Age–sex differences in the global burden of lower respiratory infections and risk factors, 1990–2019: results from the Global Burden of Disease Study 2019

GBD 2019 LRI Collaborators*

Summary

Background The global burden of lower respiratory infections (LRIs) and corresponding risk factors in children older than 5 years and adults has not been studied as comprehensively as it has been in children younger than 5 years. We assessed the burden and trends of LRIs and risk factors across all age groups by sex, for 204 countries and territories.

Methods In this analysis of data for the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019, we used clinician-diagnosed pneumonia or bronchiolitis as our case definition for LRIs. We included International Classification of Diseases 9th edition codes 079.6, 466–469, 470.0, 480–482.8, 483.0–483.9, 484.1–484.2, 484.6–484.7, and 487–489 and International Classification of Diseases 10th edition codes A48.1, A70, B97.4–B97.6, J09–J15.8, J16–J16.9, J20–J21.9, J91.0, P23.0–P23.4, and U04–U04.9. We used the Cause of Death Ensemble modelling strategy to analyse 23 109 site-years of vital registration data, 825 site-years of sample vital registration data, 1766 site-years of verbal autopsy data, and 681 site-years of mortality surveillance data. We used DisMod-MR 2.1, a Bayesian meta-regression tool, to analyse age–sex-specific incidence and prevalence data identified via systematic reviews of the literature, population-based survey data, and claims and inpatient data. Additionally, we estimated age–sex-specific LRI mortality that is attributable to the independent effects of 14 risk factors.

Findings Globally, in 2019, we estimated that there were 257 million (95% uncertainty interval [UI] 240–275) LRI incident episodes in males and 232 million (217–248) in females. In the same year, LRIs accounted for 1.30 million (95% UI 1·18–1·42) male deaths and 1·20 million (1·07–1·33) female deaths. Age-standardised incidence and mortality rates were 1.17 times (95% UI 1·16–1·18) and 1.31 times (95% UI 1·23–1·41) greater in males than in females in 2019. Between 1990 and 2019, LRI incidence and mortality rates declined at different rates across age groups and an increase in LRI episodes and deaths was estimated among all adult age groups, with males aged 70 years and older having the highest increase in LRI episodes (126·0% [95% UI 121·4–131·1]) and deaths (100·0% [83·4–115·9]). During the same period, LRI episodes and deaths in children younger than 15 years were estimated to have decreased, and the greatest decline was observed for LRI deaths in males younger than 5 years (–70·7% [–77·2 to –61·8]). The leading risk factors for LRI mortality varied across age groups and sex. More than half of global LRI deaths in children younger than 5 years were attributable to child wasting (population attributable fraction [PAF] 53·0% [95% UI 37·7–61·8] in males and 56·4% [40·7–65·1] in females), and more than a quarter of LRI deaths among those aged 5–14 years were attributable to household air pollution (PAF 26·0% [95% UI 16·6–35·5] for males and PAF 25·8% [16·3–35·4] for females). PAFs of male LRI deaths attributed to smoking were 20·4% (95% UI 15·4–25·2) in those aged 5–14 years, 30·5% (24·1–36·9) in those aged 50–69 years, and 21.9% (16·8–27·3) in those aged 70 years and older. PAFs of female LRI deaths attributed to household air pollution were 21·1% (95% UI 14·5–27·9) in those aged 15–49 years and 18·2% (12·5–24·5) in those aged 50–69 years. For females aged 70 years and older, the leading risk factor, ambient particulate matter, was responsible for 11·7% (95% UI 8·2–15·8) of LRI deaths.

Interpretation The patterns and progress in reducing the burden of LRIs and key risk factors for mortality varied across age groups and sexes. The progress seen in children younger than 5 years was clearly a result of targeted interventions, such as vaccination and reduction of exposure to risk factors. Similar interventions for other age groups could contribute to the achievement of multiple Sustainable Development Goals targets, including promoting wellbeing at all ages and reducing health inequalities. Interventions, including addressing risk factors such as child wasting, smoking, ambient particulate matter pollution, and household air pollution, would prevent deaths and reduce health disparities.

