



## Original Research

## Contrasting healthcare costs of COPD and asthma in elderly

Tiina Mattila<sup>a,b,\*</sup>, Tuula Vasankari<sup>c,d</sup>, Fredrik Herse<sup>e</sup>, Riikka-Leena Leskelä<sup>e</sup>, Marina Erhola<sup>f</sup>, Heidi Avellan-Hietanen<sup>a</sup>, Sanna Toppila-Salmi<sup>g,h</sup>, Tari Haahtela<sup>h</sup>

<sup>a</sup> Department of Pulmonary Diseases, Heart and Lung Center, Helsinki University Hospital and Helsinki University, Meilahti Triangle Hospital, 6th floor, PO Box 372, 00029 HUS, Helsinki, Finland

<sup>b</sup> Finnish Institute for Health and Welfare, PO Box 30, 00271, Helsinki, Finland

<sup>c</sup> University of Turku, Department of Pulmonary Diseases and Clinical Allergy, PO Box 52, 20521, Turku, Finland

<sup>d</sup> Finnish Lung Health Association (FILHA), Sibeliuskatu 11 A 1, 00250, Helsinki, Finland

<sup>e</sup> Nordic Healthcare Group, Vattuniemenranta 2, 00210, Helsinki, Finland

<sup>f</sup> The Wellbeing Services County of Pirkanmaa, Biokatu 10, Finn-Medi 3 (5th floor), 33520, Tampere, Finland

<sup>g</sup> Skin and Allergy Hospital, Helsinki University Hospital and University of Helsinki, Helsinki, PO Box 160, 00290, Finland

<sup>h</sup> Department of Otorhinolaryngology, Kuopio University Hospital and School of Medicine, Institute of Clinical Medicine, University of Eastern Finland, Finland

## ARTICLE INFO

## Keywords:

Asthma  
COPD  
Elderly  
Epidemiology  
Public health

## ABSTRACT

**Background:** Caring for ageing populations creates new challenges for society. Obstructive pulmonary diseases, asthma and especially COPD, are responsible for considerable morbidity, mortality, and financial costs in the elderly. We present the change in the burden of asthma and COPD in those aged  $\geq 60$  years in Finland from 1996 to 2018.

**Methods:** We collected national register data from 1996 to 2018 from Statistics Finland, Care Register for Health Care, and the Social Insurance Institution. We estimated the prevalence of asthma and severe COPD, use of healthcare, social services, reimbursed inhalation medications, and societal costs.

**Results:** In subjects aged  $\geq 60$  years, the prevalence was 8% for asthma with reimbursed medication and 0.7% for severe COPD in 2018. In 1996–2018, total costs increased from 33 M€ to 58 M€ (+57%) for asthma and decreased from 38 M€ to 30 M€ (–27%) for COPD. Costs per patient decreased for asthma from 720 € to 460 € (–57%) and remained stable for COPD (2700 € in 2018). Potential years of life lost (PYLL) increased in COPD from 5000 to 6400 (+28%) and the number of emergency department visits increased from 3700 to 6000 (+62%).

**Conclusions:** In a population aged  $\geq 60$  years, the total burden caused by asthma decreased but remained stable and high in COPD. PYLL and visits in emergency care increased in COPD.

## 1. Introduction

Asthma and COPD are obstructive pulmonary diseases. Asthma can be diagnosed at any age and in both sexes [1,2]. The global and Finnish prevalence of asthma are 3.6% [1] and 4.5% [3], respectively. The global and Finnish prevalence of COPD is 3.9% [1,3–5] and increases with age [1,3–5]. Asthma and especially COPD are major causes of disability [1]. Although death rates due to these conditions are decreasing, asthma and COPD still cause 0.9% and 5.7% of global deaths, respectively [1]. Increased mortality and poor prognosis are associated with COPD in more severe forms and COPD with exacerbations and multiple comorbidities [5–7].

In asthma, chronic airway inflammation causes mainly reversible obstruction. Asthma phenotypes diagnosed in adults include late-onset non-allergic eosinophilic and non-eosinophilic asthma, asthma in obese females and in the elderly, and asthma-COPD overlap [2,5,8–10]. In contrast to classic allergic asthma, a weak response to inhaled corticosteroids is common for these phenotypes [2], which are associated with comorbidities such as obesity, cardiovascular diseases, chronic rhinosinusitis, nasal polyposis, anxiety, and depression [2,11].

