



Impact of asthma on mortality in older women: An Australian cohort study of 10,413 women



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ABSTRACT

Background: Comorbid conditions frequently coexist with asthma in older adults and can alter the natural history of asthma, complicating management and affecting overall prognosis and survival.

Objectives: This study investigates the impact of asthma on mortality among older women, with a specific interest in influence of comorbidities and social factors on survival of older women with asthma.

Design: Participants were from the Australian Longitudinal Study on Women's Health and were born between 1921 and 1926. Cox proportional hazards were used to evaluate mortality rates for women with and without asthma, after adjustment for comorbidities and other factors.

Results: Of 10,413 women aged 73–78, 829 (8%) reported having been diagnosed by a doctor for asthma. Women with asthma had a higher likelihood of heart disease, hypertension, thrombosis, bronchitis/emphysema, osteoporosis and major illnesses ($p < 0.0001$). Asthma was associated with increased risk of death (HR = 1.31, 95%CI 1.18–1.45, $p < 0.0001$). After adjusting for age, demographic factors, comorbidities, risk factors, residential area and social support, women with asthma retained a 17% increased risk of death compared to women without asthma (HR = 1.17, 95%CI 1.03–1.32, $p = 0.016$).

Conclusion: Older women with asthma have a higher rate of mortality compared with other women of the same age. This increased risk of death remains after age, demographic factors, comorbidities, risk factors, residential area and social support have been taken into account.

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1. Introduction

Asthma is a significant global health issue affecting about 235–300 million people worldwide of all ages and ethnicities [1]. According to an international health survey across 70 countries, the global prevalence of diagnosed asthma in adults is between 4.3–4.5%, with highest prevalence rates in those aged 75 years and over (7% in 2001, 8% in 2004–05 and 10% in 2007) [2,3]. The true prevalence rates in older adults may be higher than previously thought, as asthma is difficult to diagnose in this age group. These difficulties include problems performing respiratory tests due to frailty, other diseases having similar symptoms to asthma which can mask the diagnosis [2,4–6], and misdiagnosis as COPD [7].

In Australia, the prevalence of asthma in women is 10.9%

compared with 8.9% in men and is highest amongst women aged 75 years and over (13.4%) [2]. Older women also have higher death rates from asthma compared with men (10/100 000 vs. 7/100 000) [8]. It is of concern that while mortality rates associated with asthma have declined globally, they have increased in the elderly. Deaths attributed to asthma are estimated as 6 deaths per 100,000 in those aged over 65 years old [8–11]. In 2003, over two-thirds (69%) of asthma-related deaths in Australia were among older people (65 + years old) [3,8]. As the population ages, asthma death rates are expected to increase and by 2050, it is estimated that 80% of all asthma deaths will occur in people over 60 years of age [12].

Death among people with asthma is thought to be influenced by co-morbidities such as diabetes, heart disease, stroke and cancer [13]. Comorbid conditions frequently coexist with asthma and can alter the natural history of the disease, complicating management and affecting the overall prognosis and survival [14–16]. According to the Australian Institute of Health and Welfare (AIHW) asthma series, people aged 65 years and over who died from asthma often had complications of acute respiratory tract infections (36%) and cardiovascular conditions (39%) [17]. Research has also

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demonstrated that asthma mortality is affected by age, weight, physical performance and cognitive factors [18]. These factors may also impact asthma management by increasing the risk of drug interactions or decreasing medication adherence [15].

Demographic and social factors can also affect asthma mortality. Older people living alone are more likely to have difficulties in adhering to medications due to forgetfulness or financial problems [15]. Women who care for their spouses are more likely to suffer from bad health and are more susceptible to social isolation. These circumstances may affect asthma outcomes [14].

While some studies have investigated the factors that influence asthma in children and early adulthood [19,20], few studies have examined the natural history and outcomes of asthma in the elderly [21,22]. The aims of this study were two-fold: (1) to determine if asthma is a predictor of mortality in older women, taking into account possible misclassification of the disease; and (2) to evaluate whether asthma is an independent predictor of mortality rates in older women, after controlling for known predictors of survival including comorbidities and social factors.

