Predictors of chronic obstructive pulmonary disease in women who have never smoked: a cohort study

Roger M. Engel 1, Katie de Luca1, Petra L. Graham 2, Masoumeh Kaboli Farshchi1,3, Subramanyam Vemulpad1,4 and Julie Byles5

1Dept of Chiropractic, Faculty of Medicine, Health and Human Sciences, Macquarie University, Sydney, Australia. 2School of Mathematical and Physical Sciences, Macquarie University, Sydney, Australia. 3School of Persian and Complementary Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. 4Dept of Molecular Sciences, Faculty of Science and Engineering, Macquarie University, Sydney, Australia. 5School of Medicine and Public Health, University of Newcastle, Callaghan, Australia.

Corresponding author: Roger M. Engel (roger.engel@mq.edu.au)

Shareable abstract (@ERSpublications)
A history of breathing difficulties, asthma, allergies, hay fever and sinusitis are associated with an increased risk of developing COPD later in life in women who have never smoked. Lung function testing should be considered for these women. https://bit.ly/3jDX9Mp

Cite this article as: Engel RM, de Luca K, Graham PL, et al. Predictors of chronic obstructive pulmonary disease in women who have never smoked: a cohort study. ERJ Open Res 2022; 8: 00532-2021 [DOI: 10.1183/23120541.00532-2021].

Abstract
COPD is responsible for an increasing number of deaths worldwide. Smoking is the most reliable predictor for developing COPD later in life. However, women make up the majority of patients with COPD who have never smoked. There is therefore a need to identify other factors that can predict COPD in women. The aim of this study is to identify factors associated with increasing the risk of developing COPD later in life in women who have never smoked.

Data from the Australian Longitudinal Study on Women’s Health (ALSWH) cohort born between 1946 and 1951 were used to investigate potential predictors of COPD. Retrospective analyses were performed on data from two of the ALSWH surveys: wave 1 (1996) and wave 9 (2019).

There were 3584 women who self-reported as being never-smokers (at waves 1 and 9) and did not have COPD at baseline, of which 109 had developed COPD at wave 9. Logistic regression showed a significant relationship between COPD at wave 9 and baseline breathing difficulties (p<0.001), asthma (p<0.001) and allergies (p=0.026), though significance of asthma and allergies disappeared when included together in a single model, implying that women with these symptoms earlier in life were more likely to be diagnosed with COPD later in life compared to women without these symptoms.

Our study supports the inclusion of lung function testing in primary care settings for women over the age of 45 years who have never smoked and have a history of breathing difficulties, asthma or allergies.

Introduction
The term chronic respiratory disease (CRD) refers to diseases of the airways and other structures of the lung, with asthma and COPD the most common [1]. However, asthma and COPD differ substantially with respect to worldwide mortality. Recent estimates put the number of deaths from asthma at 461 000 [2] whereas for COPD, ranked as the third leading cause of death, the number of deaths reached 3.23 million in 2019 [1]. Identifying predictors of COPD therefore has a greater potential to impact morbidity and mortality.

Clinically, COPD presents as chronic bronchitis or emphysema and includes symptoms such as breathlessness, cough and sputum production, chest tightness and chest pain [3, 4]. The disease affects both men and women and is characterised by progressive airflow limitation, decreasing exercise capacity and deteriorating quality of life [5]. However, a recent review highlighted that the prevalence of COPD is increasing more rapidly in women than in men, mainly due to personal susceptibility and environmental risk factors [6].
People with COPD have lower levels of physical activity compared to people without COPD [7]. Lower levels of physical activity lead to decreased exercise capacity, a prognostic indicator for COPD [8]. Many people with early-stage COPD are unaware they have the condition or are reluctant to consult a doctor, dismissing the onset of symptoms as being part of “normal” ageing. This often results in a delay in diagnosis until the disease has become more advanced [9, 10], a situation which can affect long-term health as early diagnosis facilitates earlier intervention and a more favourable prognosis [11].

To date, smoking has been identified as the most important risk factor associated with developing COPD later in life [12, 13]. However, up to 45% of people with COPD are nonsmokers [14]. Identifying risk factors other than smoking for developing COPD later in life may be of particular relevance to women given that they make up the majority of patients with COPD who have never smoked [14].

