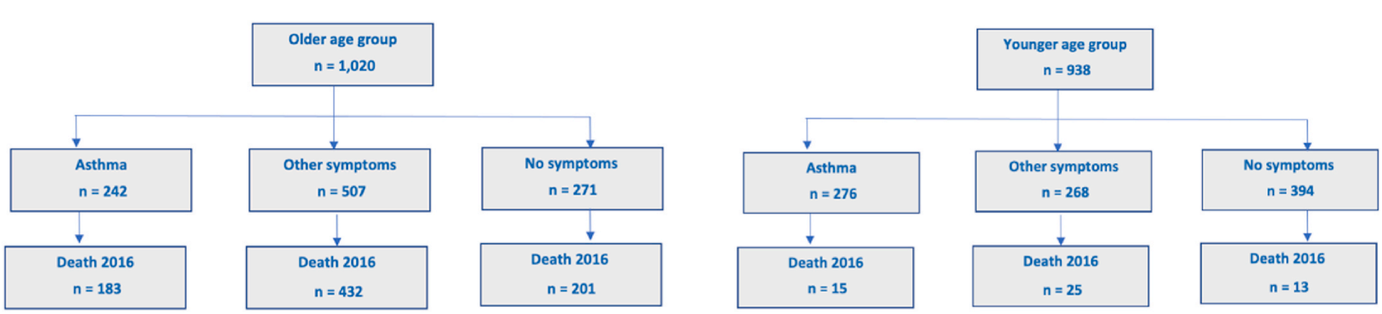

Fig. 1. Study participants flowchart showing the division into older and younger age groups, with subgroups for asthma, other respiratory symptoms, and no respiratory symptoms.

Table 1
Descriptive characteristics for the study participants, n (%) or mean (SD).

	Older age group, n = 1020				Younger age group, n0938			
	Asthma (n=242)	**Other symptoms (n=507)**	**No symptoms (n=271)**	**P-value**	**Asthma (n=276)**	**Other symptoms (n=268)**	**No symptoms (n=394)**	**P-value**
N (%)								
Male sex	98 (40)	280 (55)	118 (44)	0.10	118 (43)	139 (52)	188 (48)	<0.01
Ex-smoking	69 (35)	181 (49)	85 (40)	<0.01	69 (44)	51 (40)	98 (35)	<0.01
Current smoking	43 (18)	141 (28)	37 (14)		115 (42)	139 (28)	112 (29)	
Never smoking	128 (53)	182 (36)	144 (54)		87 (32)	72 (36)	178 (46)	
Passive smoking in childhood	108 (45)	200 (41)	108 (40)	0.48	199 (72)	193 (72)	250 (64)	0.02
Passive smoking current	41 (17)	144 (29)	51 (21)	<0.01	100 (36)	102 (39)	85 (22)	<0.01
Snus	21 (9)	47 (9)	15 (6)	0.19	48 (17)	40 (15)	84 (21)	0.10
FEV_1 % predicted <80 %	84 (35)	298 (60)	51 (20)	<0.01	47 (17)	51 (19)	31 (8)	<0.01
Means (SD)								
Skin-prick test positive	59 (24)	78 (16)	55 (20)	0.01	186 (68)	96 (36)	153 (39)	<0.01
FEV_1 (L)	2.4 (0.65)	2.1 (0.82)	2.6 (0.69)	<0.01	3.5 (0.78)	3.7 (1.00)	3.9 (0.89)	<0.01
FEV_1 (L) after bronchodilator	2.5 (0.68)	2.2 (0.82)	2.7 (0.71)	<0.01	3.7 (0.80)	3.8 (0.98)	3.9 (0.87)	<0.01
FEV_1 % predicted	85.1 (15.28)	73.2 (24.69)	93.2 (16.00)	<0.01	91.7 (14.52)	93.4 (15.98)	99.4 (13.64)	<0.01
FEV_1 after bronchodilator % predicted	90.9 (14.55)	77.0 (23.96)	96.0 (16.56)	<0.01	97.1 (2.79)	96.4 (15.39)	101.8 (13.15)	<0.01
Reversibility%	6.1 (8.99)	3.5 (6.97)	2.8 (6.00)	<0.01	5.5 (7.78)	3.1 (5.85)	2.5 (5.74)	<0.01
VC (L)	3.2 (0.91)	3.1 (0.98)	3.5 (0.97)	<0.01	4.5 (1.02)	4.7 (1.18)	4.8 (1.08)	0.01

List of Abbreviations: FEV_1 = forced expiratory volume in 1 s; L = liter; VC = vital capacity.