In COPD, continuous inhaled exposure (tobacco smoke being the most important), leads to chronic inflammation. This results in a syndrome with mostly non-reversible lung changes, such as small airway fibrosis leading to bronchus obstruction and parenchymal tissue

\* Corresponding author. Helsinki University Hospital, Department of Pulmonary Diseases, Meilahti Triangle Hospital, 6th floor, PO Box 372, 00029 HUS, Helsinki, Finland.

E-mail address: [tiina.m.mattila@hus.fi](mailto:tiina.m.mattila@hus.fi) (T. Mattila).

<https://doi.org/10.1016/j.rmed.2023.107477>

Received 13 September 2023; Received in revised form 8 November 2023; Accepted 16 November 2023

Available online 22 November 2023

0954-6111/© 2023 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

destruction, which in turn leads to emphysema [5]. Comorbidities are generally associated with multi-morbidity, such as cardiovascular diseases, diabetes, sarcopenia, and depression [5,6,12].

The global population is ageing [12]. The number of persons aged  $\geq 65$  years has increased from 427 000 (9% of the population) in 1970 to 1 279 000 (23%) in 2021. This number is estimated to be 1 518 000 (27%) in 2040. In Finland, most of the population retired in 2008–2022 at the age of 60–65 years and only very few worked after the age of 65 [13,14].

Changes in lifestyle and environment in the 20th century have also apparently affected respiratory health in the elderly. Finland has developed from a poor agricultural country to an urbanized high-income country, where everyday life requires less mandatory physical activity [13,15]. Among persons aged  $\geq 65$  years in Finland, 10% of men and 5% of women smoked in 2017; this trend does not appear to be decreasing [16]. The prevalence of obesity ( $\text{BMI} \geq 30 \text{ kg/m}^2$ ) in this age group in Finland is 25% for men and over 30% for women in 2017 [16]. Obesity complicates breathing in asthma and COPD and predicts more severe asthma, especially in women [2,5,17]. In addition, increasing age causes physiological changes that weaken respiration, such as decreasing elasticity and muscle strength in the lungs, increasing rigidity of the chest wall, and airway remodelling [9].

Caring for ageing populations creates new challenges for society. Here, we report the change in the burden and costs due to asthma and COPD in the Finnish population aged  $\geq 60$  years from 1996 to 2018. We also provide recommendations to address this increased burden.

## 2. Material and methods

### 2.1. Study population

Data were collected from national registers from the years 1996–2018. These data include all Finnish persons aged  $\geq 60$  years who have used public health and social care services. The Finnish national health system is described in Supplement 1.

### 2.2. Study design

We report the annual change from the years 1996–2018 in the burden and costs of asthma and COPD in those aged  $\geq 60$  years according to national register data.

### 2.3. Data

The Finnish national authorities compile statutory health registers. In this study, we used data from the Care Register for Health Care (primary diagnosis code) from secondary healthcare with separate data for inpatient (hospitalisations including number of inpatient days) and outpatient services (outpatient visits) and from primary healthcare for inpatient services [18]; Social Insurance Institution (SII) special reimbursements for chronic asthma and severe COPD medications [19]; and Statistics Finland for deaths [13].

The Finnish special reimbursement criteria for chronic asthma needing regular medication have been described previously [3,19–21]. For severe COPD, the criteria for special reimbursed medication includes forced expiratory volume in 1 s ( $\text{FEV}_1$ )  $< 40\%$  of reference values or  $< 50\%$  and at least one severe or two other disease exacerbations [3,19]. Due to special reimbursement criteria (demonstrated reversibility as in asthma), some cases of mild-to-moderate COPD may have been special reimbursed as asthma. However, most cases of mild-to-moderate COPD are not special reimbursed and are thus not included in the reimbursement register.

### 2.4. Disease classification

We used Anatomical Therapeutic Chemical (ATC) codes for asthma

and COPD medications for the SII special reimbursement registry [19, 22]. Otherwise, for Care Register for Health Care, SII, and Statistics Finland, we used codes from the International Classification of Diseases 10 (ICD-10) (asthma J45, J46; COPD J44, J43, J42) and from the International Classification of Primary Care 2 (ICPC 2) codes (asthma R96; COPD R95, R79). In Finland, ICD-9 was replaced by ICD-10 in 1996; therefore, ICD-9 was used for care episodes and medication reimbursements initiated before 1996.