Several studies have investigated other potential predictors of COPD [15–17]. Bu et al. [15] used the trajectories of forced expiratory volume in 1 s (FEV1) to identify modifiable early-life exposures that might minimise COPD risk later in life. They included maternal smoking and immunisation. Other studies identified chronic systemic inflammation as being associated with increasing the risk of developing COPD later in life [18]. While there have been studies on the factors associated with developing COPD in women who have a history of smoking, there is a gap in the literature around the identity of these factors in women who have never smoked.

The aim of this study is to identify factors associated with increasing the risk of developing COPD later in life in women who have never personally smoked.

Methods

The Australian Longitudinal Study on Women’s Health (ALSWH) is a population-based survey that explores the factors that contribute to the health and wellbeing of Australian women [18]. It collects data from four cohorts of women based on their year of birth: those born between 1921 and 1926; 1946 and 1951; 1973 and 1978; and 1989 and 1995. Data are collected across a range of health-related fields including arthritis, back pain, osteoporosis, diabetes, cardiac, respiratory, reproductive and mental health, cancer, ageing, tobacco, alcohol and other drug use, and exercise capacity [19]. In the field of respiratory health, the surveys include specific questions about chronic bronchitis, emphysema and COPD. The baseline survey (wave 1) was conducted in April 1996. Participants are surveyed every 3 years with the most recent survey conducted in 2019 (wave 9). Data being reported here were from the 1946 to 1951 cohort with analyses performed on the results from waves 1 and 9.

The 1946 to 1951 cohort of women were between 45 and 50 years of age at wave 1 and between 65 and 70 years at the time of completing wave 9. The factors of interest in the ALSWH surveys relating to respiratory health and wellbeing were physician-based diagnosis of COPD (the ALSWH survey question relating to COPD groups chronic bronchitis, emphysema, lung disease and COPD together), asthma, presence of allergies, hay fever and/or sinusitis, difficulty breathing, the presence of chest and/or back pain, limitations in walking various distances, and overall physical and mental health. Presence and/or treatment for COPD in the previous 3 years was used as the primary outcome for analysis. Potential predictors of COPD at wave 9 included the baseline (wave 1) variables “presence and frequency of allergies, hay fever and/or sinusitis”, “breathing difficulty”, “chest pain” and “back pain” in the last 12 months for which the following ordinal responses were provided: Never/Rarely/Sometimes/Often; presence and/or treatment for “asthma” in the past 3 years; “limitations in walking” 1 km, ½ km and 100 m for which the following ordinal responses were provided for each distance: Not limited/Limited a little/Limited a lot; and 36-item Short-Form Health Survey (SF-36) summary scores, i.e. the physical component summary (PCS) and mental component summary (MCS), for which higher scores indicate better health.

Statistical analysis

Demographic and other variables considered for analysis were summarised using means and standard deviations for continuous variables and count with percentage for categorical/ordinal variables. Differences between the COPD and no COPD groups by baseline predictor were compared using two-sample t-tests for the continuous variables, Fisher’s exact tests for the binary categorical variables and Kruskal–Wallis tests for ordinal variables. Logistic regression models were used to determine the odds of having COPD in wave 9 for each of the baseline predictor variables described, after adjusting for body mass index (BMI) as a measure of obesity, education level (less than high school, high school/trade/diploma, university or higher) and a measure of socioeconomic status of the area in which the participants live called the Socioeconomic Indexes for Areas (SEIFA) index of relative socioeconomic disadvantage (IRSD). The SEIFA IRSD is an
index developed by the Australian Bureau of Statistics that summarises measures of economic and social resources in an area including percentage of households with low income, low education, high unemployment and unskilled occupations [20]. In the SEIFA IRSD, lower scores mean more disadvantage. Predictor variables with small group sizes for some categories were collapsed into the previous category for logistic modelling. All variables significant at the 10% level in the initial analysis were included in a multivariable model which used backwards elimination to arrive at the most parsimonious final model. Only participants with observations at both baseline (wave 1) and wave 9 were included in the analyses. Participants with bronchitis/emphysema present at baseline were excluded from the analysis. Results are presented as odds ratios with 95% confidence intervals. Intervals excluding 1 imply significantly different odds compared to the reference level. p-values <0.05 were deemed significant. All analyses were completed using R version 4.1.0 statistical software [21].

