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Original Research Article

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The epidemiological burden and societal cost of 14 respiratory conditions in the WHO European region: systematic evidence map and economic analysis

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Conflicts of Interest. Pippa Powell works for and Lauren Anderson is contracted by the European Lung Foundation (ELF), which was founded and is partly funded by the European Respiratory Society (ERS), and is part of the International Respiratory Coalition. Amy Auer is an employee of the European Respiratory Society. Ane Johannessen is the Head of ERS Assembly 6 Epidemiology and Environment 2023-2026. Guy Joos has received personal payments for work unrelated to this project from AstraZeneca, Chiesi, GlaxoSmithKline, and Sanofi, and payments to his institution from AstraZeneca and Diadyc Intl - CR20. He also has unpaid roles with the International Respiratory Coalition (Chair) and as a GINA advocate. Joan B Soriano has received pharmaceutical company grants from Chiesi, GSK, Linde and Novartis via Hospital Universitario de La Princesa. He has participated in speaking activities, advisory committees, and consultancies sponsored by Air Liquide, Almirall, AstraZeneca, Boehringer Ingelheim, CHEST, Chiesi, CNPT, ERS, FTH, Gebro, Grifols, GSK, IHME, Laminar Pharma, Linde, Lipopharma, Menarini, Mundipharma, Novartis, OMS/WHO, Pfizer, ResApp, RiRL, ROVI, SEPAR, SAPIO, Seqirus, WHO EUR, Takeda and Zambon. All other authors declare that they have no conflicts of interest in relation to this work.

ABSTRACT (250 words)

Introduction

Our systematic evidence map aimed to identify lung-related epidemiological estimates to populate the International Respiratory Coalition's Lung Facts website. We highlight important evidence gaps, suggest how they could be filled, and provide bespoke societal cost estimates to inform resource allocation.

Methods

We examined 14 lung conditions across 53 WHO Europe countries, seeking incidence, prevalence, mortality, years of life lost, years lived with disability, and disability-adjusted life year (DALY) estimates by age/sex. Global Burden of Disease (GBD) study estimates were obtained for 9 GBD-included lung conditions: asthma, chronic obstructive pulmonary disease, interstitial lung disease and pulmonary sarcoidosis, lower respiratory infections, lung cancer / tracheal, bronchus and lung cancer, tuberculosis, mesothelioma, COVID-19 and pulmonary arterial hypertension. Systematic searches of bibliographic databases were necessary for 5 non-GBD-included lung conditions: cystic fibrosis (CF), obstructive sleep apnoea (OSA), influenza, alpha-1 antitrypsin deficiency (A1AD), and bronchiectasis. All-age country-specific DALY estimates were multiplied by Gross Domestic Product (GDP) per capita as a proxy for a country's wealth and prosperity to estimate societal costs.

Results

Complete data for 9 lung conditions for all countries were extracted from GBD, enabling societal cost estimation. Significant gaps were found for A1AD (only prevalence for 24 countries) and bronchiectasis (incidence, prevalence, and mortality for 1 to 5 countries), with more but incomplete estimates for CF, OSA, and influenza.

Conclusions

More epidemiological evidence is required for A1AD, bronchiectasis, CF, OSA, and influenza. Inclusion in the GDB study could help address these gaps. Lung Facts provides comprehensive lung-related epidemiological and societal cost estimates covering 53 countries to support policy makers advocating for respiratory interventions.

1. INTRODUCTION

Respiratory diseases contribute greatly to morbidity and mortality worldwide. [1] To raise public and decision-maker awareness of lung health importance and increasing disease burden, a European Lung White Book was launched in 2003 (updated 2013) [2, 3]. The European Respiratory Society (ERS) founded the International Respiratory Coalition (IRC) [4] in 2021, to promote lung health and improve respiratory care by setting up WHO Europe-based national respiratory strategies. An update of the White Book epidemiological and economic data was urgently needed. Thus, the 'Lung Facts' website was launched in 2022[5] to meet this need: https://international-respiratory-coalition.org/lung-facts/

Lung Facts provides key epidemiological and economic data for 14 major chronic respiratory conditions within the 53 WHO Europe countries. [5] The IRC updates Lung Facts every two-years; a key data source being the Global Burden of Disease (GBD) study. [6] The GBD collates epidemiological data from multiple sources (e.g., registries, epidemiological surveillance, primary scientific studies), alongside survey data on self-reported health and health-related risk behaviours. Global data are integrated into a single statistical model to estimate incidence, prevalence, and mortality. A demographic model estimates Years of Life Lost (YLL), Years Lived with Disability (YLD), and subsequently Disability-Adjusted Life Years (DALYs). However, the GBD does not provide evidence for all lung conditions (e.g., cystic fibrosis, sleep apnoea) nor economic considerations (e.g., societal costs).

We identify and describe the epidemiology of 14 respiratory diseases in the WHO Europe region for 2010 onwards. When all-age DALY estimates are available, we subsequently estimate societal costs by monetising these DALYs using Gross Domestic Product (GDP) per capita as a proxy for a country's wealth and prosperity. The Lung Facts website provides all identified and bespoke estimates. [5] This article summarises our methodology and key findings, including evidence gaps with suggestions to fill these gaps.

2. METHODS

The 14 conditions included in Lung Facts are 9 diseases reported within GBD, with a selected group of 5 other important respiratory diseases. These include frequent

disorders (obstructive sleep apnoea (OSA), influenza), alongside less common (bronchiectasis) and rare disorders (A1AD, cystic fibrosis (CF)). The selection of diseases was based on those that were included in the Lung White Book. This selection was reviewed and revised. They were considered to be the key respiratory conditions to include based on expert consultation.

Our methods have three elements. First, collating relevant GBD-sourced evidence. Second, collating non-GBD-sourced evidence using bibliographic searches. Third, estimating societal cost evidence not available in GBD. [6] Initial work was in 2022, with a 2024 update.

2.1. GBD data

The nine GBD-represented conditions are: asthma; COPD; interstitial lung disease and pulmonary sarcoidosis; lower respiratory infections; lung cancer / tracheal, bronchus and lung cancer; tuberculosis; mesothelioma; pulmonary arterial hypertension (PH; 2024 only); Covid-19 (2024 only). Data were downloaded from the GDB website[7] for 2015 and 2019 (in 2022), then 2021 (in 2024) (Table 1). GBD focuses on epidemiological estimates: incidence, prevalence, mortality, YLL, YLD, and DALYs. Absolute population counts and rates per 100,000 people estimates were extracted. Estimates were stratified by age, sex, country, region, and across Europe. Data samples were checked manually against the GBD website to ensure fidelity.

2.2. Non-GBD data: bibliographic searches

Focused bibliographic searches for the five conditions not within GBD (CF; OSA; influenza; A1AD; bronchiectasis) sought systematic reviews for commonly studied conditions, and any-design studies for less commonly-studied conditions (see Table **1** 1, "Exposure & Study design"). Searches were run in 2022 in Medline and updated in 2024 with Medline, Embase and the Cochrane library. Searches were structured around terms for the conditions and terms for the outcomes. The bibliographic searches were necessarily focussed due to time and resource constraints. To mitigate the risk of missing important studies (see also Discussion section 4.3), we selected Medline as the principle database, as it has been shown to retrieve over 90%[8] of studies that are findable using

bibliographic database searches. We also used additional search techniques (i.e., citation chasing, reference list checking, focused searches on Google scholar, and consultation with experts) to identify additional studies (Online Supplementary File 1). Search results were exported into Endnote and duplicates removed. PH was included in the 2022 searches, but not in 2024 since it was added to the GBD study.

Table 1 details the eligibility criteria and PESOS (Population, Exposure, Study Design, Outcomes, Setting). Studies were selected for inclusion by two reviewers. Disagreements were resolved through discussion between the reviewers, or with topic experts. Data could be expressed in any format, e.g., absolute numbers, ratios, per capita, per 100,000 people. Where possible, rate data were converted to rate per 100,000 people.