### 2.5. Analysis methods

The yearly age-group specific prevalence of asthma and severe COPD was estimated from the SII registry according to the number of people with special reimbursed medications. SII data did not differentiate between asthma and severe COPD prior to 2005. Accordingly, the proportion of COPD patients was extrapolated based on the trend in the proportion of COPD patients from the years 2005–2018, which was decreasing (23% of all patients in 2005 and 18% in 2018). Similarly, medication costs prior to 2005 were extrapolated based on the estimated ratio of cost per patient in COPD vs. asthma in 2005–2018, which was increasing (medication costs for a COPD patient were 1.4 times higher in 2005 and 1.8 times higher in 2018 than those of an average asthma patient).

In cost-of-illness (COI) analysis, we estimated direct age group-specific costs according to the disease in question. For direct cost calculations, we included inpatient episodes and outpatient visits with the primary diagnosis code related to asthma or COPD. Medication costs included those with special reimbursed medication for asthma or severe COPD.

The number of yearly outpatient visits in secondary care was available from 1998. For the preceding 2 years, the number of outpatient visits was extrapolated based on the annual prevalence of each year and the average number of visits per patient in 1998, 1999, and 2000.

To estimate the yearly burden, direct costs (out- and inpatient care in secondary care, inpatient care in primary care, and use of medication for asthma and severe COPD) were calculated based on the service use and unit costs for each service. The 22-year follow-up results are presented as an annual time series. For primary care, the data on outpatient visits were available only from 2013 and were thus omitted from the analysis.

Data, available to us, for estimating indirect cost would have included costs of productivity losses from work absenteeism in the form of sick leaves and disability pension. Our data include almost only persons who have retired, and therefore, in our study we estimated only direct health care costs [3,14].

Potential years of life lost (PYLL) were calculated based on asthma and COPD mortality in 5-year age groups and the average life expectancy in each age group. Average life expectancy was defined as the average age of the total population that died each year. PYLLs were obtained as the difference between age at death and life expectancy multiplied by the number of asthma and COPD death in each age group [23].

All costs were converted into 2018 prices using the consumer price index from Statistics Finland [13].

### 2.6. Ethical aspects

We used data obtained from national registers without personal identifiers.

## 3. Results

The Finnish population aged  $\geq 60$  years increased from 983 200 (19% of the entire population) in 1996 to 1 567 400 (28%) in 2018. During the same period, the prevalence of asthma increased from 4639 per 100 000 inhabitants to 8055 per 100 000 inhabitants (+170%); the prevalence of severe COPD decreased from 1407 to 679 per 100 000

inhabitants aged  $\geq 60$  (–210%) years (Fig. 1d). Actual prevalence rates in 2018 were 8% for asthma and 0.7% for severe COPD.

During the follow-up period from 1996 to 2018, there was some increase in the yearly number of outpatient visits in secondary care. Inpatient days in secondary care decreased from 31 400 to 4800 (–650%) for asthma and from 74 200 to 22 000 (–340%) for COPD. For primary care, the decrease was from 22 700 to 7900 (–290%) for asthma and from 55 700 to 33 300 (–170%) for COPD (Fig. 1a–c).

Total costs for asthma increased from 33 M€ in 1996 to 58 M€ in 2018 (+57%) in those aged  $\geq 60$  years. In 2018, this was 47% of the total direct costs of asthma in the adult population. For COPD, costs decreased from 38 M€ to 30 M€ (–27%); this is explained mostly by the decrease in inpatient care in secondary care (from 31 M€ to 19 M€; –63%). In 2018, 91% of COPD costs were for those aged  $\geq 60$  years (Fig. 2a–d). Costs per patient in those aged  $\geq 60$  years decreased from 720 € to 460 € (–57%) for asthma and remained stable in the 2000s for COPD (2700 € in 2018) (Fig. 3a–d).

During the follow-up period for those with COPD aged  $\geq 60$  years, PYLL increased from 5000 to 6400 (+28%) in 2018 and the number of emergency department visits increased from 3700 to 6000 (+62%) (Fig. 4 a–b). Total mortality for COPD increased from 1005 in 1996 to 1238 in 2018 (+23%).

#### 4. Discussion

In this study on a Finnish population with asthma aged  $\geq 60$  years, we observed that the need for care and costs are decreasing although the number of patients is increasing. Although the prevalence of severe COPD is unchanged, PYLL, emergency department visits, and mortality are increasing.