### Table 1: Summary statistics for baseline demographics and predictor variables

| Baseline variable                      | COPD in wave 9 | p-value   | Overall |
|---------------------------------------|----------------|-----------|---------|
|                                       | No             | Yes       |         |
| **Subjects n**                        | 3475           | 109       | 3584    |
| **Age years**                         | 47.6±1.5       | 47.7±1.4  | 0.205a  |
| **BMI kg·m⁻²**                        | 25.4±4.7       | 26.5±5.5  | 0.059a  |
| **SF-36 PCS**                         | 51.9±7.5       | 49.9±9.3  | 0.035a  |
| **SF-36 MCS**                         | 49.5±10.0      | 46.4±11.1 | 0.004a  |
| **SEIFA IRSD**                        | 1011±86        | 1002±77   | 0.160a  |
| **Education level**                   |                |           |         |
| Less than high school                 | 1748 (42.8)    | 61 (56.0) | 1539 (43.2) |
| High school/trade/diploma            | 1328 (38.5)    | 33 (30.3) | 1361 (38.2) |
| University/postgraduate               | 645 (18.7)     | 15 (13.8) | 660 (18.5) |
| **Presence of back pain**             |                |           | 0.077a  |
| Never                                 | 901 (26.0)     | 20 (18.3) | 921 (25.8) |
| Rarely                                | 932 (26.9)     | 31 (28.4) | 963 (27.0) |
| Sometimes                             | 1100 (31.8)    | 37 (33.9) | 1137 (31.8) |
| Often                                 | 529 (15.3)     | 21 (19.3) | 550 (15.4) |
| **Presence of chest pain**            |                |           | 0.204a  |
| Never                                 | 2769 (80.4)    | 82 (75.2) | 2851 (80.2) |
| Rarely                                | 419 (12.2)     | 18 (16.5) | 437 (12.3) |
| Sometimes/often                       | 256 (7.4)      | 9 (8.3)   | 265 (7.5) |
| **Breathing difficulties**            |                |           | <0.001a |
| Never                                 | 2723 (78.9)    | 62 (57.4) | 2785 (78.3) |
| Rarely                                | 367 (10.6)     | 23 (21.3) | 390 (11.0) |
| Sometimes/often                       | 361 (10.5)     | 23 (21.3) | 384 (10.8) |
| **Asthma**                            |                |           | <0.001a |
| No                                    | 3104 (89.4)    | 82 (75.2) | 3186 (89.0) |
| Yes                                   | 368 (10.6)     | 27 (24.8) | 395 (11.0) |
| **Presence of allergies, hay fever, sinusitis** |                |           | 0.002a  |
| Never                                 | 1478 (42.8)    | 31 (28.7) | 1509 (42.4) |
| Rarely                                | 613 (17.7)     | 22 (20.4) | 635 (17.8) |
| Sometimes                             | 911 (26.4)     | 33 (30.6) | 944 (26.5) |
| Often                                 | 453 (13.1)     | 22 (20.4) | 475 (13.3) |
| **Walking 100 m**                     |                |           | 0.113c  |
| Not limited                           | 3317 (96.5)    | 101 (93.5) | 3418 (96.4) |
| Limited (a little or a lot)           | 122 (3.5)      | 7 (6.5)   | 129 (3.6) |
| **Walking ½ km**                      |                |           | 0.049c  |
| Not limited                           | 3204 (93.3)    | 95 (88.0) | 3299 (93.2) |
| Limited (a little or a lot)           | 229 (6.7)      | 13 (12.0) | 242 (6.8) |
| **Walking 1 km**                      |                |           | 0.024c  |
| Not limited                           | 2951 (85.9)    | 84 (77.8) | 3035 (85.7) |
| Limited (a little or a lot)           | 483 (14.1)     | 24 (22.2) | 507 (14.3) |

Data presented as n (%) or mean±SD unless otherwise indicated. BMI: body mass index; SF-36 PCS: physical component summary; SF-36 MCS: mental component summary; SEIFA IRSD: Socioeconomic Indexes for Areas index of relative socioeconomic disadvantage. p-values are from: a: two-sample t-test; b: Kruskal–Wallis test; c: Fisher’s exact test.
The ALSWH project received ethics approval from the University of Newcastle Human Research Ethics Committee (approval number H 076 0795) with approval for this study given by the ALSWH Steering Committee (project number A754).