Funding Bill & Melinda Gates Foundation.

Copyright © 2022 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.
Introduction

Lower respiratory infections (LRIs), mainly caused by bacteria such as Streptococcus pneumoniae and Haemophilus influenzae type b and viruses such as influenza and respiratory syncytial virus, are a leading cause of death globally, killing more than 2 million people every year.1 LRIs are also the leading underlying cause of sepsis, which is a major cause of health loss and death worldwide.2 Global initiatives to tackle LRIs, such as the Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea,1 the Stop Pneumonia Initiative,3 and the Integrated Management of Childhood Illness initiative,3 are targeted at children younger than 5 years. Current literature on the burden of LRIs also focuses primarily on children younger than 5 years; less attention is paid to the LRI burden among children older than 5 years and adults. Evidence indicates that males are more susceptible to LRIs than females, possibly due to factors such as differences in immune response to infection and behavioural factors such as smoking.3 Understanding the current burden and trends of LRIs across all age groups by sex is essential for identifying areas of intervention.

Although measuring the burden of LRIs is a crucial input in policy decision making, the assessment of modifiable risk factors for LRIs can inform preventive interventions. With the ageing of populations, it is increasingly important to assess LRI risk factors, especially those for which exposure is not declining, such as ambient particulate matter air pollution, and compare them to risk factors for which exposure is decreasing, such as household air pollution.7 Understanding the changing LRI burden attributable to various risk factors across the entire age spectrum can assist in identifying priorities for targeted interventions. To our knowledge, the global burden of LRIs attributable to risk factors for age groups other than those younger than 5 years has not been comprehensively studied. The objective of this study is to assess the burden and trends of LRIs and risk factors across all age groups by sex for 204 countries and territories. This manuscript was produced as part of the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) Collaborator Network and in accordance with the GBD Protocol.

Methods

Overview

Detailed methods for GBD 2019 have been published elsewhere.8 Here, we describe the methods and estimation strategies for LRIs and risk factors. In compliance with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER), input data sources and code for each step of the estimation process are available on the Global Health Data Exchange.

Case definition

We used clinician-diagnosed pneumonia or bronchiolitis as our case definition for LRIs. We included...
LRI mortality

The GBD Cause of Death database collates all available data from vital registration systems, surveillance systems, and verbal autopsy studies. Input data for LRI mortality estimation included 23,109 site-years (the number of years for which data are available for a particular location) of vital registration data, 825 site-years of sample vital registration data (ie, data covering a sample of the population), 1,766 site-years of verbal autopsy data, and 681 site-years of mortality surveillance data. Country-specific data sources and citations are available on the Global Health Data Exchange. Vital registration data were adjusted for completeness and garbage coding.1,8 Data before and after garbage code redistribution are available in the online data visualisation tool.

We used the Cause of Death Ensemble modelling (CODEm) strategy13 to generate LRI mortality estimates by location, year, age, and sex. CODEm assesses a vast array of sub-models with varying combinations of predictive covariates (eg, undernutrition and air pollution) that are run through four model categories (ie, mixed-effects regression models and spatiotemporal Gaussian process regression models for cause fractions and mortality rates; appendix 1 pp 13–14). Sub-models are evaluated using out-of-sample predictive validity and combined into an ensemble with the best predictive performance.

LRI morbidity

To estimate age–sex-specific incidence and prevalence of LRIs, we used data identified via systematic reviews of the literature. Additionally, we used population-based survey data, claims data, and inpatient data to estimate incidence and prevalence (appendix 1 pp 6–10. For GBD 2019, we used an enhanced standardised approach, compared with previous GBD iterations, to adjust definitions in data sources that did not use our reference case definition to be comparable with our reference case definition (ie, clinician-diagnosed pneumonia or bronchiolitis). To do so, we first computed the ratio of the data based on alternative case definitions to the data based on the reference case definition, on the basis of all available data matched by location, year, age, and sex. We then ran a meta-regression to pool the ratios and used the pooled ratio to adjust the data based on alternative case definitions to the level of the data based on the reference case definition (appendix 1 pp 8–10).