The global population is ageing and the overall prevalence of asthma is decreasing [1]. However, in Finland the prevalence of asthma is increasing [3], also in the elderly. The overall prevalence of COPD is increasing in high-income countries but remains stable in Finland [1,4]. The prevalence of severe COPD is also stable both in the overall Finnish population [3] and those aged  $\geq 60$  years.

The national *Asthma (1994–2004)*, *COPD (1998–2007)*, and *Allergy Programme (2008–2018)* played a central role in Finland in increasing awareness and synchronizing diagnostics and treatment of these diseases (Supplement 2) [21,24,25]. For instance, the *COPD Programme* highlighted the cause-and-effect relationship of COPD and smoking,

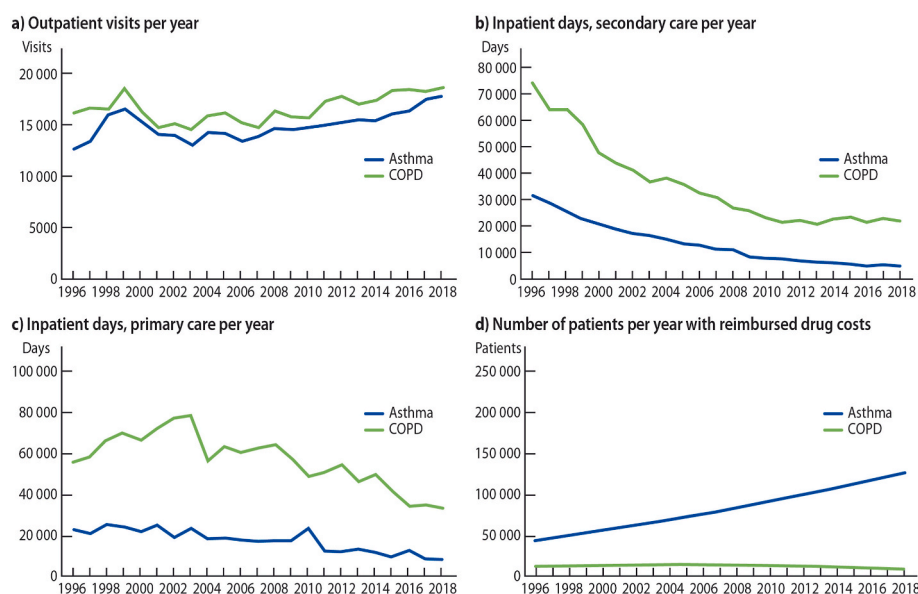
emphasised earlier diagnosis with objective lung-function measurements, and pressured decision makers to renew anti-smoking legislation to support various anti-smoking campaigns. This resulted in smoking bans in workplaces in 1995 and in restaurants in 2007 [24]. Smoking is decreasing in Finland and in other high-income countries [1,5,16,24]; accordingly, the prevalence of COPD may decrease in future.

Although the total burden and costs of asthma in the elderly are decreasing in Finland, the prevalence of asthma is increasing. This could be interpreted that asthma in most elderly patients is a treatable disease that has minimal impact on daily life. It has been shown that most Finnish adult asthma patients need less care than before, have minimal symptoms, and severe symptoms are rare [21,26]. It is also likely that nowadays less severe asthma is diagnosed, which may explain in part these positive results [21].