Results

There were 13,714 women in the 1946–1951 cohort who completed wave 1 in 1996 (baseline) and 7,956 women who completed wave 9 in 2019. Of these, 3,584 self-reported as personally being never-smokers (at both waves 1 and 9; note that information on passive smoking was not available) and did not have bronchitis or emphysema at wave 1. At wave 9, 109 women had been diagnosed or treated for COPD in the previous 3 years while 3,475 women had not. Summary statistics for included participants are shown in table 1. Women with COPD in wave 9 were not significantly different in age or BMI from women who did not have COPD (p>0.05). Women with COPD at wave 9 were more likely to have breathing difficulties (p<0.001), asthma (p<0.001), allergies, hay fever and sinusitis (p=0.002), and limitations in walking ½ km (p=0.049) and 1 km (p=0.024) at baseline compared to women who did not have bronchitis or emphysema at wave 9. There were no differences in the proportion of those with baseline back and chest pain, or limitation in walking 100 m for women with versus without COPD at wave 9.

After adjusting for BMI, education level and socioeconomic status (via the SEIFA IRSD), logistic regression analysis of each predictor separately (table S1) showed a significant relationship between COPD and baseline breathing difficulties (versus never; Rarely: OR 2.74, 95% CI 1.64–4.43; Sometimes/often: OR 2.62, 95% CI 1.55–4.27; p<0.001), baseline presence of asthma (OR 2.73, 95% CI 1.70–4.27; p<0.001), and allergies, hay fever or sinusitis at baseline (versus never; Often: OR 2.29, 95% CI 1.30–3.98; p=0.027), implying women with these symptoms earlier in life were more likely to be diagnosed with COPD later in life compared to women without these symptoms. Women with higher (better) baseline SF-36 summary scores for both PCS and MCS had significantly lower odds of being diagnosed with COPD at wave 9 than women with lower baseline summary scores (OR 0.79, 95% CI 0.64–0.99; p=0.041 and OR 0.76, 95% CI 0.65–0.91; p=0.002, respectively) per 10-point change in those scores. There were no significant differences in odds of COPD at wave 9 by limitations in walking ½ km and 1 km at wave 1 though odds of COPD for both variables, which were significant in table 1 (OR 1.91, 95% CI 1.01–3.35 for ½ km; and OR 1.75, 95% CI 1.08–2.73 for 1 km), combined with the small change in odds, suggests a potential lack of power rather than a lack of association.

Backwards elimination of all variables significant at the 10% level in the initial modelling included in a subsequent analysis resulted in a final model containing breathing difficulties, presence of asthma, SF-36 MCS and SF-36 PCS as well as BMI, education level and SEIFA index of relative disadvantage (see table 2). Odds ratios were similar to those observed in the initial modelling except that asthma and PCS were no longer significant after adjusting for the other variables.

| Predictor variable | OR (95% CI) | p-value |
|--------------------|-------------|---------|
| BMI                | 1.01 (0.97–1.05) | 0.736   |
| Education level    |             | 0.042   |
| Less than high school | Reference |         |
| High school/trade/diploma | 0.63 (0.40–0.98) |         |
| University/postgraduate | 0.58 (0.30–1.03) |         |
| SEIFA (per 100 units) | 0.95 (0.76–1.21) | 0.692   |
| Breathing difficulties |            | <0.001  |
| Never              | Reference |         |
| Rarely             | 2.31 (1.34–3.86) |         |
| Sometimes/often    | 1.68 (0.89–3.08) |         |
| Presence of asthma |             | 0.083   |
| No                 | Reference |         |
| Yes                | 1.65 (0.92–2.89) |         |
| SF-36 PCS (per 10 units) | 0.84 (0.67–1.05) | 0.115   |
| SF-36 MCS (per 10 units) | 0.78 (0.66–0.94) | 0.008   |