Our inclusion criteria for scientific literature included a study duration of at least 1 year to avoid bias in the seasonal timing of LRIs and a sample size of at least 100 people (the sample size threshold was chosen arbitrarily). Survey data were adjusted for seasonality by fitting a generalised additive mixed-effects model with a forced periodicity for each GBD region, accounting for the year of the survey and the case definition used. The percentage difference between the monthly model-fit LRI prevalence and the corresponding regional mean LRI prevalence was computed to adjust survey data by month and geography. The mean duration of LRIs was 7–79 days (uncertainty interval [UI] 6·20–9·64); this was determined on the basis of a systematic review and meta-analysis,9 and was used to convert incidence data to prevalence. We modelled these data together with LRI mortality estimates using DisMod-MR 2.1,11 a Bayesian meta-regression tool that imposes coherence between data for different parameters, to produce final incidence and prevalence estimates. Details on the preparation of data sources and the modelling in DisMod can be found in appendix 1 (pp 6–11).

Risk factors

Detailed methods for GBD risk factor estimation have been published elsewhere.7 In summary, we first selected risk–outcome pairs (eg, LRIs attributable to smoking) on the basis of evidence of a convincing or probable causal relationship between the risk and the outcome. A full list of LRI risk factors and the mechanism through which each risk factor could cause LRIs can be found in appendix 1 (pp 15–17). The population attributable fractions (PAFs) of risk factors were quantified by estimating the risk factor exposure distributions and the relative risk of the association between each risk factor and the outcome, and determining the theoretical minimum-risk exposure level. The PAF is the fraction of LRI mortality that would have been reduced if the exposure to the risk factor had been at the theoretical minimum-risk exposure level. The attributable burden was computed by multiplying the location–year–age–sex-specific PAFs of risk factors by corresponding LRI deaths. We also calculated risk-deleted mortality rates to represent the LRI mortality rate that would have been observed had the risk factors been set to their corresponding theoretical minimum-risk exposure levels. Full details of the methods used for estimating each of the 14 LRI risk factors are provided in appendix 1 (pp 18–79).

Uncertainty intervals and age-standardisation

We computed 95% UIs based on 1000 draws from the posterior distribution of each stage in the estimation process using the 2.5th and 97.5th percentiles of the 1000 ordered values.

We used the GBD world population age standard12 to calculate age-standardised LRI incidence and mortality rates.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.
Results

On a global scale, in 2019, the total number of LRI incident episodes was 257 million (95% UI 240–275) for males and 232 million (217–248) for females, reflecting an increase of 20.0% (95% UI 15.8–24.5) for males and 15.8% (11.9–19.7) for females since 1990 (appendix 2 pp 3, 5). The age-standardised incidence rate was 1.17 (95% UI 1.16–1.18) times greater in males than in females in 2019. When looking at specific age–sex groups, we estimated that there was a decrease in LRI episodes between 1990 and 2019 in children younger than 15 years and an increase in this period in all adult age groups (figure 1; appendix 2 pp 3, 34). Among children, the decrease varied from 20.8% (95% UI 16.2–25.6) among males aged 5–14 years to 49.9% (48.5–51.6) among females younger than 5 years. Among adult age groups, the increase varied from 26.1% (23.2–29.1) for females aged 15–49 years to 126.0% (121.4–131.1) for males aged 70 years and older during the same period (appendix 2 p 34).

Between 1990 and 2019, children younger than 5 years saw the greatest improvement, with a decrease in incidence rate per 100,000 population of 51.7% (95% UI 50.0–53.5) for males and 52.1% (50.7–53.7) for females. Among adult age groups, the increase varied from 8.6% (6.6–10.5) decrease in incidence rate for males aged 70 years and older and only an 11.2% (9.2–13.0) decrease in incidence rate for females aged 70 years and older during the same period (appendix 2 p 34).