In 2022, data were extracted by one reviewer and checked by a second (Online Supplementary File 1). In 2024, summary data were extracted into a table by one reviewer to create an evidence map. ERS disease experts used the evidence-map to decide if a Lung Facts update was required. No 2024 update data were deemed superior to the existing 2022 data, thus full data extraction with double checking was not performed. Links to new studies are provided within Lung Facts.

2.3. Societal cost estimation

When operationalising health-related metrics (e.g., DALYs or quality-adjusted life years [QALYs]) to inform resource allocation, applying a monetary value to (i.e., monetising) those health-related metrics is needed to determine the 'opportunity cost' from any financial investment, i.e., what is foregone when investing in health-related outputs because the resources are no longer available to spend elsewhere. We refer to monetised health-related metrics as a societal cost, i.e., the health burden's monetary value. It is important to recognise that these monetised health-related metrics represent the monetised burden-of-illness (i.e., monetised DALYs), not the cost-of-illness such as the amount of money the healthcare system pays to prevent/treat such conditions.

DALY monetisation using GDP stems from the WHO's Choosing Interventions That Are Cost Effective (WHO-CHOICE) initiative, whereby 1 to 3*GDP per capita was suggested as a country-specific cost-effectiveness threshold (e.g., the amount of money a country is willing to pay to prevent one DALY) for cost-effectiveness analysis. [9-12] Robinson et al. [12] describes the GDP-based threshold rationale. In essence, GDP is a standard measure of value created through goods and services in a country during a certain period: it measures the income earned from production, or the total amount spent on final goods and services (less imports). [13] GDP guides policymakers, investors, and businesses in strategic decision making given an economy's activity, with GDP per capita being the GDP per person in a country's population. Thus, the WHO report suggested a DALY prevented should be equivalent to the per capita income, or extra market income, created from an intervention's outcome. However, benefits may be (up to three times) higher due to non-income-based benefits (e.g., reducing pain/suffering). [9] Therefore, without a defined and/or evidence-based DALY monetary value, 1 to 3*GDP per capita could be used. More recently, WHO-CHOICE moved away from using any defined cost-effectiveness threshold, not just GDP-based thresholds. [14]

Franklin et al (2023) rationalises why, in the absence of a defined or evidence-based DALY monetary value, using 1*GDP per capita as a benchmarked value (i.e., a reference point) of what countries should aim to invest in health-related outcomes could still have many benefits for transparent and consistent decision making, citing others who debate for and against this point. Franklin et al (2023) [15] subsequently suggests using 1*GDP per capita specifically, as it better aligns with monetised QALY valuations as a similar, widely used health-related metric.

Thus, we use GDP per capita to estimate the resources available in each country that could be invested in lung interventions (e.g., preventative strategies and medical care) to address the DALY burden of lung condition(s). That is, 1*GDP per capita is multiplied by the all-age DALY burden at a population-level or rate per 100,000 people to estimate the societal cost, to be used as a reference point for negotiation with policymakers investing in lung interventions. GDP per capita is obtained from the WHO Global Health Expenditure Database, [16] presented in 2021 values based on US Dollars (USD$2021),

international dollars (Int$2021), Euros (EUR€2021), and National Currency Units (NCU|2021).

3. RESULTS

To complement Lung Facts, we describe example GBD and non-GBD epidemiological estimates, and bespoke societal cost estimates, in Table 2-3 and Figure 1. Lung Facts provides all estimates by country, lung condition, age, and sex: https://international-respiratory-coalition.org/lung-facts

3.1. GBD data covering nine lung conditions

Lung Facts provides GBD-reported epidemiological estimates for 9 lung conditions, by age and sex, by and across all 53 WHO European countries and associated regions. Table 2 provides illustrative results for asthma.

3.2. Non-GBD data covering five lung conditions

Data relating to conditions not in the GBD were systematically sought. A PRISMA flow diagram relating to the process of study selection is provided in Online Supplementary File 2. In 2022, 1622 records were identified by the bibliographic and supplementary searches. Of these, 1493 were excluded based on their title or abstract. Full texts of 129 records were obtained, with 16 studies' data extracted: two CF reviews[17 18] (one non-systematic) [18], one OSA systematic review[19], one influenza GBD study[20], one A1AD systematic review[21], six bronchiectasis primary studies[22-27], and five PAH studies (two systematic reviews, 3 primary studies) [28-32].

In 2024, the updated search found 199 unique records; 172 were excluded based on their title or abstract. Full text of 27 records were obtained, with 10 [33-42] included in the mapping review. Ten additional studies were identified through citation tracking; eight were excluded, with two[43 44] included in the mapping review.

Figure 1 provides an evidence map of the data sourced for Lung Facts for non-GBD-included conditions. Online Supplementary File 2 shows a PRISMA flow diagram relating to the process of study selection and reasons for study exclusions are provided in Supplementary File 3.

<Figure-1>

3.2.1. Cystic fibrosis (CF)

No data were identified for some countries across all outcomes, with no data broken down by age or sex. One systematic review[17] estimated prevalence across 40 European countries. One non-systematic review[18] reported incidence-ratios across 19 European countries. One 2024 study provided Iceland, [37] and another whole-Europe only, [36] estimates. Overall, the systematic review data were considered more consistent and included in Lung Facts.

3.2.2. Obstructive sleep apnoea (OSA)

No data were identified for incidence or mortality. One systematic review[19] modelled world-wide country-specific (50 European-specific) prevalence rates/numbers, based on 18 countries' data (six European: Poland, Germany, Iceland, Norway, Spain, and Switzerland) including by age and sex. Four prevalence-related systematic reviews[35 38 40 42] were identified in 2024, but none were superior to the previous review[19] as they included fewer countries[35 40 42], reported less outcome data, [35 38 42] or were in specific age groups only (one in children; [40] one in people aged ≥65 years[38])

3.2.3. Alpha-1 antitrypsin deficiency (A1AD)

There were no data on incidence or mortality. One review[21] based on a systematic search calculated expected prevalence rates/numbers for 26 countries using Z-allele frequency and autosomal recessive inheritance. Four new studies[33 34 43 44] were identified in 2024 covering Denmark, Germany, Madeira, and La Palma; however, previous review data was retained to maintain consistency between countries.

3.2.4. Bronchiectasis

There was little data across countries and outcomes. Six primary studies[22-27] found in 2022 reported incidence, prevalence and mortality data for the UK, Poland, Germany, Italy, and Spain. No new studies were found in 2024.

3.2.5. Influenza

One GBD study found in 2022, using data from 2017, attributed influenza to a fraction of the GBD's "lower respiratory tract infections" incidence and mortality estimates. One new study[39] found in 2024 was based on data older than 2017.

3.3. Societal cost estimates

Table 3 provides illustrative asthma mean societal costs for 53 WHO Europe countries per 100,000 people. We focus on mean societal costs, with DALYs' 95% confidence intervals presented to indicate uncertainty impacting the societal cost estimates.

Based on two example countries chosen because they have quite different GDP per capita, but similar asthma DALY burden, ways to use these societal costs (USD$) could be to state:

- Türkiye should aim to invest up to $2,357,340 to eradicate the 244.7 (175.7 to 332) DALY burden associated with asthma per 100,000 people (i.e., $23.57 per person);
- Austria should aim to invest up to $11,077,984 to eradicate the 206.0 (138.9 to 291.7) DALY burden associated with asthma per 100,000 people (i.e., $110.78 per person).