2. Methods

2.1. Study population and data source

Participants were recruited from the Australian Longitudinal Study on Women's Health (ALSWH, www.alswh.org.au), a prospective cohort study that commenced in 1996. This study examines the health and wellbeing of over 40,000 Australian women through surveying three birth cohorts born 1921–1926, 1946–1951 and 1973–1978. Recruitment procedures and participant characteristics for the original ALSWH sample have been described elsewhere [23]. This paper examines data from the 1921–1926 cohort. In 1996, 12,432 women completed the first survey (aged 70–75). The cohort has been surveyed a further five times at regular three-year intervals until 2011.

Eligibility for this study was defined as participants who responded to the questions about recently diagnosed asthma, bronchitis/emphysema and breathing difficulties in Survey 2 completed in 1999 and for whom follow-up time could be determined by March 2012 (end of Survey 6 follow-up). Human Research Ethics Committees at the Universities of Newcastle and Queensland approved this research.

2.2. Variables

2.2.1. Mortality

Deaths were confirmed from the National Death Index (NDI) [24]. Participants who had not died were censored at the return date of their sixth survey or 15th March 2012, whichever occurred first. Given the delay in notification from the NDI, this cut-off time was appropriate to allow complete information on deaths within the cohort. A binary variable was assigned for each participant to indicate death or censoring.

2.2.2. Asthma case definitions

At survey 2, women were asked “In the last 3 years have you been told by a doctor that you have: Asthma” (Yes/No), as well as “In the last 3 years have you been told by a doctor that you have: Bronchitis/Emphysema” (Yes/No). Additionally, women also responded to a question about whether they had experienced any breathing difficulties in the past 12 months, with response options of “Never” and “Rarely” being classified as ‘No’ while “Sometimes” and “Often” responses were classified as ‘Yes’.

As there may be misclassification in the diagnosis of asthma for older women [14,18,25], we evaluated four different definitions

using self-reported asthma with and without the inclusion of other respiratory conditions or symptoms, namely: (i) asthma; (ii) asthma or bronchitis/emphysema; (iii) asthma or breathing difficulties; and (iv) asthma or bronchitis/emphysema or breathing difficulties.

2.2.3. Other variables of interest

Participant's area of residence was classified as either major city, regional area or remote area, according to the ARIA + geographical classification criteria [26]. Participants were asked about their current marital status with response options of: married; de facto relationship; separated; divorced; widowed; or never married. Women who had responded as either married or in a de facto relationship were classified as having a current partner, while all other responses were classified as not having a current partner. Alcohol consumption was measured in terms of frequency and quantity over a typical week and then categorised as per the NHMRC guidelines [27]. Risky drinking was defined as drinking more than four drinks on any one occasion or drinking more than two drinks per day in a typical week. Low risk drinking was defined as drinking less than 4 drinks on any one occasion, 1 or 2 drinks per day in a typical day or 3 or 4 drinks no more than 4 days a week [27]. According to their smoking responses, women were categorised as either non-smoker, ex-smoker or current smoker. Body Mass Index (BMI) was calculated and categorised according to WHO guidelines [28]. Social support was measured using modified version of Duke's Social Support Index (DSSI) [29]. Data on other comorbidities was collected at Survey 2. These included heart disease, thrombosis, osteoporosis, low iron level, hypertension, diabetes, stroke and cancer (excluding skin cancers).

2.2.4. Analysis

The prevalence for each of the case definitions was calculated and reported. Descriptive characteristics between women with asthma (case definition (i)) and its respective control group were compared. Kaplan-Meier methods were used to estimate survival probabilities over time for women with and without asthma with survival defined as the time between the date of completing Survey 2 and death/censor. The cumulative mortality according to asthma status was graphed, truncated at 12 years of follow-up. Cox proportional hazard models were used to estimate the effect of asthma on risk of death. Nested multivariate proportional hazard models demonstrated the sequential impact of age, demographic data, risk factors, social support and comorbidities on the association between the asthma case definition and mortality risk and were defined as:

- (i) Asthma;
- (ii) Asthma + age
- (iii) Asthma + age + demographics;
- (iv) Asthma + age + demographics + health behaviours;
- (v) Asthma + age + demographics + health behaviours + Duke's Support Scale Index (DSSI);
- (vi) Asthma + age + demographics + health behaviours + Duke's Support Scale Index (DSSI) + comorbidities.