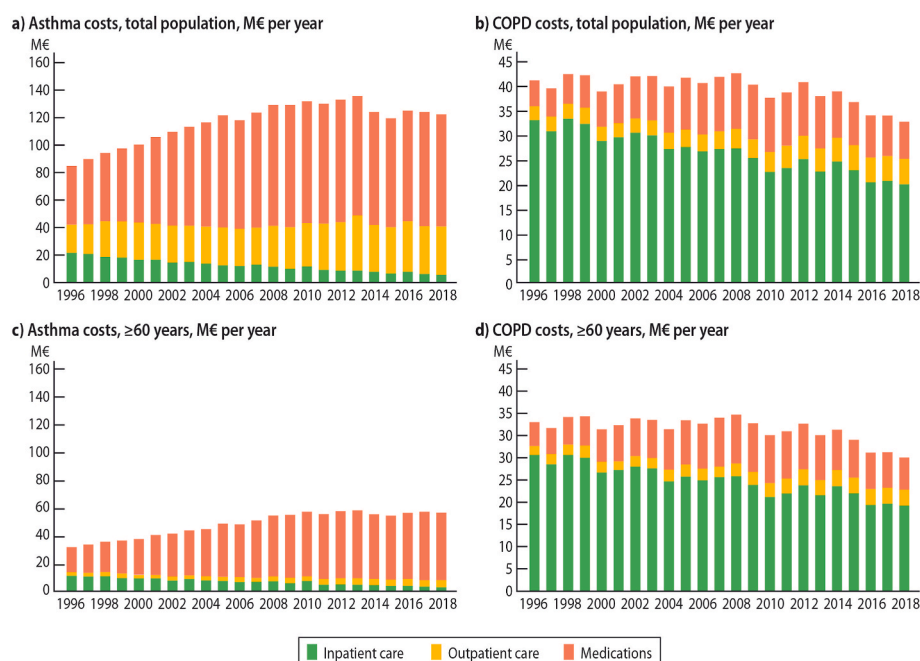
However, severe or difficult-to-treat phenotypes are responsible for much of the burden of asthma [11]. Additionally, increased burden is associated with asthma in the elderly and with exacerbations. Poor asthma control is associated with comorbidities, multimorbidity, and polypharmacy, leading to hospitalizations and increased costs [8,11,27]. For COPD, the more severe forms, phenotypes with exacerbations and comorbidities, sedentary lifestyle, and ageing predict increased burden and costs [5,7]. In the elderly, physiological changes and obesity lead to less effective breathing [5,9,11]. Furthermore, ageing may complicate treatment of asthma and COPD [5,10,28].

Although global life expectancy has increased, the disease-free life-span has not increased accordingly [12]. Ageing increases the risk for multimorbidity, frailty, and chronic terminal diseases [6,12]. COPD is an example of a progressive syndrome with multimorbidity that causes frailty and early death [5,6]. COPD is responsible for 3.3% of the global disability-adjusted life years, and rates are increasing [1]. In our study, PYLL, emergency department visits (likely due to COPD exacerbations), and mortality due to COPD were increasing. According to previous data, the mortality risk in COPD is associated with COPD severity, amount and severity of comorbidities, sedentary lifestyle, and exacerbations [5,29]. Global mortality due to COPD is increasing [1]. In Britain, mortality due to COPD increased in those aged  $\geq 85$  years from 2000 to 2015 [30]. Furthermore, patients with COPD often have concomitant cardiovascular disease, malignancies, and other chronic lung disease [5,29]. Smoking is mainly responsible for mortality due to COPD [1]; the average number of lost years in Europe due to smoking is 4.8 [12].

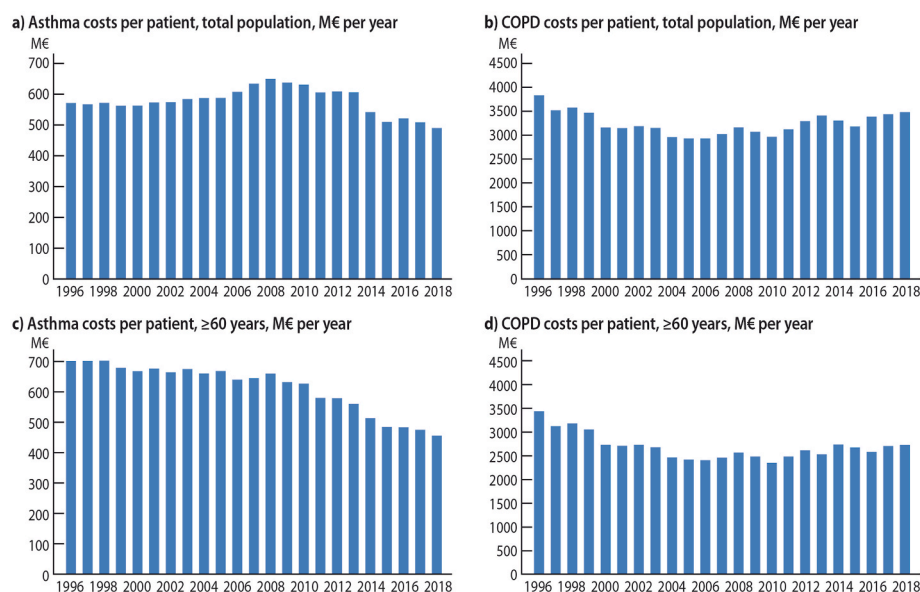
Both the global and Finnish populations are ageing [12,13]. To care