As these societal costs are presented as rates per 100,000 people, the main difference between countries is the DALY burden and GDP per capita. For example, whilst Austria has the lower asthma mean DALY burden rate compared to Türkiye (206.0 vs 244.7), Austria has the higher GDP per capita ($53,777 vs $9,661), making the societal cost higher for Austria than Türkiye. This does not mean that Austria values avoiding the asthma burden more than Türkiye, rather it means that due to Austria's wealthier economy, the amount Austria could invest in lung care is estimated to be higher than the amount Türkiye could invest. In this context, the societal cost is how much a country could consider investing in lung care to tackle the condition burden within that society. Further ways to use these societal costs to inform policy making are described by Franklin et al (2023). [15]

4. DISCUSSION

Epidemiological estimates of respiratory health need regular review as determinants (e.g., exposure patterns, socio-political factors) change over time and geographies. [45] Accurate data is a critical component to developing national respiratory health plans. Lung Fact's methodology allows for relatively easy comparisons within and across a large number of WHO European countries, helping national coalitions assess and monitor policy progress over time. Lung Facts is largely populated with GBD estimates, to facilitate replicability and regular updates.

4.1. Current evidence gaps

The GBD methodology is becoming the gold standard in population health data[46], used by most major administrations and organisations. Where GBD included the condition, estimates were complete across countries, estimates, ages, and sexes. However, for non-GBD-included conditions, there were data gaps.

A1AD has particularly poor coverage, with prevalence based on allele frequency rather than diagnoses, though the 2024 update did identify some data on diagnoses in Germany[44] and Denmark. [33] Bronchiectasis has significant data gaps, with only six primary studies covering 5 countries and no new studies found in 2024. [22-27] For CF and OSA, reviews identified cross-country epidemiological estimates using data from multiple sources, but not for mortality (both conditions) or incidence (OSA). The studies used different methodologies, thus estimates may not be interchangeable nor comparable with GBD estimates. GBD's influenza study, based on 2017 lower respiratory infections (LRIs) data, did not report prevalence, YLL, nor DALYs; no update was identified and influenza is not a current GBD condition.

4.2. Filling evidence gaps

The GBD collates and analyses a huge amount of data to produce its global estimates. Harnessing GBD's high-quality methodology and expertise would be efficient to provide reasonably consistent estimation across countries and conditions. Whilst not as comprehensive as the GBD, our research has filled evidence-gaps for some conditions (CF, OSA) while highlighting gaps for others (A1AD, Bronchiectasis). Also, increasing GBD's current four-level condition categorisation could support more granular condition-specific estimation, e.g., influenza within lower respiratory infections, sarcoidosis within interstitial lung disease.

There are a few examples of national and international initiatives to map and monitor respiratory conditions' epidemiology. [47-52] For example, ISAAC[51 52] is a project investigating variations in the prevalence of asthma rhinitis and eczema at the population-level, and their potential causes. The largest worldwide collaborative research project ever undertaken in children, it involves 306 centres in 105 countries, with nearly 2 million

children participating and >1,240 PubMed-indexed publications. Similar initiatives could be replicated across other respiratory conditions where data are sparse.

4.3. Collated data: strengths and limitations

Our evidence review has helped populate Lung Facts, providing policymakers and clinicians with a one-stop resource containing important statistics to help advocate for improved respiratory health. Lung Facts has already supported care and decision-making, e.g., the Belgian Lung Foundation used Lung Facts to emphasise the need to improve COPD patient care, and set strong objectives focusing on advocacy, better prevention, and improved rehabilitation access.

Limitations of our approach include the focussed search strategies: whilst efforts were taken to identify all relevant data (i.e., citation searching, reference checking, asking experts), some studies may have been missed. It is well-known that bibliographic searches are generally only approximately 80%[8] sensitive. Our additional search techniques identified 37.5% of the studies included in 2022 (an excess over comprehensive searches of 17.5%), and 17% in the 2024 update. However, only systematic reviews were included for some conditions, thus primary studies published since the most recent systematic review will have been missed.

4.4. Societal costs: strengths and limitations

Our GDP-based approach for generating societal cost estimates is based on theory because there are no defined or empirically-based monetary DALY values, nor sufficient direct and indirect lung health cost estimates, for all WHO European countries. Despite this, decision-makers regularly need to prioritise resource allocation within countries, across conditions and associated population groups. As such, understanding the monetary cost of lung conditions is vital, but evidence is lacking.

The strengths and limitations of this GDP-based approach is described in detail elsewhere.[15] A key point is that monetised DALYs based on GDP are by intention and design a simplistic approach to valuing DALYs. The approach's simplicity also aids its usefulness, if decision-makers are willing to utilise the valuation as a reference point.[15] For example, Drake (REF)[53] suggests a monetary DALY value, even with limitations and flaws, could be justified as it could "radically improve transparency and efficiency of

priority setting in global health", providing examples including the Millennium Development Goals and absolute poverty threshold.

Internationally, monetary valuations of the QALY for health technology assessment cost-effectiveness thresholds are also not evidence-based; rather they are decided by decision-makers as 'approval norms' to support and rationalise resource allocation and care price negotiation within a fixed budget[15 54]. The logic and necessity are similar to the GDP-based approach, but our DALY valuation is based on an economic activity metric (GDP per capita) rather than the QALY's 'expert opinion' valuation. [15]

The monetised DALY figures in Lung Facts do not replace the need for rigorously estimated economic data (e.g., understanding the care costs for conditions), but the benchmarked figures can be used as a reference point for investment to alleviate condition burden, even if the underlying model for monetising DALYs has flaws. [15]

5. CONCLUSION

There are evidence gaps for several respiratory conditions that have an epidemiological and economic burden on people, their families/carers, and society. Researchers, including the GBD study, should extend their scope to additional respiratory conditions, including A1AD, cystic fibrosis, obstructive sleep apnoea, and bronchiectasis. New evidence is needed to benefit more people burdened by poor lung health internationally. Lung Facts provides epidemiological and economic data for WHO European countries for a range of lung conditions, to support clinicians and policy makers in advocating for lung health and in setting up respiratory plans.

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Table 1. Inclusion criteria for GBD data bibliographic searches for non-GBD data to identify systematic reviews and primary studies

Item	Inclusion criteria	
Population	**1) GBD data** <5 years; 5-9 years; 5-year increments to 90-94; 95+ years, age standardised **2) Bibliographic searches** Data by any age range, e.g. everyone, adults, children, etc	
Exposure & Study design	**1) GBD data:** 1. Asthma 2. Chronic obstructive pulmonary disease 3. Interstitial lung disease and pulmonary sarcoidosis 4. Lower respiratory infections 5. Lung cancer / tracheal, bronchus and lung cancer 6. Tuberculosis **7.** Mesothelioma 8. Pulmonary arterial hypertension* 9. Covid-19* **2) Bibliographic searches** **a) Systematic reviews**:** 1. Cystic fibrosis 2. Obstructive sleep apnoea 3. Influenza **b) Primary studies:** 1. Alpha-1 antitrypsin deficiency 2. Bronchiectasis 3. Pulmonary hypertension*	
Outcomes	Rates and absolute numbers of: • Incidence • Prevalence • DALY • YLL • Mortality Any type of reporting of the outcome. For example, rates may be age standardised, reported per capita, reported as a ratio (1 case per X head of population) reported by sex etc.	
Settings	**WHO European Region** **Central Asia** Armenia Azerbaijan Georgia	**Western Europe** Andorra Austria Belgium Cyprus Denmark***

Item	Inclusion criteria	
	Kazakhstan Kyrgyzstan Tajikistan Türkiye Turkmenistan Uzbekistan **Eastern Europe** Albania Bosnia and Herzegovina Bulgaria Croatia Czech Republic Hungary Macedonia Montenegro Poland Romania Serbia Slovakia Slovenia **Central Europe** Belarus Estonia Latvia Lithuania Moldova Russia Ukraine	Finland France Germany Greece Greenland*** Iceland Ireland Israel Italy Luxembourg Malta Monaco Netherlands Norway Portugal San Marino Spain Sweden Switzerland United Kingdom

Acronyms. DALYs, disability adjusted life years; GBD, global burden of disease study; YLL, years of life lost; WHO, World Health Organisation.