Between 1990 and 2019, children younger than 5 years had the lowest global incidence rate of LRI episodes per 100,000 population among all age groups: 4128.1 (95% UI 3726.8–4583.5) for males and 3944.6 episodes (3541.5–4421.4) for females (figures 1, 2; appendix pp 34–37). Individuals aged 70 years and older, on the other hand, had the highest incidence rate per 100,000 population of all age groups: 25786.6 (23182.5–28975.4) for males and 19819.9 (17921.3–22072.6) for females. Of all super-regions, South Asia had the highest incidence rate per 100,000 population among both males aged 70 years and older (48185.3 [95% UI 42327.6–56191.8]) and females aged 70 years and older (38852.6 [34264.3–44606.1]; appendix 2 pp 34–37).

Globally, in terms of absolute numbers, LRIs accounted for 1.30 million (95% UI 1.18–1.42) deaths in 2019 among males and 1.20 million (1.07–1.33) deaths among females (appendix 2 p 38). The age-standardised mortality rate was 1.31 (95% UI 1.23–1.41) times greater in males than in females in 2019. We estimated an increase in LRI deaths among all adult age groups between 1990 and 2019 (figure 1; appendix 2 p 4), with males aged 70 years and older having the highest increase in deaths (100.0% [95% UI 83.4–115.9]; table). In high-income countries, we estimated a 70.7% (95% UI 58.3–77.9) increase in death counts for males aged 70 years and older and a 54.3% (39.7–63.0) increase for females aged 70 years and older (table). This increase in the number of deaths between 1990 and 2019 is visible regardless of age, with 20 countries showing an increase of more than 100% in death counts attributable to LRIs for males and 19 countries for females (appendix 2 pp 38–67).

Between 1990 and 2019, children younger than 5 years showed the greatest improvement in death rates for LRIs

Figure 1: Incidence and mortality counts (A) and rates (B) due to lower respiratory infections for both sexes combined in 1990 and 2019, by age group
In contrast, children aged 5–14 years had the lowest mortality rates, with a mortality rate per 100 000 people of only 3·3 (2·8–3·9) for males and 3·3 (2·7–3·9) for females. We estimated that sub-Saharan Africa was the super-region with the highest mortality rate in individuals aged 70 years and older, with a mortality rate per 100 000 people of 850·8 (758·1–941·4) for males and 672·1 (553·9–766·2) for females (table).

Globally, in 1990, we estimated that 876 000 LRI deaths (95% UI 770 000–987 000) among males (PAF 67·6% [95% UI 62·9–72·1]) and 725 000 deaths (95% UI 629 000–826 000) among females (PAF 60·6% [95% UI 55·6–65·6]) were attributable to all evaluated LRI risk factors (appendix 2 p 68). Globally, the number of LRI deaths attributable to all risk factors decreased by 41·4% (95% UI 32·0–49·3) for males and 44·5% (34·9–53·9) for females between 1990 and 2019. Children younger than 5 years had the greatest percentage decrease in number of deaths and mortality rate attributable to all risk factors between 1990 and 2019 (appendix 2 p 97). The greatest percentage increase in attributable deaths between 1990 and 2019 was estimated to be in males aged 70 years and older (66·6% [95% UI 50·4–82·8]).

Global age-standardised attributable mortality rate per 100 000 population due to all risk factors in 2019 was 26·2 (95% UI 23·1–29·5) for males and 19·4 (16·8–22·2) for females. Between 1990 and 2019, this rate decreased by 56·1% (95% UI 50·0–60·9) for males and 59·1% (52·5–65·6) for females (appendix 2 p 68).