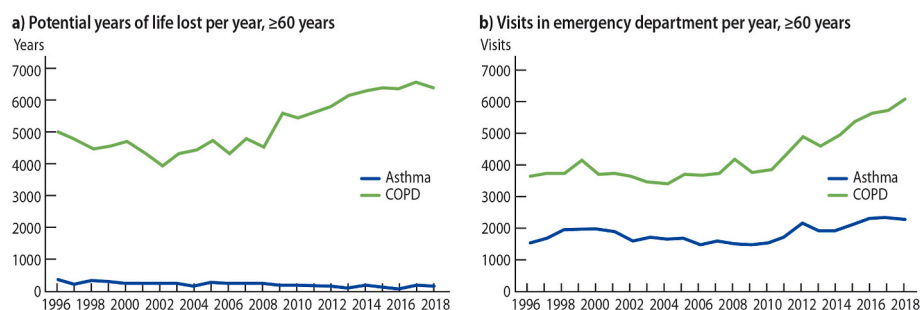
**Fig. 1.** Disease burden of asthma and COPD in those aged  $\geq 60$  years: a) outpatient visits, b) inpatient days in secondary care, c) inpatient days in primary care, and d) number of patients with asthma and severe COPD entitled to special reimbursement for their drug costs.



**Fig. 2.** Direct healthcare costs in total population and in those aged  $\geq 60$  years, divided into cost components: a) asthma, total, b) COPD, total, c) asthma,  $\geq 60$  years, and d) COPD,  $\geq 60$  years.



**Fig. 3.** Average cost per patient in total population and in those aged  $\geq 60$  years: a) asthma, total, b) COPD, total, c) asthma,  $\geq 60$  years, and d) COPD,  $\geq 60$  years.



**Fig. 4.** Potential years of life lost (PYLL) (a) and visits to emergency department (b) in those aged  $\geq 60$  years with asthma or COPD.



for an ageing population, reducing the length and severity of late-life morbidity should be the most important goal for society [12]. The keys to preventing multimorbidity, frailty, and polypharmacy include daily decisions at the individual level that promote a healthy lifestyle, such as smoking cessation, a healthy diet, and physical activity [5,8,10,12,15,21,24,25]. The role of society is to support individuals to make appropriate decisions, and additionally, to diagnose and treat any possible diseases early and cost-effectively [12]. Increasing exposure to natural environments with rich microbiota may increase general and respiratory health [31].

However, the older and more frail the patient is, the more the goal of treatment should focus on quality of life [6,12]. There is a significant risk for over-diagnosis and over-treatment in the elderly patient with multi-morbidity, many symptoms, and reduced cooperation [6,28]. At the individual level, this may cause possible side-effects due to over-medication without any increase in quality of life [12,28]. At the population level, this may result in increased disease burden and costs. Additionally, advanced age and multimorbidity are often exclusion criteria for clinical trials, and data on the benefits of new medications in elderly populations remain scarce [28].

#### 4.1. Limitations

We performed a retrospective, descriptive, and register-based study. The limitations of this study are those typically associated with this kind of design. These include missing information on certain confounders, such as changes in lifestyle factors. However, we used nationwide real-world data with long-term follow up, which is expected to reduce bias. National and international diagnostic criteria and treatment guidelines for asthma and COPD and their phenotypes have varied during follow-up [2,5,10], which complicates comparisons between studies. However, our data with nationwide, systematically collected diagnoses showed long-term changes in prevalence rates and burden.

The prevalence rates were concentrated on more severe forms of asthma and COPD that require regular medication (special reimbursed diseases). Due to Finnish special reimbursement criteria, some COPD with significant reversibility may have been registered as asthma. On the other hand, the outpatient and inpatient visits included all cases with a diagnosis of COPD. During the follow-up period, documentation of causes of deaths may have changed and the mean life expectancy increased (from 73 to 79 years in men and from 81 to 84 in women) [13], which may have slightly affected our results.

## 5. Conclusion

In asthma, routine diagnostics and treatment are also appropriate in the elderly regarding the risk of over-diagnostics and over-medication. However, to prevent premature deaths and decrease the burden and costs at the population level, the focus should be prevention, diagnostics, and treatment of severe and very severe COPD. This includes smoking cessation, early diagnostics, patient education, targeted medication, and increasing daily physical activity. Digitalisation and e-health applications will bring solutions for management and prevention. Nevertheless, effective primary care will remain a prerequisite for effective control of asthma and COPD.

## Contributions

FH, R-LL, and TM collected and analysed most of the data. TM outlined the first version of the manuscript. All authors interpreted the data, contributed to the writing process, and have read and agreed to the published version of the manuscript.