* Pulmonary arterial hypertension and Covid-19 were added to the GBD in 2024. Therefore, pulmonary hypertension was dropped from search 2b in 2024, and both conditions were added to search 1.

**where no systematic reviews were available, the criteria were widened to include non-systematic reviews, if these provided data of use to the review.

*** Greenland is part of Denmark, but is reported by the GBD separately.

Table 2: Asthma GBD 2021: age-standardised estimates per 100,000 people for 54 countries and WHO European sub-regions.

Country/region	Incidence (95% UI)	Prevalence (95% UI)	DALYs (95% UI)	YLL (95% UI)	Mortality (95% UI)
WHO European sub-regions	**535.4 (434.1 - 673.4)**	**4607.1 (3907.7 - 5378.7)**	**204.1 (137.5 - 292.3)**	**22.6 (21.1 - 24.2)**	**0.9 (0.9 - 1)**
Central Asia	**409.3 (338.4 - 509.6)**	**2577.2 (2227.1 - 2979.2)**	**198.8 (158.9 - 245.6)**	**97.9 (84.5 - 114)**	**4.3 (3.8 - 5.1)**
Armenia	322.9 (250.7 - 419)	1753.8 (1411.3 - 2210)	77.6 (49.4 - 111.4)	7.6 (6.7 - 8.7)	0.4 (0.3 - 0.4)
Azerbaijan	379.9 (310.9 - 480)	2247.7 (1909.2 - 2633.4)	168.2 (128.9 - 222.2)	79.9 (58.8 - 116.1)	3.6 (2.7 - 4.8)
Georgia	370.4 (296.8 - 470.7)	2016.7 (1680.7 - 2434.5)	114.8 (84.7 - 157.4)	34.5 (29.6 - 40.8)	1.6 (1.4 - 1.9)
Kazakhstan	284.4 (233.7 - 357.9)	1599.8 (1361 - 1888.6)	250.4 (200.8 - 310.8)	187.9 (146.1 - 241.2)	8.6 (6.7 - 11.3)
Kyrgyzstan	421.5 (343.4 - 536.1)	2572.9 (2149.4 - 3076)	134.6 (96.5 - 185.3)	32.8 (26.4 - 40)	1.3 (1.1 - 1.6)
Tajikistan	378.7 (311.7 - 476.5)	2170.6 (1869.8 - 2590.1)	212.5 (156.8 - 273.4)	127.5 (90.6 - 175.6)	6.6 (4.7 - 8.8)
Türkiye	711.3 (593.5 - 869.4)	4888.7 (4199.5 - 5680.4)	249.1 (176.9 - 342)	58.4 (46.8 - 71.9)	3.1 (2.4 - 4)
Turkmenistan	318.9 (254.1 - 407.4)	1750 (1442.3 - 2138.7)	118.1 (86.1 - 159.1)	48.4 (32.7 - 70.5)	1.6 (1.1 - 2.2)
Uzbekistan	532.7 (441.5 - 652.7)	3791.6 (3314.2 - 4312.9)	237.1 (181.8 - 307.1)	89.5 (75.6 - 107.7)	3.9 (3.4 - 4.7)
Central Europe	**898.7 (725.3 - 1136.9)**	**5643 (4722.7 - 6691.6)**	**239.1 (156.5 - 350.5)**	**15.7 (14.4 - 17.3)**	**0.8 (0.7 - 0.9)**
Albania	471.2 (382.9 - 589.6)	2687.2 (2244 - 3207.9)	164.3 (117.4 - 221.4)	58 (40.8 - 82.4)	3.4 (2.3 - 4.8)
Bosnia and Herzegovina	746.3 (605.8 - 943.4)	4972.2 (4133.3 - 6036.3)	214.3 (139.4 - 308)	18.6 (14.3 - 24)	0.9 (0.7 - 1.2)

Bulgaria	587.2 (470.3 - 744.4)	3606.6 (2945.8 - 4410.9)	150.2 (94.5 - 221.2)	7.3 (6.2 - 8.5)	0.3 (0.3 - 0.4)
Croatia	639.3 (520.1 - 806.4)	4070.4 (3362.3 - 4977)	172.9 (111.9 - 249.8)	12.3 (10 - 15)	0.7 (0.6 - 0.9)
Czech Republic	517.4 (413.3 - 666)	3043.3 (2488.7 - 3715.8)	130.5 (82.5 - 189.1)	9.6 (8.4 - 10.8)	0.5 (0.4 - 0.6)
Hungary	544.2 (437.9 - 696.5)	3282.8 (2700.8 - 3982.4)	140.1 (89.3 - 205.9)	9.9 (8.6 - 11.1)	0.5 (0.4 - 0.5)
Macedonia	796.4 (663.8 - 986.2)	5654.9 (4836.5 - 6652.9)	261.4 (180.7 - 362.7)	41.6 (30 - 63.9)	2.3 (1.8 - 3.4)
Montenegro	591.6 (473.4 - 753.5)	3594.6 (2887.7 - 4497.3)	149.1 (93.8 - 218.8)	6.1 (4.7 - 7.7)	0.3 (0.3 - 0.4)
Poland	1467.9 (1163.4 - 1879.8)	9329.1 (7839.4 - 11200.3)	384.9 (251.4 - 567.2)	15.9 (14.5 - 17)	0.8 (0.7 - 0.8)
Romania	699.7 (560.4 - 881.4)	4526.6 (3745.4 - 5513.6)	192.2 (123.1 - 277.7)	12.7 (11.1 - 14.2)	0.6 (0.5 - 0.7)
Serbia	536.9 (434.5 - 675.9)	3234.9 (2734.7 - 3871.5)	163.7 (113.7 - 227.2)	35.9 (29.1 - 44.2)	1.9 (1.5 - 2.3)
Slovakia	515.6 (414.6 - 652)	3060.8 (2533.7 - 3742.6)	131.1 (83.7 - 192.8)	9.6 (7.8 - 12.5)	0.5 (0.4 - 0.6)
Slovenia	777.4 (631.1 - 977.5)	5374.8 (4469.3 - 6479.2)	218 (138.1 - 318.9)	5.7 (4.9 - 6.5)	0.3 (0.3 - 0.4)
Eastern Europe	**460.1 (360.8 - 601.7)**	**2622 (2125 - 3234)**	**116.5 (76.3 - 169.5)**	**12.5 (11.6 - 13.4)**	**0.5 (0.4 - 0.5)**
Belarus	627.8 (494.7 - 793)	4210.1 (3487.4 - 5059.4)	172.8 (111.2 - 252)	7.2 (5.9 - 8.6)	0.2 (0.2 - 0.3)
Estonia	463 (372.9 - 591.7)	2789.3 (2330.5 - 3387.6)	121.8 (80.1 - 174.5)	11.6 (10.1 - 13.1)	0.6 (0.5 - 0.6)
Latvia	510.1 (408.5 - 647.2)	3094.6 (2578.2 - 3753.2)	138.1 (91.7 - 198.7)	15.5 (13.4 - 17.8)	0.7 (0.6 - 0.8)
Lithuania	476.5 (381.4 - 609.4)	2819.6 (2331.8 - 3408.3)	121.6 (77.8 - 176)	10 (8.7 - 11.2)	0.4 (0.4 - 0.5)
Moldova	464.5 (366.5 - 598.2)	2692.8 (2203.9 - 3279.2)	117.9 (76 - 172.1)	10.7 (9.4 - 12.2)	0.4 (0.3 - 0.4)
Russia	431.1 (337.9 - 565.9)	2418.9 (1960.8 - 2967.8)	111 (74.2 - 160.6)	15.1 (14 - 16.2)	0.6 (0.5 - 0.6)
Ukraine	534.2 (408.2 - 709.5)	2970.9 (2345.2 - 3690.8)	123.9 (76.2 - 182.6)	5.4 (3.9 - 7.1)	0.2 (0.1 - 0.2)
Western Europe	**498.8 (404.7 - 632.6)**	**5886.8 (4944 - 6943.6)**	**248.3 (161.3 - 359.5)**	**16.4 (15.5 - 17)**	**0.7 (0.6 - 0.7)**