In 2019, the leading risk factor for LRI mortality in children younger than 5 years was child wasting, in both males (PAF 53·0% [95% UI 37·7–61·8]) and females (56·4% [40·7–65·1]; figure 3; appendix p 117). Child wasting was also the largest risk factor in children younger than 5 years in 1990 and had decreased only slightly by 2019 (figure 3). For children younger than 5 years in 2019, the second largest PAF was for household air pollution; male and female children in this age group had near identical PAFs (31·4% [95% UI 21·5–41·5] vs 31·2% [21·3–41·5]; appendix p 117). Household air pollution was the second largest PAF in 1990 and had decreased substantially by 2019 (figure 3).

In 2019, the largest risk factor for children aged 5–14 years was household air pollution (PAF 26·0% [95% UI 16·6–35·5] vs 31·2% [21·3–41·5]; appendix p 117). Househould air pollution was the second largest PAF in 1990 and had decreased substantially by 2019 (figure 3).
Males aged 50–69 years in 2019 had the highest PAF from smoking (30·5% [95% UI 24·1–36·9]) and the lowest PAF from high temperature (3·0% [1·3–6·4]; figure 4; appendix p 160). Females in the same age group had the highest PAF from ambient particulate matter (11·7% [8·2–15·8]), and the lowest PAF from alcohol use (1·8% [0·5–3·2]; figure 4; appendix p 173). Differing from females in 2019, females in 1990 had the highest PAF from household air pollution (21·2% [15·4–27·6]), and the lowest PAF from high temperature (1·8% [0·7–6·2]; figure 4).

Ambient particulate matter tended to affect males and females similarly across all age ranges (figure 4). PAFs for low temperatures were highest in North America and Western Europe, and the lowest in South Asia and Central Asia.
| Region                      | 2019 Male | Percentage change from 1990 to 2019 | 2019 Female | Percentage change from 1990 to 2019 |
|-----------------------------|-----------|------------------------------------|-------------|------------------------------------|
|                             | Number of deaths | Mortality rate (per 100 000 people) | Number of deaths | Mortality rate (per 100 000 people) |
| **North Africa and Middle East** |           |                                     |              |                                     |
| 0-4 years                   | 15 300    | (11 800 to 19 500)                  | 50 0        | (38 6 to 63 6)                      |
| 5-14 years                  | 18 000    | (14 000 to 23 000)                  | 3 0         | (2 3 to 3 8)                        |
| 15-49 years                 | 6 500     | (5 400 to 7 800)                    | 3 7         | (3 1 to 4 5)                        |
| 50-69 years                 | 11 600    | (9 700 to 13 700)                   | 28 2        | (23 6 to 33 3)                      |
| ≥70 years                   | 23 200    | (20 100 to 26 700)                  | 238 7       | (206 3 to 274 0)                    |
| **Southeast Asia, east Asia, and Oceania** |           |                                     |              |                                     |
| 0-4 years                   | 87 800    | (69 700 to 111 000)                 | 101 3       | (81 3 to 129 1)                     |
| 5-14 years                  | 6 600     | (5 000 to 8 500)                    | 3 6         | (2 7 to 4 6)                        |
| 15-49 years                 | 16 900    | (13 800 to 20 700)                  | 3 4         | (2 8 to 4 2)                        |
| 50-69 years                 | 48 200    | (38 600 to 58 300)                  | 39 2        | (31 4 to 47 5)                      |
| ≥70 years                   | 102 600   | (83 800 to 122 000)                 | 309 2       | (253 6 to 368 1)                    |
| **Sub-Saharan Africa**      |           |                                     |              |                                     |
| 0-4 years                   | 30 600    | (25 800 to 35 800)                  | 41 2        | (34 7 to 48 2)                      |
| 5-14 years                  | 2 200     | (1 900 to 2 600)                    | 2 9         | (1 4 to 1 8)                        |
| 15-49 years                 | 16 700    | (14 800 to 19 000)                  | 3 4         | (2 6 to 3 3)                        |
| 50-69 years                 | 47 900    | (41 100 to 54 500)                  | 19 4        | (12 7 to 22 1)                      |
| ≥70 years                   | 138 000   | (122 000 to 154 000)                | 221 4       | (195 1 to 246 0)                    |
| **Global Burden of Diseases, Injuries, and Risk Factors Study** |           |                                     |              |                                     |

95% uncertainty intervals are shown in parentheses. *Six-digit numbers are reported to the nearest 1000 deaths and all other numbers are reported to the nearest 100 deaths.