BMI: body mass index; SEIFA: Socioeconomic Indexes for Areas; SF-36 PCS: physical component summary; SF-36 MCS: mental component summary.
Discussion

In Australian women aged 45–50 years and who have never smoked, the presence of breathing difficulties, asthma and/or allergies, hay fever and sinusitis at baseline were statistically significant predictors of developing COPD >20 years later. Moreover, the odds of developing COPD were more than twice the rate for women who rarely have breathing difficulties, any asthma, or allergies, hay fever and sinusitis often, compared to women who do not have these symptoms. Women who smoke are more susceptible to developing COPD than men because they have smaller airway size and therefore receive a greater dose of toxin for the same amount of inhaled smoke [22, 23]. While the prevalence of COPD among women who are never-smokers is lower than for men, the proportion of never-smokers with COPD is much higher for women than it is for men [24]. This has led to speculation that as women age, the high proportion of never-smokers with COPD may be the result of the effect changing hormonal levels have on lung function during menopause [25]. When considered in conjunction with our findings, measuring lung function using spirometry in women over the age of 45 years who have never smoked and have a history of breathing difficulties, asthma, allergies, hay fever or sinusitis would facilitate earlier detection of a CRD such as COPD. In the presence of a history of childhood asthma, measuring lung function in these women would be even more pertinent given the link between asthma and an increase in risk of developing COPD later in life [26, 27].

As early diagnosis facilitates earlier intervention and a more favourable prognosis [11], this approach would suit primary care settings where the respiratory history of a patient is known. Complicating this scenario is a level of uncertainty surrounding the diagnosis of COPD where patients considered to have the disease may not meet the threshold for airflow obstruction or simply be misdiagnosed. In an audit of >1000 patients in primary care, approximately one-third were found to not meet the guideline-specified FEV1/forced vital capacity (FVC) criteria for airflow obstruction [28]. Furthermore, in patients presenting with chronic cough, failure to recognise the syndrome of chronic cough can result in a misdiagnosis of exacerbation of COPD [29].

Given the uncertainty surrounding the diagnosis of COPD in primary care, additional steps may need to be taken to confirm the diagnosis before applying intervention. One suggestion in the presence of a normal examination and a chest radiograph is to use FEV1 % predicted instead of FEV1/FVC as the diagnostic threshold [28].

Our results showing that asthma, allergies, hay fever and sinusitis are predictors of developing a CRD such as COPD later in life are supported by the literature [30, 31]. However, our results showing that back pain was not a predictor of COPD in women who have never smoked appear at odds with the literature showing that patients with COPD experience more low back pain generally compared to those without COPD [32–34]. This disagreement can be explained by two reasons. First, that men with COPD experience more low back pain than women with COPD [32–34]. As the ALSWH study only collected data from women, our analyses were unable to account for the differences in pain distribution across sexes. Second, as the incidence of low back pain increases after the onset of COPD [34], any pre-diagnosis predictive ability would be limited.

Strengths and limitations

The strengths of this study include the longitudinal design of the ALSWH, allowing for data to be regularly collected over a 23-year period, and the relevance of the research question about identifying factors associated with the risk of developing COPD later in life in women who have never smoked. There are several limitations associated with the study. The collection of only women’s data may limit generalisability to the broader population. However, population studies support the view that men may be similarly affected by COPD as women [35–37]. While our study used data from a single country, Australia, the rates of COPD in many developed countries are similar [38]. There is therefore no basis for assuming our results would not be applicable to other developed countries. The ALSWH study relies on self-reporting of physician-diagnosed COPD in the past 3 years. While this method increases the level of confidence regarding diagnosis, self-reporting of symptoms has been shown to include a degree of inaccuracy in studies related to other chronic diseases such as arthritis [39]. Furthermore, given the level of uncertainty surrounding the diagnosis of COPD in primary care and the risk of misdiagnosis in patients with chronic cough syndrome, we acknowledge the potential that our data and therefore analyses could contain a degree of error.

Conclusion

Identifying predictors of COPD is important for improving the implementation of strategies designed to manage CRD. The results from our study provide support for the inclusion of lung function testing in
primary care settings for women over the age of 45 years who have never smoked and have a history of breathing difficulties, asthma, allergies, hay fever and/or sinusitis, albeit with additional confirmation required in some settings. This approach has the potential to reduce the burden of disease by facilitating early identification of women at risk of developing CRD and allowing for the earlier introduction of measures designed to slow or prevent disease progression.