All four asthma case definitions were evaluated within these six models.

As there may be misclassification between asthma and COPD, a sensitivity analysis was performed with mutually exclusive restrictions for asthma and COPD (ie. bronchitis/emphysema). Against women with no reported respiratory conditions (ie. no asthma and no bronchitis/emphysema), we also examined mortality for (a) women with asthma with no bronchitis/emphysema (“asthma only”), (b) women with bronchitis/emphysema with no

asthma (“bronchitis only”; to represent women with COPD) and (c) women with asthma and bronchitis/emphysema.

All data analysis was performed using SAS 9.3[30].

3. Results

In 1999, 10,413 women aged 73–78 years old completed Survey 2. The prevalence of asthma and the expanded case definitions are presented in Table 1, with 829 (8.0%) women indicating that they had been told by a doctor that they had asthma within the last three years (case definition [i]). Women reporting asthma were also five times more likely to report bronchitis/emphysema (OR = 5.87, 95% CI = 4.87, 7.08) and were more than 10 times more likely to report breathing difficulties (OR = 11.56, 95% CI = 9.88, 13.54). Nearly one fifth of women (19.7%) reported a respiratory condition which included any asthma, bronchitis/emphysema or breathing difficulties, using case definition [iv].

Table 2 presents descriptive characteristics for women according to asthma status (using case definition [i]). Compared with women without asthma, women with asthma were more likely to be overweight, ex-smokers and have more comorbidities (all $p < 0.0001$).

Fig. 1 shows the cohort profile according to asthma status. The median time of follow-up was 11.9 years, while the maximum follow-up time was 12.9 years. By 2012, surviving women were aged 85–90 years old and a total of 4170 women had died (40.0%). Among women who indicated that they had doctor diagnosed asthma in the past 3 years, 391 (47.2%) had died compared with 3779 (39.4%) women who did not have asthma. Over 12 years follow-up, women with asthma were 31% more likely to die than women with no asthma (HR: 1.31, 95%CI: 1.18–1.45, $p < 0.0001$, see Fig. 2). Factors that were associated with asthma or likely to be associated with mortality were included in the nested multivariate models sequentially (see Table 3). After accounting for the influence of age, demographic factors, health behaviours, social factors and comorbid conditions, the effect of asthma on mortality remained statistically significant. Once other factors were controlled for, women who indicated that they had asthma were still 17% more likely to have died over the 12 year period than women without asthma (HR: 1.17, 95%CI: 1.03–1.32, $p = 0.016$). Comparable models for the other three asthma case definitions showed similar and consistent associations between asthma-related respiratory conditions and mortality.

In the sensitivity analyses, there were 639 (6.1%) women who reported asthma only with no bronchitis/emphysema, 451 (4.3%) women or who reported bronchitis/emphysema only with no asthma and 190 women (1.8%) who reported having been diagnosed with both asthma and bronchitis (Table 4). While 38.9% of women with no reported respiratory conditions in the survey died during the average 12 year follow-up, higher mortality rates were observed among women with asthma only; bronchitis/emphysema only; and asthma with bronchitis/emphysema (42.7%, 49.2% and 62.1% respectively). Women with asthma only were 15% more likely to have died over 12 years compared with women without asthma and without bronchitis/emphysema (Model 1). After controlling for age, demographic factors, health behaviours, and social factors,

women with asthma only were 17% more likely to have died (Model 5). However, after controlling for comorbidities (Model 6), there was no longer evidence of a difference in mortality risk between women with asthma only and women with no reported respiratory conditions. Women who reported a diagnosis of bronchitis/emphysema only appeared to have a consistently higher risk of mortality. After controlling for other factors, these women were 33% more likely to have died over 12 years compared with women with no reported respiratory conditions. Having both asthma and bronchitis/emphysema resulted in twice the risk of mortality when compared to women with no reported respiratory conditions (HR: 2.08, Model 1). This association was attenuated slightly after taking into account other risk factors but remained strong (HR: 1.78, Model 6).