Andorra	494 (401.2 - 626.5)	6536.6 (5337.2 - 7774.3)	274.9 (177.1 - 406.9)	17.3 (12.1 - 23)	0.6 (0.4 - 0.8)
Austria	416.6 (339.9 - 532.7)	4788.8 (3942.2 - 5796.4)	203.1 (131.4 - 297.4)	14.1 (13.2 - 15)	0.5 (0.5 - 0.6)
Belgium	407 (329.6 - 530.6)	4618.8 (3855.3 - 5517.6)	197.9 (128.9 - 283.9)	16 (14.9 - 17.1)	0.6 (0.5 - 0.7)
Cyprus	524.6 (417.5 - 661.2)	7411.9 (6003.5 - 9009.1)	327.1 (214.7 - 474.7)	36.5 (30.5 - 43.9)	2 (1.7 - 2.5)
Denmark*	460.5 (371.7 - 582.5)	4631.3 (3772.2 - 5507.2)	201.3 (132.7 - 287.3)	18.6 (17.1 - 20)	0.8 (0.7 - 0.8)
Finland	462.6 (378.3 - 586.9)	6163 (5111.4 - 7331)	255.5 (165.8 - 365.9)	14 (12.7 - 15)	0.7 (0.6 - 0.7)
France	484.6 (392.3 - 611.2)	6244.6 (5192.7 - 7435.8)	261.2 (167.8 - 381.1)	15.6 (14.5 - 16.6)	0.6 (0.6 - 0.7)
Germany	388.8 (315.8 - 498.4)	4262.2 (3529.5 - 5050.3)	183.5 (119 - 260.6)	15.5 (14.5 - 16.5)	0.6 (0.5 - 0.6)
Greece	411.5 (328.4 - 522.7)	4781.9 (3914.3 - 5721.5)	194.3 (122.7 - 283.2)	6 (5.7 - 6.4)	0.2 (0.2 - 0.2)
Greenland*	1067.7 (865.6 - 1350.2)	7632.2 (6612.9 - 8851)	350.6 (241.7 - 494.6)	51.6 (42.5 - 62.4)	1.5 (1.3 - 1.8)
Iceland	634.6 (511.8 - 817.3)	7330.5 (5957.6 - 8914.1)	306.5 (193.1 - 453.2)	16.6 (15 - 18.2)	0.6 (0.6 - 0.7)
Ireland	525.5 (417.6 - 670.5)	6914.5 (5760.1 - 8351.5)	288.1 (181 - 418.3)	15.4 (14.1 - 16.5)	0.6 (0.5 - 0.7)
Israel	365.5 (294.4 - 472.9)	3765.6 (3130.6 - 4472.4)	169.5 (112.3 - 240.2)	20.6 (18.6 - 22)	1 (0.8 - 1.1)
Italy	415.1 (323.4 - 540.1)	3722.9 (2995.2 - 4569)	152.4 (96.5 - 227.4)	5.6 (5.1 - 5.9)	0.3 (0.2 - 0.3)
Luxembourg	514.3 (417.4 - 662)	7102.3 (5964 - 8441.9)	299.8 (194.3 - 439.5)	20 (17.9 - 22.2)	0.8 (0.8 - 0.9)
Malta	502.1 (404 - 644.3)	6700.3 (5456 - 8082)	277 (175.6 - 410.3)	13.5 (11.9 - 15.3)	0.6 (0.5 - 0.6)
Monaco	474.6 (376.4 - 605.8)	6054.7 (4991 - 7148.9)	243.7 (151.6 - 370.9)	4.7 (3.6 - 6)	0.2 (0.1 - 0.2)
Netherlands	339 (280.7 - 419.6)	6507.1 (5455.3 - 7766.1)	265.9 (169.1 - 388.9)	9.7 (9 - 10.4)	0.4 (0.4 - 0.5)
Norway	644.3 (511 - 823.6)	6050.4 (4949.5 - 7293.2)	255.7 (167.2 - 375.3)	16.7 (15.6 - 17.5)	0.8 (0.7 - 0.9)
Portugal	621.8 (514.9 - 792.4)	9465.4 (7816.9 - 11402.8)	386.8 (246.2 - 572.9)	15.8 (14.7 - 16.7)	0.6 (0.6 - 0.7)

San Marino	474.2 (382.8 - 600)	5999.9 (4970.9 - 7191.1)	243.4 (154.8 - 364.1)	7 (4.5 - 9.7)	0.3 (0.2 - 0.4)
Spain	402.7 (322.2 - 512.9)	4332.6 (3602.4 - 5189.6)	187 (122.3 - 264.8)	16.3 (14.4 - 17.5)	0.9 (0.7 - 1)
Sweden	679.6 (541.4 - 872.6)	7522.6 (6140.8 - 9106.1)	309.1 (199 - 459.2)	12.5 (11.2 - 13.9)	0.6 (0.5 - 0.7)
Switzerland	465.8 (375.8 - 604.2)	5655.5 (4527 - 6839.2)	235.2 (149.9 - 345)	12.4 (11.4 - 13.4)	0.5 (0.5 - 0.6)
United Kingdom	793.7 (643.1 - 999)	10029.8 (8450.2 - 11747.4)	427.7 (282.7 - 620.1)	33.1 (31.5 - 34.1)	1.3 (1.1 - 1.3)

Abbreviations: DALY, Disability Adjusted Life Year; UK, United Kingdom; YLL, Years of Life Lost; WHO, World Health Organisation.

***** Greenland is part of Denmark, but is reported by the GBD separately.

Table 3: Asthma societal cost examples based on GBD 2021 DALY rates and GDP per capita by 53 countries and WHO European region

Country/region	NCU	DALY rates per 100,000 people, Mean (95% CI)	GDP per capita (2021)				Societal cost per 100,000 people (2021)*			
			Int$**	USD$	EUR€	NCU	Int$**	USD$	EUR€	NCU
Albania	ALL	191.2 (142.7 - 250)	$15,572	$6,395	€5,407	662,007	$2,974,258	$1,221,439	€1,032,720	126,443,404
Andorra	EUR	280.6 (188.7 - 401.3)	$58,885	$42,066	€35,567	35,567	$16,487,824	$11,778,492	€9,958,644	9,958,644
Armenia	AMD	72.5 (48.6 - 102.1)	$15,592	$4,967	€4,199	2,501,981	$1,122,659	$357,589	€302,340	180,142,615
Austria	EUR	206 (138.9 - 291.7)	$60,118	$53,777	€45,468	45,468	$12,384,331	$11,077,984	€9,366,369	9,366,369
Azerbaijan	AZN	161.9 (123.4 - 214.1)	$15,585	$5,296	€4,478	9,004	$2,509,216	$852,730	€720,978	1,449,641
Belarus	BYN	177.6 (118.3 - 251.5)	$21,160	$7,121	€6,021	18,078	$3,745,273	$1,260,403	€1,065,663	3,199,785
Belgium	EUR	199.8	$59,035	$51,438	€43,490	43,490	$11,747,995	$10,236,127	€8,654,584	8,654,584