Table: Lower respiratory infection deaths and mortality rates in 2019 and the percentage change in deaths and mortality rates between 1990 and 2019 by age, sex, and GBD super-region.

70 years and older than for the younger age ranges. In 2019, second-hand smoke produced differing patterns of effect between males and females: males aged 5–14 years had a higher PAF (7·9% [95% UI 4·5–11·5]) than other age categories, whereas females aged 15–49 years were estimated to have a slightly higher PAF from second-hand smoke (10·1% [5·8–14·4]) than other age categories. Alcohol-use PAFs were much higher in males across all age categories than in females. Lastly, high temperature PAFs were consistent across both sexes and tended to show a greater effect on individuals in younger age categories.
Mortality and incidence ratios were calculated between males and females across countries for the year 2019 (figure 5). Male-to-female ratios of age-standardised incidence rates were the highest in Ukraine and Moldova (figure 5A). Male-to-female ratios of age-standardised mortality rates were the highest in Russia, Belarus, Ukraine, Estonia, Lithuania, Japan, Ghana, and Moldova (figure 5B).

In 2019, the male-to-female ratio in global age-standardised mortality rates was 1·31 (95% UI 1·23–1·41). When all risk factors for LRIs were removed, the global age-standardised mortality rate per 100 000 population in 2019 in males was 13·5 (95% UI 11·4–15·7), and in females was 11·1 (9·2–12·7; appendix 2 p 102). Therefore, the ratio of risk-deleted mortality rates between males and females in 2019 was 1·22 (95% UI 1·12–1·36).
Figure 5: Male-to-female ratio of age-standardised lower respiratory infection incidence rates (A) and mortality rates (B), 2019
Comparatively, in 1990, the male-to-female ratio in global age-standardised mortality rates was 1·24 (95% UI 1·15–1·33). The global risk-deleted mortality rates per 100 000 population were 15·6 (95% UI 13·0–18·3) for males and 13·4 (11·2–15·7) for females (appendix p 102). The risk-deleted mortality rate between males and females in 1990 was 1·17 (95% UI 1·07–1·28). In 2019, the central Europe, eastern Europe, and central Asia region had the largest risk-deleted male-to-female ratio of all regions at 1·62 (95% UI 1·43–1·83). South Asia had the lowest male-to-female ratio at 0·88 (95% UI 0·67–1·14), where females had a higher risk-deleted mortality rate than males (appendix p 110).

Discussion

Between 1990 and 2019, the greatest progress in reducing LRI incidence and mortality rates was observed in children younger than 5 years, indicating the success of initiatives targeting children in this age bracket. Much less progress has been made to reduce LRI incidence and mortality rates in adults, particularly in older age groups. Over the same period, in terms of absolute numbers, an increase in LRI incident episodes and deaths was estimated among all adult age groups due to population growth and aging. Globally, in 2019, age-standardised incidence rates were 1·2 times greater in males than in females and mortality rates were 1·3 times greater. Smoking was the leading risk factor for LRI mortality in adult males, responsible for about one-third of LRI deaths in those aged 50–69 years and one-fifth of LRI deaths in other age groups in 2019. PAFs of LRI deaths attributable to ambient particulate matter pollution have gone up for both males and females of all ages since 1990. On the other hand, PAFs of LRI deaths due to household air pollution have decreased among all age groups since 1990. PAFs of LRI deaths due to child wasting, stunting, and being underweight have also decreased among children younger than 5 years during the same period.