## Funding

The Finnish Institute for Health and Welfare, The Hospital District of

Helsinki and Uusimaa (HUH), Finland, and the Research Foundation of the Pulmonary Diseases, Finland.

## Data sharing statement

The data analysed in this study are not directly available to others. Anyone may apply for a study permit and access to the data from the appropriate registers from Findata and from the relevant hospital districts. Other related documents, including memos and plans for this study (mainly in Finnish), will be available 2 years after publication for researchers upon reasonable request ([tiina.m.mattila@hus.fi](mailto:tiina.m.mattila@hus.fi)).

## CRediT authorship contribution statement

**Tiina Mattila:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Visualization, Project administration, Funding acquisition. **Tuula Vasankari:** Conceptualization, Methodology, Writing – review & editing. **Fredrik Herse:** Conceptualization, Methodology, Validation, Software, Formal analysis, Investigation, Visualization, Writing – review & editing. **Riikka-Leena Leskelä:** Conceptualization, Methodology, Validation, Software, Formal analysis, Investigation, Visualization, Writing – review & editing. **Marina Erhola:** Conceptualization, Writing – review & editing. **Heidi Avellan-Hietanen:** Conceptualization, Writing – review & editing. **Sanna Toppila-Salmi:** Conceptualization, Writing – review & editing. **Tari Haahetla:** Conceptualization, Methodology, Writing – review & editing.

## Declaration of competing interest

There is no conflict of interest.

## Acknowledgement

The Finnish Institute for Health and Welfare funded the data collection. Financial support from the Hospital District of Helsinki and Uusimaa and the Research Foundation of the Pulmonary Diseases awarded to the first author allowed for write-up of our analysis.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rmed.2023.107477>.

## References

- [1] GBD Chronic Respiratory Disease Collaborators, Prevalence and attributable health burden of chronic respiratory diseases, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017, *Lancet Respir. Med.* 8 (2020) 585–596.
- [2] R. Kaur, G. Chupp, Phenotypes and endotypes of adult asthma: moving toward precision medicine, *J. Allergy Clin. Immunol.* 144 (2019) 1–12.
- [3] T. Mattila, M. Erhola, T. Vasankari, et al., Controlling chronic respiratory diseases in Finland from 1996 to 2018, *Eur. Respir. J.* 60 (2022), 2200318.
- [4] T. Vasankari, O. Impivaara, M. Heliövaara, et al., No increase in the prevalence of COPD in two decades, *Eur. Respir. J.* 36 (2010) 766–773.
- [5] A. Agustí, B.R. Celli, G.J. Criner, et al., Global initiative for chronic obstructive lung disease 2023 report: GOLD executive summary, *Eur. Respir. J.* 61 (2023), 2300239.
- [6] M.E. Salive, Multimorbidity in older adults, *Epidemiol. Rev.* 35 (2013) 75–83.
- [7] I. Iheanacho, S. Zhang, D. King, M. Rizzo, A.S. Ismaila, Economic burden of chronic obstructive pulmonary disease (COPD): a systematic literature review, *Int. J. Chronic Obstr. Pulm. Dis.* 15 (2020) 439–460.
- [8] J. Hsu, J. Chen, M.C. Mirabelli, Asthma morbidity, comorbidities, and modifiable factors among older adults, *J. Allergy Clin. Immunol. Pract.* 6 (2018) 236–243.e7.
- [9] R.M. Dunn, P.J. Busse, M.E. Wechsler, Asthma in the elderly and late-onset adult asthma, *Allergy* 73 (2018) 284–294.
- [10] H.K. Reddel, J.M. FitzGerald, E.D. Bateman, L.B. Bacharier, A. Becker, G. Brusselle, Gina, A fundamental change in asthma management: treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents, *Eur. Respir. J.* 53 (2019), <https://doi.org/10.1183/13993003.01046-2019>, 2019.