		(136.6 - 277.3)								
Bosnia and Herzegovina	BAM	223.5 (155.9 - 306.8)	$17,701	$7,230	€6,113	11,956	$3,947,385	$1,612,331	€1,363,216	2,666,161
Bulgaria	BGN	138.9 (92.8 - 194.2)	$27,948	$12,156	€10,278	20,099	$3,856,862	$1,677,509	€1,418,324	2,773,594
Croatia	EUR	183 (125.2 - 253.3)	$33,381	$17,094	€14,453	14,453	$6,108,703	$3,128,256	€2,644,922	2,644,922
Cyprus	EUR	354.3 (236.8 - 499.1)	$44,610	$31,709	€26,810	26,810	$15,791,768	$11,224,953	€9,490,630	9,490,630
Czech Republic	CZK	122.9 (83.4 - 169.1)	$44,783	$26,331	€22,263	570,813	$5,463,524	$3,212,413	€2,716,076	69,639,227
Denmark[*,**]	DKK	202.6 (140.3 - 279.1)	$65,069	$68,202	€57,664	428,794	$13,144,001	$13,776,822	€11,648,220	86,616,440
Estonia	EUR	129.1 (91.1 - 177)	$43,505	$27,962	€23,642	23,642	$5,612,158	$3,607,080	€3,049,764	3,049,764
Finland	EUR	280.3 (191.6 - 389)	$54,756	$53,538	€45,266	45,266	$15,331,708	$14,990,728	€12,674,570	12,674,570

France	EUR	271.4 (183.9 - 380.4)	$51,434	$43,719	€36,964	36,964	$13,938,692	$11,847,840	€10,017,278	10,017,278
Georgia	GEL	127.2 (101.1 - 163.6)	$16,790	$4,956	€4,190	15,967	$2,132,325	$629,435	€532,183	2,027,786
Germany	EUR	186.8 (129.1 - 256.3)	$58,813	$51,229	€43,314	43,314	$10,939,237	$9,528,564	€8,056,344	8,056,344
Greece	EUR	193.1 (125.4 - 275.5)	$31,185	$20,122	€17,013	17,013	$6,018,737	$3,883,519	€3,283,492	3,283,492
Hungary	HUF	134 (90.9 - 186.5)	$36,694	$18,732	€15,838	5,678,391	$4,917,050	$2,510,069	€2,122,248	760,904,392
Iceland	ISK	302.7 (196.6 - 436.3)	$58,524	$68,999	€58,338	8,762,068	$17,674,220	$20,837,612	€17,618,075	2,646,144,575
Ireland	EUR	285.6 (185.1 - 404.9)	$107,142	$100,709	€85,149	85,149	$30,535,405	$28,702,112	€24,267,462	24,267,462
Israel	ILS	173.2 (116.3 - 241.9)	$46,365	$54,890	€46,409	177,306	$8,021,149	$9,496,016	€8,028,824	30,674,011
Italy	EUR	154.3	$46,593	$35,694	€30,179	30,179	$7,175,390	$5,496,821	€4,647,529	4,647,529

		(102.7 - 222.9)								
Kazakhstan	KZT	240.2 (192.3 - 296)	$28,393	$10,268	€8,682	4,373,284	$6,814,272	$2,464,357	€2,083,599	1,049,588,067
Kyrgyzstan	KGS	128.5 (90.1 - 179.8)	$5,548	$1,339	€1,132	113,334	$710,122	$171,393	€144,911	14,506,805
Latvia	EUR	142.9 (102 - 194.8)	$34,887	$21,001	€17,756	17,756	$4,953,944	$2,982,144	€2,521,384	2,521,384
Lithuania	EUR	118.7 (82.3 - 164)	$43,866	$23,759	€20,088	20,088	$5,176,246	$2,803,555	€2,370,389	2,370,389
Luxembourg	EUR	311.6 (208.1 - 448.1)	$132,583	$134,713	€113,899	113,899	$41,233,169	$41,895,685	€35,422,549	35,422,549
Macedonia	MKD	286.2 (202.5 - 390.1)	$18,006	$6,573	€5,558	342,511	$5,149,786	$1,879,961	€1,589,496	97,958,192
Malta	EUR	293.1 (195.3 - 419.4)	$50,230	$34,406	€29,090	29,090	$14,717,393	$10,080,814	€8,523,268	8,523,268
Moldova	MDL	108.8 (73.1 -	$15,572	$5,293	€4,475	93,575	$1,681,737	$571,597	€483,282	10,106,120

		152.3)								
Monaco	EUR	240.1 (154.9 - 348.9)	$238,509	$234,317	€198,114	198,114	$57,242,067	$56,236,100	€47,547,284	47,547,284
Montenegro	EUR	136.7 (88.2 - 197.1)	$23,111	$9,335	€7,893	7,893	$3,143,127	$1,269,576	€1,073,418	1,073,418
Netherlands	EUR	276.6 (180.5 - 396.8)	$63,562	$57,898	€48,953	48,953	$17,543,085	$15,979,966	€13,510,965	13,510,965
Norway	NOK	259.3 (176.2 - 365.5)	$82,124	$90,940	€76,890	781,178	$21,270,165	$23,553,569	€19,914,400	202,325,157
Poland	PLN	368.2 (249.6 - 525)	$38,148	$18,006	€15,224	69,538	$14,038,408	$6,626,198	€5,602,411	25,589,828
Portugal	EUR	419 (279.9 - 598.5)	$36,734	$24,663	€20,852	20,852	$15,391,422	$10,333,680	€8,737,064	8,737,064
Romania	RON	185.6 (125.9 - 258.5)	$36,114	$14,864	€12,567	61,839	$6,681,035	$2,749,766	€2,324,911	11,440,127
Russia	RUB	107.7 (76.2 - 148.4)	$34,222	$12,659	€10,703	932,408	$3,661,751	$1,354,539	€1,145,254	99,767,678

San Marino	EUR	247.5 (163 - 356.4)	$67,831	$51,809	€43,805	43,805	$16,754,356	$12,796,916	€10,819,715	10,819,715
Serbia	RSD	186.1 (140.9 - 242.9)	$21,525	$9,180	€7,762	912,472	$4,003,580	$1,707,514	€1,443,693	169,719,864
Slovakia	EUR	124.2 (84.4 - 174.4)	$34,449	$21,733	€18,375	18,375	$4,271,725	$2,694,874	€2,278,499	2,278,499
Slovenia	EUR	218.7 (144.6 - 313.2)	$43,944	$29,279	€24,755	24,755	$9,579,871	$6,382,812	€5,396,629	5,396,629
Spain	EUR	202.6 (142.5 - 278.8)	$40,666	$30,114	€25,462	25,462	$8,214,595	$6,083,099	€5,143,224	5,143,224
Sweden	SEK	316.8 (212.7 - 453.5)	$60,323	$61,358	€51,878	526,244	$19,062,098	$19,389,233	€16,393,480	166,293,052
Switzerland	CHF	238.3 (158.3 - 339.7)	$76,251	$92,343	€78,075	84,387	$18,147,637	$21,977,593	€18,581,922	20,084,136
Tajikistan	TJS	150.9 (109.8 - 198.8)	$4,382	$917	€775	10,367	$657,306	$137,504	€116,259	1,555,005

Türkiye	TRY	244.7 (175.7 - 332)	$30,452	$9,661	€8,169	85,506	$7,430,312	$2,357,340	€1,993,116	20,863,416
Turkmenistan	TMT	115 (83.3 - 156)	$17,219	$10,150	€8,581	35,523	$1,980,216	$1,167,196	€986,857	4,085,186
Ukraine	UAH	101.9 (65.7 - 147.2)	$13,516	$4,596	€3,886	125,417	$1,365,147	$464,231	€392,505	12,667,102
United Kingdom	GBP	429.9 (293.4 - 600.2)	$49,818	$46,410	€39,240	33,743	$21,371,750	$19,909,987	€16,833,774	14,475,855
Uzbekistan	UZS	213 (160.5 - 279.2)	$8,705	$2,031	€1,718	21,553,886	$1,854,229	$432,699	€365,844	4,590,977,788
WHO European Region	N/A	211.7 (148.1 - 288.8)	$39,501	$27,553	€23,296	N/A	$8,334,703	$5,813,713	€4,915,459	N/A

Acronyms. CI, confidence intervals; DALY, Disability Adjusted Life Year; EUR, Euros; GBP, Great British Pound; GDP, Gross Domestic Product; HUF, Hungarian Forint; ISL, Israeli New Shekel; Int$, International Dollars; MDL, Moldovan Leu; NCU, National Currency Unit; PLN, Polish Złoty; RON, Romanian Leu; SEK, Swedish Krona; TRY, Turkish lira; USD, United States Dollars; UAH, Ukrainian hryvnia; WHO, World Health Organisation.