Table 2
Causes of mortality categorised as respiratory, cancer, cardiovascular, and other causes in the older and the younger age groups, with subgroups for asthma, other respiratory symptoms, and no respiratory symptoms, n (%).

Cause of mortality	Older age group			Yonger age group		
	Asthma	Other symptoms	No symptoms	Asthma	Other symptoms	No symptoms
Respiratory	39 (21)	100 (23)	56 (28)	7 (47)	7 (28)	7 (54)
Cancer	12 (7)	61 (14)	12 (06)	1 (7)	1 (4)	0 (0)
Cardiovascular	85 (46)	182 (42)	91 (45)	3 (20)	6 (24)	3 (23)
Other	47 (26)	92 (21)	43 (21)	4 (27)	11 (44)	3 (23)

The lowest survival rate was observed in the group with other respiratory symptoms. Therefore, we additionally stratified this group into those with FEV_1 % predicted <80 % and ≥80 % in Supplementary Fig. 1. Those with FEV_1 % predicted <80 % showed significantly higher mortality, whereas mortality in those with FEV_1 % predicted ≥80 % was similar to that in asthmatics.

3.4. Predictors of mortality in all participants

In the Cox Proportional Hazards presented in Fig. 3, which included subgroup variables, sex, smoking status, skin prick test results, and FEV_1 % predicted, we found that asthma was not a predictor of mortality as compared to the other two subgroups in either age group, as shown in Fig. 3. In the older age group, significant predictors of mortality included increasing age, male sex, ex- or current smoking, and lower FEV_1 % predicted. In the younger age group, the significant predictors of mortality were other respiratory symptoms and age.

The model presented in Fig. 4 was adjusted with the same variables as in Fig. 3, with the additional inclusion of the GQL tool, and showed no significant correlation between any well-being domains and mortality in either age group. In the older age group, having 6–9 symptoms was significant for mortality, but this correlation was not observed in the younger age group. In both age groups, age was a significant predictor for mortality.

3.5. Predictors of mortality in asthmatics

In a model, which included only asthmatics (Table 3), increasing age, male sex and exposure to passive smoking (current) were significant predictors of mortality in the older age group. In the younger age group of asthmatics, only male sex was a significant predictor of mortality.

4. Discussion

The main finding of the present study is that at this 26-year follow-up, having asthma at baseline was not associated with increased mortality. Cardiovascular causes were the leading cause of death in the older group, while respiratory disease was the most common cause in younger asthmatics. In the older group, significant predictors of mortality were increasing age, male sex, smoking, lower lung function, and the number of symptoms in the quality-of-life questionnaire. In younger participants, male sex and having other respiratory symptoms were significant predictors of mortality. When considering only mortality in asthmatics, increasing age, male sex and experiencing passive smoking were significantly associated with mortality in the older group, while male sex was the only significant predictor of mortality in the younger group.

Consistent with our previous study at the 18-year follow-up in the same cohort of participants, we showed that asthmatics did not have a significantly different mortality rate than those without asthma [7]. Our result contrasts with a recent study on the population from Sweden and Norway with a 10-year follow-up, which demonstrated that asthmatics had significantly higher mortality as compared to those without this condition [15]. Additionally, a study on the Danish population of asthmatics with a median follow-up of 30 years, starting at a median age of 30 years, found significantly higher mortality in asthmatics than in the general population [16]. The differences between our study and others may be attributed to the characteristics of the included asthma and non-asthmatic subjects. Our study did not include information on asthma severity, which is well known to impact mortality [17]. Notably, a recent study from China with a mean follow-up of 7.5 years on