- [11] R.F. McLoughlin, V.M. McDonald, The management of extrapulmonary comorbidities and treatable traits; obesity, physical inactivity, anxiety, and depression, in adults with asthma, *Front Allergy* 2 (2021), 735030.
- [12] L. Partridge, J. Deelen, P.E. Slagboom, Facing up to the global challenges of ageing, *Nature* 561 (2018) 45–56.
- [13] Statistics Finland. <https://www.stat.fi/>. (Accessed 21 June 2023).
- [14] Finnish Centre for Pensions. <https://www.etk.fi/en/>. (Accessed 2 November 2023).
- [15] M. Smith, J. Hosking, A. Woodward, K. Witten, A. MacMillan, A. Field, ym, Systematic literature review of built environment effects on physical activity and active transport – an update and new findings on health equity, *Int. J. Behav. Nutr. Phys. Activ.* 14 (2017) 158.
- [16] P. Koponen, K. Borodulin, A. Lundqvist, K. Sääksjärvi, S. Koskinen, National FinHealth Survey - Terveys, Toimintakyky Ja Hyvinvointi Suomessa - FinTerveys 2017-tutkimus, National Institute for Health and Welfare, Helsinki, Finland, 2018 (in Finnish, abstract in English). (Accessed 20 June 2023).
- [17] R. Barros, P. Moreira, P. Padrao, V.H. Teixeira, P. Carvalho, L. Delgado, ym, Obesity increases the prevalence and the incidence of asthma and worsens asthma severity, *Clin. Nutr.* 36 (2017) 1068–1074.
- [18] Care Register for Health Care (HILMO), National Institute for health and Welfare, Helsinki, Finland. [https://www.thl.fi/fi/tilastot/tiedonkeruut/hoitoilmoitus\\_jarjestelma-hilmo](https://www.thl.fi/fi/tilastot/tiedonkeruut/hoitoilmoitus_jarjestelma-hilmo). (Accessed 7 May 2022).
- [19] Social insurance institution of Finland, statistics, reimbursement system, Available at: <https://www.kela.fi/>; <https://www.kela.fi/tilastot-aiheittain-tilasto-korvatuista-resepteista>, 2019.
- [20] A. Karjalainen, K. Kurppa, R. Martikainen, J. Karjalainen, T. Klaukka, Exploration of asthma risk by occupation—extended analysis of an incidence study of the Finnish population, *Scand. J. Work. Environ. Health* 28 (2002) 49–57.
- [21] T. Haahtela, F. Herse, J. Karjalainen, et al., The Finnish experience to save asthma costs by improving care in 1987–2013, *J. Allergy Clin. Immunol.* 139 (2016) 408–414.e2.
- [22] ATC-Codes. <https://www.whocc.no/>; [https://www.whocc.no/atc/structure\\_and\\_principles/](https://www.whocc.no/atc/structure_and_principles/). Accessed June 20 2021.
- [23] J.W. Gardner, J.S. Sanborn, Years of potential life lost (YPLL)—what does it measure? *Epidemiology* 1 (1990) 322–329.
- [24] V.L. Kinnula, T. Vasankari, E. Kontula, A. Sovijärvi, O. Saynajakangas, A. Pietinalho, The 10-year COPD Programme in Finland: effects on quality of diagnosis, smoking, prevalence, hospital admissions and mortality, *Prim. Care Respir. J.* 20 (2011) 178–183.
- [25] T. Haahtela, E. Valovirta, J. Bousquet, M. Makela, Allergy Programme Steering Group, The Finnish Allergy Programme 2008–2018 works, *Eur. Respir. J.* 49 (2017), <https://doi.org/10.1183/13993003.00470-2017>.
- [26] H. Hisinger-Mölkänen, P. Pallasaho, T. Haahtela, A. Lindqvist, A. Sovijärvi, P. Piirilä, The increase of asthma prevalence has levelled off and symptoms decreased in adults during 20 years from 1996 to 2016 in Helsinki, Finland, *Respir. Med.* 155 (2019) 121–126.
- [27] P.W. Sullivan, V.H. Ghushchyan, J.D. Campbell, G. Globe, B. Bender, D.J. Magid, Measuring the cost of poor asthma control and exacerbations, *J. Asthma* 54 (2017) 24–31.
- [28] S. Battaglia, A. Benfante, M. Spatafora, N. Scichilone, Asthma in the elderly: a different disease? *Breathe* 12 (2016) 18–28.
- [29] D.D. Sin, N.R. Anthonisen, J.B. Soriano, A.G. Agusti, Mortality in COPD: role of comorbidities, *Eur. Respir. J.* 28 (2006) 1245–1257.
- [30] D.E. Shaw, C.M. Gaynor, A.W. Fogarty, D.E. Shaw, Changes in asthma mortality in England and Wales since 2001 brief communication, *Thorax* 74 (2019) 1174–1175.
- [31] T. Haahtela, A biodiversity hypothesis, *Allergy* (2019) all.13763.