Provenance: Submitted article, peer reviewed.

Acknowledgements: We would like to acknowledge the support of the Australian Longitudinal Study on Women’s Health (ALSWH), the University of Newcastle and the University of Queensland. We would also like to acknowledge the Australian Government Dept of Health for its support and the women who completed the ALSWH surveys.

Author contributions: R.M. Engel, K. de Luca, M. Kaboli Farshchi and S. Vemulpad were involved in the study design, interpreting the results and drafting the manuscript. P.L. Graham conducted the statistical analyses, and helped draft the methods and results section of the manuscript. R.M. Engel and J. Byles supervised the study. All authors read, revised and approved the final manuscript.

Conflict of interest: R.M. Engel has nothing to disclose. K. de Luca has nothing to disclose. P.L. Graham has nothing to disclose. M. Kaboli Farshchi has nothing to disclose. S. Vemulpad has nothing to disclose. J. Byles reports grants from Australian Dept of Health during the conduct of the study.

References

1 World Health Organization. Chronic respiratory diseases. www.who.int/health-topics/chronic-respiratory-diseases Date last accessed: 25 March 2022.
2 Vos T, Lim SS, Ababati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020; 396: 1204–1222.
3 Lung Foundation Australia. The COPD-X Plan: Australian and New Zealand guidelines for the management of chronic obstructive pulmonary disease 2021. 2.64: June 2021; p. 19. www.copdx.org.au Date last updated: 2 May 2022.
4 Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. 2021. Available from: http://goldcopd.org/
5 Liu W, Liu Y, Li X. Impact of exercise capacity upon respiratory functions, perception of dyspnea, and quality of life in patients with chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis 2021; 16: 1529–1534.
6 Jenkins CR, Chapman KR, Donohue JF, et al. Improving the management of COPD in women. Chest 2017; 151: 686–696.
7 Watz H, Pitta F, Rochester CL, et al. An official European Respiratory Society statement on physical activity in COPD. Eur Respir J 2014; 44: 1521–1537.
8 Waschki B, Kirsten A, Holz O, et al. Physical activity is the strongest predictor of all-cause mortality in patients with COPD: a prospective cohort study. Chest 2011; 140: 331–342.
9 Peña VS, Miravitlles M, Gabriel R, et al. Geographic variations in prevalence and underdiagnosis of COPD: results of the IBERPOC multicentre epidemiological study. Chest 2000; 118: 981–989.
10 Toelle BG, Xuan W, Bird TE, et al. Respiratory symptoms and illness in older Australians: the Burden of Obstructive Lung Disease (BOLD) study. Med J Aust 2013; 198: 144–148.
11 Laucho-Contreras ME, Cohen-Todd M. Early diagnosis of COPD: myth or a true perspective. Eur Respir Rev 2020; 29: 200131.
12 American Lung Association. COPD causes and risk factors. www.lung.org/lung-health-diseases/lung-disease-lookup/copd/what-causes-copd#:~:text=Smoking%20is%20the%20biggest%20risk,developing%20and%20byinger%20from%20COPD Date last accessed: 2 May 2022.
13 Australian Institute of Health and Welfare. Chronic obstructive pulmonary disease (COPD), associated comorbidities and risk factors. www.aihw.gov.au/reports/web/105/copd-associated-comorbidities-risk-factors/contents/risk-factors-associated-with-copd Date last accessed: 2 May 2022.
14 Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. Lancet 2009; 374: 733–743.
15 Bui DS, Lodge CJ, Burgess JA, et al. Childhood predictors of lung function trajectories and future COPD risk: a prospective cohort study from the first to the sixth decade of life. Lancet Respir Med 2018; 6: 535–544.
16 Cavailles A, Brinchall-Rabin G, Dixmier A, et al. Comorbidities of COPD. Eur Respir Rev 2013; 22: 454–475.
17 Fuller-Thomson E, Howden KEN, Fuller-Thomson LR, et al. A strong graded relationship between level of obesity and COPD: findings from a national population-based study of lifelong nonsmokers. J Obes 2018; 2018: 6149263.
18 ALSWH. Australian Longitudinal Study on Women’s Health. www.alswh.org.au/ Date last accessed: 25 March 2022.