4. Discussion

In this nationally representative sample of older women, our estimates for self-reported, doctor diagnosed asthma prevalence (8.0%) were consistent with other studies in Australia [2]. However, there is no gold standard definition or diagnosis of asthma, making the estimation of prevalence difficult [8,31]. In our study, we used self-reported diagnosis of asthma by a doctor; this is a commonly used measure of asthma in epidemiological studies [31] and has been shown to have good agreement with objective measures [32]. Hansen et al. investigated the agreement between self-reported and GP-reported (BHR) asthma in multi-morbid older adults. Their findings showed strong agreement with no discernible difference between men and women [32]. Likewise, studies that have examined the agreement between self-reported and clinical investigation conclude that in large scale epidemiological studies, self-reported diagnosis of asthma can be employed as a reasonable marker for asthma [32–34]. Some studies also suggest combining responses to questions about asthma and respiratory symptoms [31,35,36]. In our study, 19.7% of women had a respiratory condition when combining self-reported doctor diagnosed asthma and bronchitis/emphysema with the symptom of breathing difficulties. A review by Sa-Sousa and colleagues demonstrated that the range of prevalence estimates (5.3%–24.4%) for different case definitions reflects the non-specific characterization of asthma and diagnosis confusion with other respiratory diseases [31]. Additionally, other studies have shown that FEV1 measures are important predictors of mortality in other age groups with asthma [37,38]. Therefore, the use of self-reported asthma without clinical measures or detailed symptomology remains a limitation of epidemiological studies, particularly for older people.

Recognising there are high numbers of false positive and false negative reports of asthma, the Global Initiative for Asthma in 2011 stated that mortality rates for asthma in older people could not be established [39]. The results of our study indicate that before considering confounders, older women reporting asthma with or without bronchitis/emphysema, have a higher mortality rate compared with women without asthma or without asthma and bronchitis/emphysema (Tables 3 and 4). In our study, controlling for age, demographic factors, health behaviours, social factors and comorbid conditions did not eliminate the higher mortality rate in

Table 1
Classification of asthma-related case definitions.

Asthma-related case definitions	(N = 10,423)
(i) Asthma	829 (8.0%)
(ii) Asthma OR (bronchitis/emphysema)	1280 (12.3%)
(iii) Asthma OR breathing difficulties	1795 (17.2%)
(iv) Asthma OR (bronchitis/emphysema) OR breathing difficulties	2057 (19.7%)

Table 2
Characteristics of women according to asthma status (n = 10,413).

Demographics, risk factors, social support and comorbidities		Asthma N = 829 n (%)	No asthma N = 9584 n (%)
Age	(mean ± SD)	75.3 ± 1.48	75.4 ± 1.46
Marital status	Partnered	397 (48.2%)	4901 (51.3%)
	Not partnered	427 (51.8%)	4647 (48.6%)
Area	Major city	488 (58.9%)	5644 (59.0%)
	Regional area	311 (37.6%)	3713 (38.8%)
	Remote area	29 (3.5%)	208 (2.2%)
BMI*	Underweight	33 (4.2%)	314 (3.4%)
	Healthy	323 (40.7%)	4634 (50.2%)
	Overweight/Obese	430 (56.2%)	4172 (46.7%)
Alcohol consumption	No drinking	318 (38.6%)	3296 (34.6%)
	Low risk drinking	227 (27.6%)	2957 (31.1%)
	Risky drinking	278 (33.8%)	3267 (34.3%)
Smoking*	Non-smoker	460 (58.7%)	5738 (63.9%)
	Ex-smoker	283 (36.1%)	2681 (29.9%)
	Current smoker	41 (5.2%)	553 (6.2%)
Comorbidities	Heart disease*	183 (22.1%)	1180 (12.6%)
	Thrombosis*	24 (2.9%)	137 (1.5%)
	Osteoporosis*	154 (18.6%)	1128 (12.0%)
	Low iron level	47 (5.7%)	425 (4.5%)
	Hypertension*	333 (40.2%)	3102 (33.1%)
	Diabetes	71 (8.6%)	685 (7.3%)
	Breast cancer	17 (2.1%)	153 (1.6%)
	Stroke	32 (3.9%)	254 (2.7%)
	Other major illness*	156 (18.8%)	918 (9.6%)
DSSI score	(mean ± SD)	9.1 ± 1.54	9.0 ± 1.55