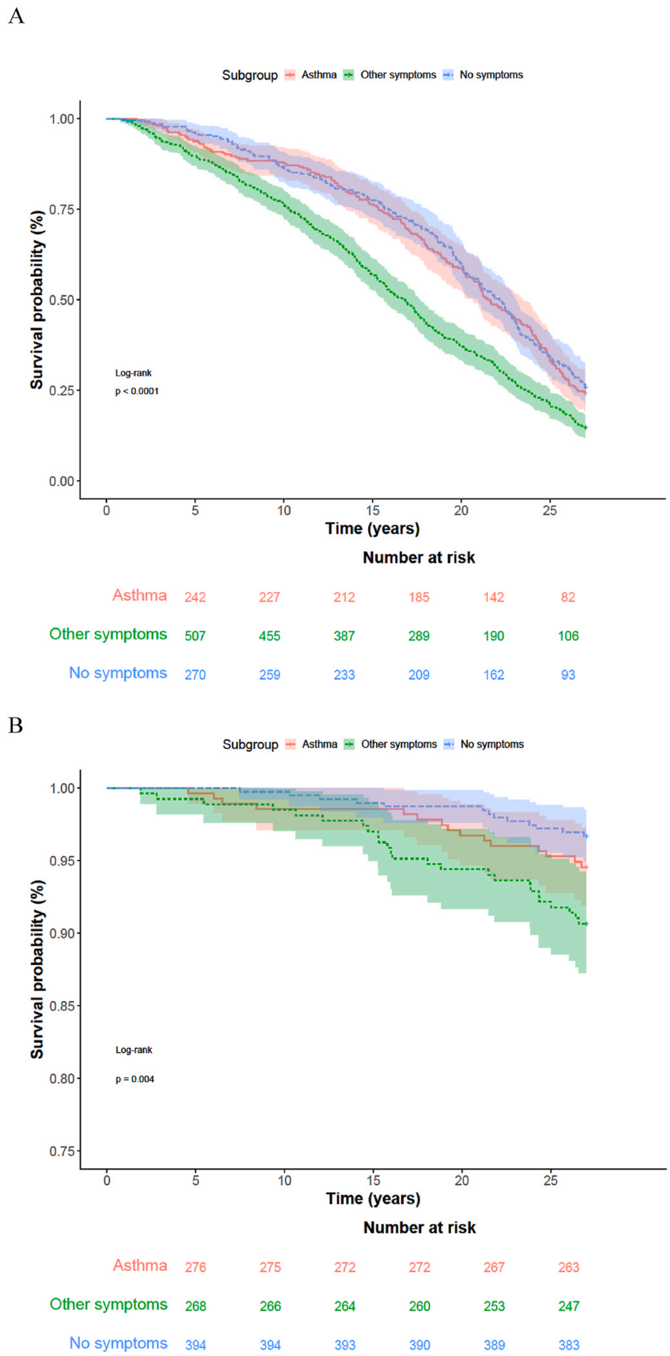

Fig. 2. Kaplan-Meier survival curves for mortality in participants with asthma, respiratory symptoms and those without respiratory symptoms in A) the older and B) the younger age groups.

mortality in asthmatics revealed that current asthma, but not former asthma, was associated with increased all-cause mortality as well as mortality due to cardiovascular disease [18].

In our previous study on a nationwide primary care asthmatic population (mean age 42 years) with an 8-year follow-up, it was found that the all-cause mortality was similar to the general population, but pulmonary-related deaths were greater in asthmatics [19]. This is in accordance with our results on younger asthmatics, where respiratory causes of death were the most common. However, in the older age group of asthmatics, the most common cause of death was cardiovascular disease. This is in line with the Swedish general population mortality reports [20].

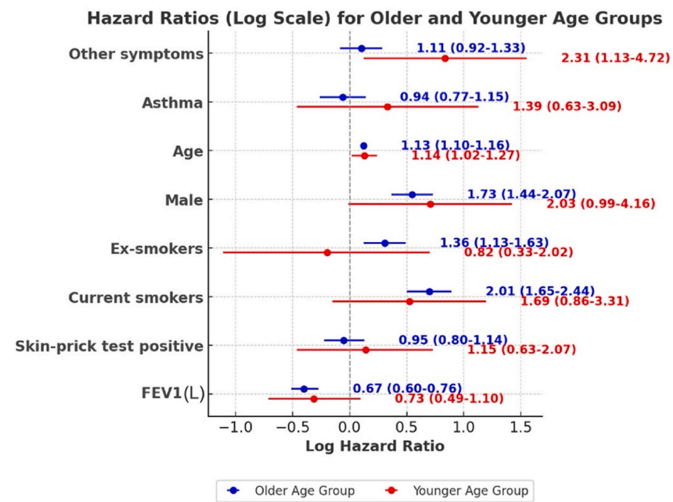

Fig. 3. Independent predictors of mortality in all participants were assessed using the Cox Proportional Hazards Model, with hazard risk ratios and 95 % confidence intervals (CI) for all participants. Model 1 included the variables: subgroup, sex, age, smoking status, skin prick test results, and forced expiratory volume in 1 s (FEV_1) in liters (L).