***** An example way for how to use these societal cost estimates, is to state that WHO Europe should seek to invest $5,813,713 to eradicate the 211.7 (95%CI:148.1 - 288.8) DALY burden associated with asthma per 100,000 people (i.e., $58.14 per person). Other examples based on Austria and Türkiye are provided in the main article.

** Data on GDP per capita are converted to a common currency (i.e., international dollars, Int$) using a purchasing power parity (PPP) adjustment (Int$2021). Relative to converting all currencies to a common currency using an exchange rate (e.g. USD$), PPP-adjusted figures are more stable overtime and allow a better comparison between countries.

*** Although Greenland is reported separate to Denmark in Table 2, our GPD per capita data source does not provide estimates for Greenland thus Greenland is not reported separately here

	INCIDENCE Range of rates per 100,000 population across countries Range of absolute numbers of people across countries Estimate for whole of Europe		PREVALENCE Range of rates per 100,000 population across countries Range of absolute numbers of people across countries Estimate for whole of Europe		MORTALITY Range of rates per 100,000 population across countries Range of absolute numbers of people across countries Estimate for whole of Europe	
Cystic Fibrosis	Rates 12 countries[11] Range: 10.0 (RUS) to 154-192* Europe: NR	Numbers 0 countries	Rates 40 countries[10] Range: 0.5 (KG) to 25.4 (IRL)** Europe: 5.48 ± SD4.8	Numbers 40 countries[10] Range: 12 (KG) to 10,509 (GBR) Europe: 47,650	No estimates found	
Obstructive sleep apnoea	No estimates found		Rates 50 countries (AHI 5+ events per hour***)[12] Range: 0.5% (ARM) to 72% (CHE) Europe: NR	Numbers 50 countries (AHI 5+ events per hour***)[12] Range: 25,372 (ISL) to 40,203,912 (RUS) Europe: NR	No estimates found	
Alpha-1 antitrypsin deficiency	No estimates found		Rates 24 countries (based on Z allele frequency)[14] Range: 0.58 (KG) – 204 (LVA) Europe: NR	Numbers 24 countries (based on Z allele frequency)[14] Range: 0 (ISL) – 20,611 (DEU) Europe: 119,594 (error NR)	No estimates found	
Bronchiectasis	Rates 4 countries[15,17,18,20] Range: 16.3 (ITA) to 35.2 (GBR, females) Europe: NR	Numbers 1 country[20] Estimates: M: 4,331 F: 3,587 Pooled: 7,918 (ESP) Europe: NR	Rates 3 countries[15, 18, 19] Range: 94.8 (95% CI 91.7–97.9) (DEU) to 566 (GBR, females)	Numbers 1 country[19] Estimate: 78,450 (DEU) Europe: NR	Rates 1 country[16] Range: 1463 (95% CI: 1439–1488) (GBR) Europe: NR	Numbers 1 country[16] Estimate: 5,446 (error NR) (GBR) Europe: NR
Influenza	Rates 51 countries[13] Range: 63·4 (ITA) to 2489·6 (LTU) Europe: NR	Numbers 51 countries[13] Range: <1000***** to 3,504,000 (RUS) Europe: NR	Rates NR	Numbers NR	Rates 51 countries[13] Range: 0.7 (MKD) to 6.1 (ROU) Europe: NR	Numbers 51 countries[13] Range: <1000****** to 8000 (RUS) Europe: NR

Red= Systematic Review Blue = Primary Studies Yellow = Non-systematic review

Figure 1

Online Supplementary File: Search strategies and data extraction

This document contains:

1. Search strategy from 2024
2. Search strategy from 2022
3. Data extraction fields

1. Search strategy from 2024

An update search was run in May 2024, based on the original search conducted in May 2022. Two separate searches were conducted; 1) to identify systematic reviews on cystic fibrosis, sleep apnoea, and influenza, 2) Alpha-1 and Bronchiectasis with no limits on study design. Searches were conducted on MEDLINE, Embase, and the Cochrane Library, and limited to studies published since May 2022. The full search strategies and the number of records found in each database can be found below. Experts were also consulted for any missed studies.

Search 1: Systematic Reviews - Cystic Fibrosis, Sleep Apnoea, Influenza

Database	**Date Search**	**No. of records retrieved**
Ovid MEDLINE(R) Epub Ahead of Print and In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <May 21, 2024>	22/05/24	59
Embase <1974 to 2024 Week 20>	22/05/24	106
Cochrane Database of Systematic Reviews Issue 5 of 12, May 2024	22/05/24	6
Total		171
Total after duplicates removed		**125**

Search 1 Search Strategies

Ovid MEDLINE(R) Epub Ahead of Print and In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <May 21, 2024>

1 cystic fibrosis.ti. 32758

2 sleep apn?ea*.ti. 29743

3 osahs.ti. 216

4 (influenza* or flu or grippe).ti. 95574

5 or/1-4 158151

6 Epidemiologic Studies/ 9546

7 (epidemiology or epidemiological).ti.120322

8 Incidence/ or incidence.ti. 356530

9 Prevalence/ or prevalence.ti. 412622

10 Disability-Adjusted Life Years/ 292

11 disability adjusted life.mp. 6206

12 (DALY or DALYS).mp. 5440

13 "years of life lost".mp. 2611

14 YLL.ti.19

15 Mortality/ 49936

16 mortality.ti. 167904

17 or/6-161021634

18 5 and 17 9975

19 meta analysis.mp,pt. or review.pt. or search:.tw. 3848319

20 18 and 19 1150

21 ("20220528" or "20220529" or "20220530" or "20220531").dt. 17216

22 (2023* or 2024*).dt. 2198413

23 21 or 22 2215629

24 20 and 23 59

Embase <1974 to 2024 Week 20>

1 cystic fibrosis.ti. 49534

2 sleep apn?ea*.ti. 45377

3 osahs.ti. 306

4 (influenza* or flu or grippe).ti. 101561

5 or/1-4 196544

6 *epidemiology/ 48559

7 (epidemiology or epidemiological).ti.140150

8 *incidence/ 40577

9 incidence.ti. 155850

10 *prevalence/ 105512

11 prevalence.ti. 237746

12 *disability-adjusted life year/618

13 disability adjusted life.mp. 9232

14 (DALY or DALYS).mp. 7030

15 "years of life lost".mp. 3284

16 YLL.ti.20

17 *mortality/ 118224

18 mortality.ti. 217917

19 or/6-18814671

20 (2022* or 2023* or 2024*).dc. 5182087

21 5 and 19 and 20 1165

22 (((systematic or state-of-the-art or scoping or literature or umbrella) adj (review* or overview* or assessment*)) or "review* of reviews" or meta-analy* or metaanaly* or ((systematic or evidence) adj1 assess*) or "research evidence" or metasynthe* or meta-synthe*).tw. or systematic review/ or "systematic review (topic)"/ or meta analysis/ or "meta analysis (topic)"/ 962200

23 21 and 22 106

Cochrane Library (CDSR & CENTRAL)