19 Brown W, Bryson L, Byles J, et al. Women’s Health Australia: Establishment of The Australian Longitudinal Study on Women’s Health. *J Womens Health* 1996; 5: 467–472.

20 Australian Bureau of Statistics. Socio-Economic Indexes for Areas (SEIFA) 2011. www.ausstats.abs.gov.au/ausstats/subscriber.nsf/0/22CEDA8038AFTA0DCA257B3B00116E34/$File/2033.0.55.001%20seifa%202011%20tec%20hnical%20paper.pdf

21 R Core Team. R: A language and environment for statistical computing. Vienna, Austria, R Foundation for Statistical Computing, 2020. www.R-project.org/

22 Sin DD, Cohen SB, Day A, et al. Understanding the biological differences in susceptibility to chronic obstructive pulmonary disease between men and women. *Proc Am Thorac Soc* 2007; 4: 671–674.

23 Chapman KR. Chronic obstructive pulmonary disease: are women more susceptible than men? *Clin Chest Med* 2004; 25: 331–341.

24 von Hertzen L, Reunanen A, Impivaara O, et al. Airway obstruction in relation to symptoms in chronic respiratory disease – a nationally representative population study. *Respir Med* 2000; 94: 356–363.

25 Matheson MC, Bowatte G, Perret JL, et al. Prediction models for the development of COPD: a systematic review. *Int J Chronic Obstruct Pulmon Dis* 2018; 13: 1927–1935.

26 Tai A, Tran H, Roberts M, et al. The association between childhood asthma and adult chronic obstructive pulmonary disease. *Thorax* 2014; 69: 805–810.

27 McGeachie MJ. Childhood asthma is a risk factor for the development of chronic obstructive pulmonary disease. *Curr Opin Allergy Clin Immunol* 2017; 17: 104–109.

28 Hamad G, Rigby A, Morice AH. An audit of COPD: diagnosis and management in general practice. *ERJ Open Res* 2020; 6: 00330-2020.

29 Morice AH, Millqvist E, Bielsiensen K, et al. ERS guidelines on the diagnosis and treatment of chronic cough in adults and children. *Eur Respir J* 2020; 55: 1901136.

30 Silva GE, Sherrill DL, Guerra S, et al. Asthma as a risk factor for COPD in a longitudinal study. *Chest* 2004; 126: 59–65.

31 Jamieson DB, Matsui EC, Belli A, et al. Effects of allergic phenotype on respiratory symptoms and exacerbations in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2013; 188: 187–192.

32 de Miguel-Díez J, López-de-Andrés A, Hernández-Barrera V, et al. Prevalence of pain in COPD patients and associated factors: report from a population-based study. *Clin J Pain* 2018; 34: 787–794.

33 Bentsen SB, Miaskowski C, Cooper BA, et al. Distinct pain profiles in patients with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2018; 13: 801–811.

34 Bordoni B, Marelli F, Morabito B, et al. Low back pain and gastroesophageal reflux in patients with COPD: the disease in the breath. *Int J Chron Obstruct Pulmon Dis* 2018; 13: 325–334.

35 Watson L, Vonk JM, Löfdahl CG, et al. Predictors of lung function and its decline in mild to moderate COPD in association with gender: results from the Euroscop study. *Respir Med* 2006; 100: 746–753.

36 Garcia-Aymerich J, Lange P, Benet M, et al. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: a population-based cohort study. *Am J Respir Crit Care Med* 2007; 175: 458–463.

37 Hopkinson NS, Polkey MI. Does physical inactivity cause chronic obstructive pulmonary disease? *Clin Sci (Lond)* 2010; 118: 565–572.

38 Blanco I, Diego I, Bueno P, et al. Geographic distribution of COPD prevalence in the world displayed by Geographic Information System maps. *Eur Respir J* 2019; 54: 1900610.

39 Lo TKT, Parkinson L, Cunich M, et al. Discordance between self-reported arthritis and musculoskeletal signs and symptoms in older women. *BMC Musculoskelet Disord* 2016; 17: 494.