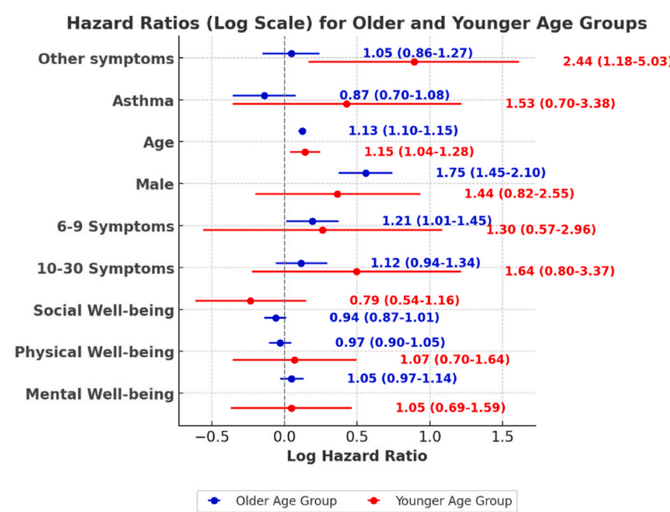

Fig. 4. Independent predictors of mortality in all participants were assessed using the Cox Proportional Hazards Model, with hazard risk ratios and 95 % confidence intervals (CI) for the whole population. This model included all variables from Fig. 3 and the **Gothenburg Quality of Life** (GQL) Instrument.

Table 3
Independent predictors of mortality in the participants with asthma assessed using the Cox Proportional Hazards Model, with hazard risk ratios and 95 % confidence intervals (CI). Model 3 used stepwise selection to identify the best predictors.

	Older age group			Younger age group		
	HR	95 % CI	P-value	HR	95 % CI	P-value
Age (years)	1.17	1.11–1.23	< 0.01			
Male sex	1.73	1.25–2.40	< 0.01	7.62	1.51–38.40	0.02
Snus	1.56	0.94–2.59	0.09	0.30	0.05–1.87	0.17
Passive smoking in childhood	1.28	0.96–1.72	0.07	0.31	0.10–1.00	0.05
Passive smoking current	2.09	1.45–3.01	< 0.01	NA		
FEV_1 (L)	*NA*			0.47	0.19–1.18	0.10

List of Abbreviations: FEV_1 = forced expiratory volume in 1 s; L = liter.

The results should be interpreted with caution regarding the mortality in the subgroup with other respiratory symptoms, as it is difficult to characterise this group. When stratified according to FEV_1 % predicted, the lowest survival rate was shown among the FEV_1 % predicted <80 % in both age groups. In the 1990s, there was no established diagnosis for COPD [21], which we believe the majority of these participants (FEV_1 % predicted <80 %), particularly within the older age group, could have had. COPD patients were shown to have a significantly higher risk of mortality than asthmatic patients in a Finish cohort with 18 years of follow-up [22]. Respiratory symptoms may also reflect other underlying conditions such as interstitial lung disease (ILD) and Preserved Ratio Impaired Spirometry (PRISm). PRISm has recently been increasingly recognised in epidemiological studies and linked to accelerated rates of lung function decline, obesity or underweight, and increased all-cause and cardiovascular mortality [23,24]. Similarly, ILD contributes to poor outcomes and was likely present in a subset of participants, especially among older individuals with respiratory symptoms and reduced lung volumes [25]. In the younger age group, this subgroup (FEV_1 % predicted <80 %) might include participants who had not yet been diagnosed with asthma, but might be diagnosed later on [2].

As in our previous 18-year follow-up [7], all-cause mortality in the entire older age group was associated with increasing age, male sex, current smoking, and a higher number of symptoms in the quality-of-life questionnaire. However, at the 26-year follow-up, even ex-smoking and lower FEV_1 % predicted became significantly associated with mortality. In line with our findings, a previous study on an international cohort of adults from 17 countries with a median follow-up of 8 years showed that FEV_1 % predicted was an independent predictor of all-cause mortality [26].

Also, in line with our study on the 18-year follow-up [7], we found that quality of life at baseline was not associated with all-cause mortality in our study participants. There have been few studies on quality of life as a predictor of mortality in asthmatics. A previous study on United States (U.S.) veterans (mean age 65 years) found that low quality of life at baseline was associated with mortality at the 5-year follow-up in self-reported obstructive pulmonary disease, without distinguishing between asthma and chronic obstructive pulmonary disease (COPD) [27]. The contrasting results compared to ours can be attributed to the short follow-up period and the fact that it was not conducted solely on asthmatics. In fact, in COPD, the quality of life was shown to be an independent predictor of mortality [28].