#1 MeSH descriptor: [Epidemiologic Studies] this term only 129

#2 (epidemiology or epidemiological):ti 1107

#3 MeSH descriptor: [Incidence] this term only 14333

#4 incidence:ti 8616

#5 MeSH descriptor: [Prevalence] this term only 7402

#6 prevalence:ti 3478

#7 MeSH descriptor: [Disability-Adjusted Life Years] explode all trees 4

#8 disability adjusted life 2822

#9 (DALY or DALYS) 1628

#10 "years of life lost" 67

#11 YLL:ti 0

#12 MeSH descriptor: [Mortality] this term only 1029

#13 mortality:ti 7809

#14 1-#13 41877

#15 cystic fibrosis:ti 4857

#16 sleep apn?ea*:ti 5540

#17 osahs:ti 57

#18 (influenza* or flu or grippe):ti 6112

#19 #15 or #16 or #17 or #18 16539

#20 #14 and #19 with Cochrane Library publication date Between Jan 2022 and May 2024 23

Search 1: Alpha-1, Bronchiectasis

Database	**Date Search**	**No. of records retrieved**
Ovid MEDLINE(R) Epub Ahead of Print and In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <May 17, 2024>	20/05/24	26
Embase <1974 to 2024 Week 20>	20/05/24	78

Cochrane Database of Systematic Reviews Issue 5 of 12, May 2024	20/05/24	1
Cochrane Central Register of Controlled Trials Issue 4 of 12, April 2024	20/05/24	1
Total		106
Total after duplicates removed		**74**

Ovid MEDLINE(R) Epub Ahead of Print and In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <May 17, 2024>

1 bronchiectas*.ti. 5321

2 ((alpha 1 or alpha-1) adj antitrypsin deficienc*).ti. 1890

3 Epidemiologic Studies/ 9545

4 (epidemiology or epidemiological).ti.120261

5 Incidence/ or incidence.ti. 356376

6 Prevalence/ or prevalence.ti. 412427

7 Disability-Adjusted Life Years/ 281

8 disability adjusted life.mp. 6191

9 (DALY or DALYS).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word] 5428

10 "years of life lost".mp. 2607

11 YLL.ti.19

12 Mortality/ 49915

13 mortality.ti. 167753

14 1 or 2 7185

15 or/2-131021095

16 14 and 15 390

17 ("20220528" or "20220529" or "20220530" or "20220531").dt. 17216

18 (2023* or 2024*).dt. 2181707

19 17 or 18 2198923

20 16 and 19 26

Embase <1974 to 2024 Week 20>

1 bronchiectas*.ti. 6274

2 ((alpha 1 or alpha-1) adj antitrypsin deficienc*).ti. 2129

3 *epidemiology/ 48559

4 (epidemiology or epidemiological).ti.140150

5 *incidence/ 40577

6 incidence.ti. 155850

7 *prevalence/ 105512

8 prevalence.ti. 237746

9 *disability-adjusted life year/618

10 disability adjusted life.mp. 9232

11 (DALY or DALYS).mp. 7030

12 "years of life lost".mp. 3284

13 YLL.ti.20

14 *mortality/ 118224

15 mortality.ti. 217917

16 1 or 2 8370

17 or/3-15814671

18 16 and 17 349

19 (2022* or 2023* or 2024*).dc. 5182087

20 18 and 19 78

Cochrane Library (CDSR & CENTRAL)

#1	(bronchiectas*):ti	923
#2	((alpha 1 or alpha-1) NEAR/1 antitrypsin deficienc*):ti	74
#3	MeSH descriptor: [Epidemiologic Studies] this term only	129
#4	(epidemiology or epidemiological):ti	1107
#5	MeSH descriptor: [Incidence] this term only	14333
#6	incidence:ti	8616
#7	MeSH descriptor: [Prevalence] this term only	7402
#8	prevalence:ti	3478
#9	MeSH descriptor: [Disability-Adjusted Life Years] explode all trees	4
#10	disability adjusted life	2821
#11	(DALY or DALYS)	1628
#12	"years of life lost"	67
#13	YLL:ti	0
#14	MeSH descriptor: [Mortality] this term only	1029
#15	mortality:ti	7809
#16	#1 OR #2	997
#17	{OR #3-#15}^{2}	41876
#18	#16 and #17	13
#19	#18 with Cochrane Library publication date Between Jan 2022 and May 2024	2

2. Search strategy from 2022

A search of Medline was conducted in May 2022. A focussed approach to searching was taken, and only one database was searched due to the large number of records that would be retrieved were more exhaustive methods used (in excess of 15,000 records) and budgetary considerations. Because Medline has been estimated to identify approximately 85% of all records in systematic reviews,[2] this was selected as the database to search. Additional search techniques were also applied, which included contact with experts, via ELF, and snowballing (checking citations in Google Scholar, and checking reference lists) from important studies,

where insufficient data were identified by the database search. For two conditions (influenza and cystic fibrosis), additional focussed searches were conducted in Google Scholar, since no relevant studies were identified by the initial Medline search.

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <1946 to May 26, 2022>

1 bronchiectas*.ti. 4836

2 cystic fibrosis.ti. 30612

3 sleep apn?ea*.ti. 26352

4 osahs.ti. 196

5 (pulmonary hypertension or pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension or CTEPH).ti. 27597

6 ((alpha 1 or alpha-1) adj antitrypsin deficienc*).ti. 1763

7 Epidemiologic Studies/ 9129

8 (epidemiology or epidemiological).ti.110794

9 Incidence/ or incidence.ti. 340250

10 Prevalence/ or prevalence.ti. 385440

11 Disability-Adjusted Life Years/ 126

12 disability adjusted life.mp. 4551

13 (DALY or DALYS).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 3973

14 "years of life lost".mp. 2125

15 YLL.ti.12

16 Mortality/ 48911

17 mortality.ti. 147292

18 meta analysis.mp,pt. or review.pt. or search:.tw. 3449004

19 or/7-17949712

20 2 or 3 or 4 57123

21	19 and 20	3685	
22	18 and 21	603	
23	limit 22 to yr="2010 -Current"	382	
24	1 or 5 or 6	34168	
25	19 and 24	1566	
26	limit 25 to yr="2010 -Current"	**1130 All studies (unfiltered) since 2010 for bronchiectas, alpha 1, PH**	
27	(influenza* or flu or grippe).ti.	89426	
28	10 or 11 or 12 or 13 or 14 or 15	391442	
29	18 and 27 and 28	90	
30	limit 29 to yr="2010 -Current"	69	
31	23 or 30	**448 Reviews since 2010 for CF, apnoea, influenza***	
		***prevalance, DALYs and YLL only for influenza**	

3. Data extraction fields

Data were extracted under the following headings:

Author, year

Study design (systematic review (SR) or primary; retrospective, prospective)

Source of extracted data (if primary study extracted from systematic review)

Year of data collection

Condition

Country

Sex & Age inclusion criteria

SR search date

Source of primary study data (registry, health insurance claims etc)

Incidence rates, incidence numbers

Prevalence rates, prevalence numbers

Mortality rates, mortality numbers

DALY rates, DALY numbers

YLL rates, YLL numbers

Notes

1. Netikul T, Palittapongarnpim P, Thawornwattana Y, et al. Estimation of the global burden of Mycobacterium tuberculosis lineage 1. *Infection, Genetics & Evolution* 2021;91:104802.
2. Booth A. Over 85% of included studies in systematic reviews are on MEDLINE. *J Clin Epidemiol* 2016;79:165-66. doi: 10.1016/j.jclinepi.2016.04.002 [published Online First: 20160421]

Online Supplementary File: PRISMA flow diagram

It should be noted that there is a difference in the number of records included in 2022 (n=16) and the number of studies included in previous versions of the review in 2024 (n=11). This is because PAH data was sourced from the GBD in 2024 when it was added as a new category, and the 5 studies on PAH from 2022 were therefore not required in 2024.