*p < 0.05.

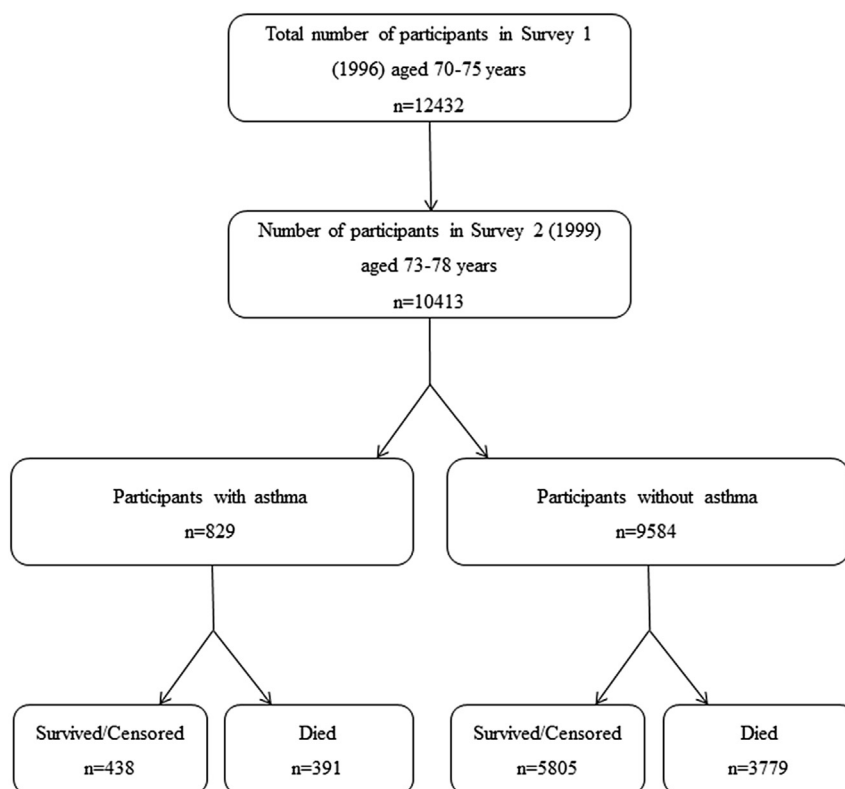


Fig. 1. Cohort profile between 1996 and 2012.

older women with asthma. The results of our sensitivity analysis indicated that while COPD alone does have a stronger impact on mortality than asthma alone, asthma still influences mortality,

particularly for women with coexisting COPD and asthma. Similarly Dantzer and colleagues found that self-reported asthma was associated with higher mortality in people aged 65 and over,