In this study, male sex was associated with a higher risk of mortality in asthma in both the younger and older groups. In contrast to our findings, other studies, including a recent meta-analysis on all-cause mortality in asthmatics, revealed a higher risk in females than males [29]. The explanation for male sex being a predictor of asthma mortality in our study could be attributed to the socioeconomic characteristics of the cohort, the variable we did not have in the current study. In a recent study with a 10-year follow-up of asthmatics from Sweden and Norway [15], a lower educational level was a significant risk factor for all-cause mortality. In addition, men have been shown to have poorer health-seeking behaviour, lower adherence to treatment, and higher rates of smoking and occupational exposures, all of which may contribute to worse outcomes in chronic respiratory disease [30,31].

In line with our study, multiple studies have revealed that ever smoking is a risk factor for all-cause mortality [32]. A study with a 50-year follow-up, published in 2004, confirmed the association between smoking habits and many severe diseases. The authors also found that men born between 1900 and 1930 who smoked cigarettes continuously died about 10 years younger than lifelong nonsmokers, while stopping at age 60, 50, 40, or 30 years gained about 3, 6, 9, or 10 years of life expectancy, respectively [33]. In our study, 18 % and 42 % of asthmatics in the older and the younger age groups were current smokers at baseline. This is in line with a Swedish study showing long-term trends in smoking, revealing that there were significantly more smokers among 30-year-old subjects than 60-year-old subjects in 1990. This study also showed that smoking rates declined significantly from 1968 to 2002 in males and females [34].

The main strength of our study is that we followed up on randomly selected patients' mortality over 26 years. There have been few studies with follow-up on mortality in asthma patients exceeding two decades. We based our study on both survey data and objective results from physical examinations and registry data. There have also been few previous studies on quality of life as a predictor of mortality in asthma. Probably no previous studies have evaluated the use of snuff as a predictor of mortality in asthma. The diagnosis of asthma was not self-reported but based on objective findings. However, the limitation is that asthma criteria are in accordance with those from 1990, which is attributed to the long follow-up. The current asthma criteria differ from these, mainly in that the diagnostic reversibility cutoff in FEV_1 was changed from a reversibility test with spirometry of 15 %–12 % and 200 mL [35]. The other diagnostic criteria remained unchanged.

This study has also several limitations, including the lack of information on sociodemographic status, which was identified as a factor influencing asthma mortality in another Swedish study [15]. We did not have information on participants' body mass index (BMI), which was shown to be significantly associated with an increased hazard of all-cause and cardiovascular mortality in adults with asthma in a previous Swedish cohort [36]. BMI data could have enhanced the characterisation of individuals in the group with 'other respiratory symptoms' and may have helped explore potential mechanisms underlying their increased mortality risk. Our study lacks information on asthma medication, whereas oral corticosteroid (OCS) use is frequent among asthma patients, and many are regular users. Regular OCS use is associated with an increased risk of mortality [37]. We do not have data on treatment regimens, so we cannot assess asthma severity in our study population. We also did not have data on comorbidities despite multimorbidity being associated with an increased risk of mortality [38]. Regarding the causes of death, we relied on registry data, and it is a known limitation that some causes may not be accurately recorded, especially in cases of multiple comorbidities, where a single primary cause of death cannot always be correctly attributed.

5. Conclusion

Asthma was not a strong independent predictor of mortality in either age group, whereas other respiratory symptoms, increasing age, male sex, smoking, and lower lung function were key risk factors. These findings highlight the importance of identifying high-risk individuals and addressing modifiable lifestyle factors such as smoking in mortality prevention strategies.

CRediT authorship contribution statement

Marta A. Kisiel: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. **Xingwu Zhou:** Writing – review & editing, Validation, Supervision, Software, Methodology, Formal analysis, Data curation. **Ida Fundberg:** Writing – review & editing, Visualization, Software, Data curation. **Amelie Barrling:** Writing – review & editing, Visualization, Software, Data curation. **Herman Sundqvist Lindelöf:** Writing – review & editing, Writing – original draft, Visualization, Validation. **Adriana-Maria Hiller:** Writing – review & editing, Validation, Supervision. **Christer Janson:** Writing – review & editing, Validation, Supervision, Methodology, Funding acquisition, Data curation, Conceptualization. **Anna Rask-Andersen:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

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Declaration of competing interest

The authors declare that they have no competing financial or personal interests that could have influenced the work reported in this manuscript (below). No funding bodies had any role in the study design, data collection, analysis, or interpretation, nor in the decision to submit this manuscript for publication.

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Appendix A. Supplementary data

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