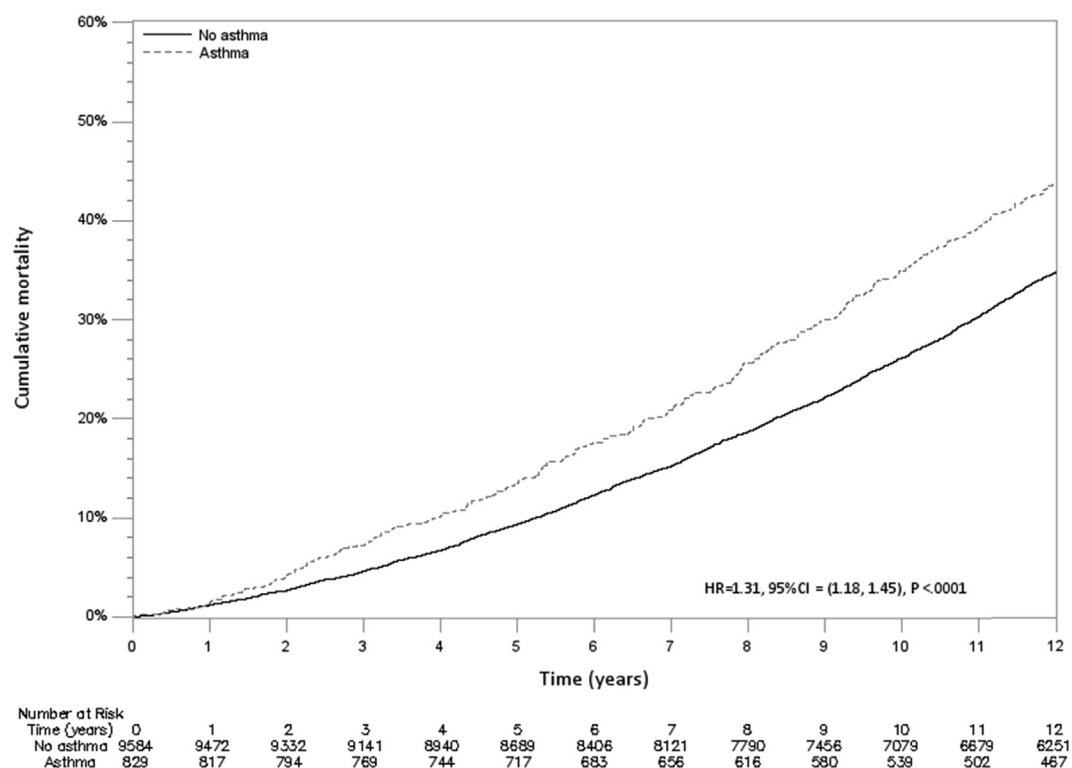


Fig. 2. Cumulative mortality for 10,413 older women, according to asthma status.

Table 3
Effect of asthma and other related respiratory conditions on mortality over an average of 12 years follow-up among 10,413 older women, after controlling for demographics, health behaviours, social support and other comorbidities.

Case definition	Death, n (%)		Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
	Case	Non-case						
(i) Asthma	391 (47.2%)	3779 (39.4%)	1.31 (1.18–1.45) <0.0001	1.31 (1.17–1.45) <0.0001	1.30 (1.17–1.44) <0.0001	1.26 (1.13–1.41) <0.0001	1.28 (1.13–1.46) <0.0001	1.17 (1.03–1.32) 0.016
(ii) Asthma or breathing difficulty	924 (51.5%)	3246 (37.7%)	1.58 (1.47–1.70) <0.0001	1.58 (1.47–1.70) <0.0001	1.58 (1.46–1.70) <0.0001	1.59 (1.47–1.72) <0.0001	1.64 (1.50–1.79) <0.0001	1.41 (1.29–1.55) <0.0001
(iii) Asthma or bronchitis/emphysema	613 (47.9%)	3557 (38.9%)	1.37 (1.26–1.49) <0.0001	1.36 (1.25–1.48) <0.0001	1.36 (1.24–1.48) <0.0001	1.30 (1.19–1.42) <0.0001	1.34 (1.21–1.49) <0.0001	1.24 (1.11–1.37) <0.0001
(iv) Asthma or breathing difficulty or bronchitis/emphysema	1035 (50.3%)	3135 (37.5%)	1.53 (1.43–1.64) <0.0001	1.54 (1.43–1.65) <0.0001	1.53 (1.42–1.64) <0.0001	1.53 (1.41–1.64) <0.0001	1.58 (1.45–1.72) <0.0001	1.38 (1.26–1.50) <0.0001

Model 1: case definition.

Model 2: case definition + age.

Model 3: case definition + age + demographics (residential area and marital status).

Model 4: case definition + age + demographics + health behaviours (BMI, smoking and alcohol).

Model 5: case definition + age + demographics + health behaviours + social support (DSSI scale).

Model 6: case definition + age + demographics + health behaviours + social support + comorbidities.

Note 1: Comorbidities include thrombosis, osteoporosis, low iron level, hypertension, diabetes, breast cancer, stroke, other major illness.

Note 2: For models 1–6, hazard ratios with corresponding 95% CI and p-values have been presented.

although the model was adjusted for only gender, marital status, educational level, cognitive impairment, smoking and comorbidities including ischemic heart disease, stroke and angina [34]. Bellia et al. reported that the difference in five year survival for 210 patients with asthma and 1027 patients with other chronic conditions was not statistically significant after covariate adjustment, including comorbidities which is in contrast with our findings [18]. Other studies have also found asthma is not associated with

mortality when other factors such as comorbidities are considered [13,18,40]. However, these studies were limited by small sample sizes and short follow-up time. A strength of our study is the large sample size and a long follow-up period (median: 11.9 years), allowing investigation of multiple potential confounders.

As populations age, the impact of asthma will be of increasing importance. It is anticipated that there will be a substantial and sustained rise in asthma-related deaths among older women. This

Table 4

Effect of asthma only, bronchitis only and their combination on mortality over an average of 12 years follow-up among 10,413 older women, after controlling for demographics, health behaviours, social support and other comorbidities.

Respiratory condition	Death n (%)	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
No asthma and no bronchitis/emphysema ^a (n = 9133)	3557 (38.9%)	1	1	1	1	1	1
Asthma only (n = 639)	273 (42.7%)	1.15 (1.02–1.30) 0.026	1.15 (1.02–1.30) 0.025	1.14 (1.01–1.29) 0.0376	1.16 (1.00–1.34) 0.0463	1.17 (1.00–1.37) 0.049	1.08 (0.92–1.26) 0.3322
Bronchitis/emphysema only (n = 451)	222 (49.2%)	1.44 (1.26–1.65) <0.0001	1.42 (1.24–1.63) <0.0001	1.31 (1.24–1.63) <0.0001	1.39 (1.11–1.54) 0.0014	1.39 (1.17–1.65) 0.0002	1.33 (1.12–1.58) 0.0012
Asthma and bronchitis/emphysema (n = 190)	118 (62.1%)	2.08 (1.74–2.50) <0.0001	2.07 (1.72–2.49) <0.0001	2.07 (1.73–2.49) <0.0001	1.95 (1.57–2.44) <0.0001	2.02 (1.55–2.55) <0.0001	1.78 (1.40–2.25) <0.0001

Model 1: respiratory condition.

Model 2: respiratory condition + age.

Model 3: respiratory condition + age + demographics (residential area and marital status).

Model 4: respiratory condition + age + demographics + health behaviours (BMI, smoking and alcohol).

Model 5: respiratory condition + age + demographics + health behaviours + social support (DSSI scale).

Model 6: respiratory condition + age + demographics + health behaviours + social support + comorbidities.

Note 1: Comorbidities include thrombosis, osteoporosis, low iron level, hypertension, diabetes, breast cancer, stroke, other major illness.

Note 2: For models 1–6, hazard ratios with corresponding 95% CI and p-values have been presented.

^a Reference group.

increased mortality risk underscores a need to improve clinical care for older women with asthma. Specific guidelines for the management of older adults with asthma and related respiratory conditions are important, particularly for older adults with other comorbidities.

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Authors' contribution

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; were involved in the drafting the manuscript and/or provided critical revision for important intellectual content; and gave final approval of the manuscript to be published.

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Ethics

Ethical approvals for the project were granted from the Human Research Ethics Committees of the University of Newcastle (HREC Ref: H-076-0795, 1996) and the University of Queensland. To preserve anonymity and confidentiality, data were de-identified prior to analysis.

Conflict of interest

The authors have not identified any conflicts of interest.

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