Despite the substantial progress made in children younger than 5 years, there were still 672 000 LRI deaths in this age group in 2019, and 93·5% (95% UI 90·4–95·7) of those deaths were attributable to preventable risk factors. Over the past two decades, global initiatives to combat wasting, the leading LRI risk factor, have focused mainly on treating wasting children, particularly in humanitarian situations. Although treatment coverage has steadily increased over time, only one-third of severely wasted children received treatment in 2019. This situation has been compounded by COVID-19 pandemic-related disruptions to nutrition and other fundamental services; the global prevalence of child wasting was estimated to increase by 14·3% during the first year of the pandemic. Given that undernutrition is the main risk factor not only for LRIs but also for other leading causes of death in children younger than 5 years such as diarrhoea and measles, long-term adverse implications are foreseeable unless the recommended actions (eg, protecting and facilitating access to healthy, nutritious, and affordable food and reactivation and scaling up of early detection and treatment services for child wasting”) are taken promptly.

In 2015, the era of the Millennium Development Goals (MDGs) ended and the global community unanimously adopted the Sustainable Development Goals (SDGs). Although substantial progress had been made towards the MDG goal of reducing under-5 mortality by two-thirds between 1990 and 2015, achieving the new SDG target of 25 or fewer deaths per 1000 livebirths by 2030 would require promoting child survival by accelerating the decline of the major causes of death in young children. LRIs, which were still the leading infectious cause of death among children younger than 5 years in 2019, are largely preventable through vaccination and addressing key risk factors. In contrast to the progress seen in children younger than five years, little has been achieved in reducing the LRI burden among adults, indicating a need for initiatives that address LRI risk factors in the adult age groups. Ambient particulate matter pollution was a leading risk factor for LRI mortality in all adult age groups in 2019. Studies from 2020 have also suggested associations between elevated exposures to particulate matter with a diameter less than 2·5 μm (PM$_{2·5}$) and higher COVID-19 cases and deaths. Contributors to global ambient particulate matter pollution include wildfires, biomass burning, sandstorms, chemical plants, and vehicle combustion sources. A study of how countries have followed the WHO ambient air quality guidelines found there were no air quality standards in 57 (34%) of the 170 countries examined. The same study also found that air quality standards for some pollutants, including PM$_{2·5}$, were non-compliant with WHO guidelines in many countries.

Our results showed that global LRI deaths attributable to household air pollution decreased among all age groups between 1990 and 2019; however, exposure to household air pollution was responsible for more than a quarter of LRI deaths among children younger than 5 years and children aged 5–14 years, and more than a fifth of LRI deaths among women aged 15–49 years, in 2019. Sub-Saharan Africa had the largest PAFs, and South Asia had the second largest PAFs, for household air pollution across all age groups in 2019. More than 890 million people do not have access to clean cooking fuels in sub-Saharan Africa. In India, the Pradhan Mantri Ujjwala Yojana, one of India’s primary policies to provide households with liquid petroleum gas, a clean cooking fuel, was scheduled to be implemented in 102 cities and towns and related villages in 2019. An evaluation study done in a rural community in Odisha found that the majority of Pradhan Mantri Ujjwala Yojana recipients did not refill their liquid petroleum gas cylinders (ie, solid fuels were still being used for cooking).
indicating the need for interventions to address challenges faced by rural households to ensure a complete transition from polluting to clean fuels.57

Consistent with previous studies,5 we found higher LRI incidence and mortality among males than females, especially among adults. Potential reasons for this difference include sex differences in the immune response to infection and behavioural factors such as smoking and alcohol use.5–10 Females generally have a stronger immune system than males.11 Smoking is not only immunosuppressive but also causes changes such as ciliary dysfunction in the respiratory tract, leading to decreased pathogen clearance.12 The highest LRI mortality rates attributable to smoking among men were observed in countries in east Asia, southeast Asia, and eastern Europe. Despite a gradual decline in smoking prevalence in most of these countries, the declines were not sufficient to compensate for population growth, leading to a steady or growing number of smokers with time.13 In many countries worldwide, progress towards reducing smoking prevalence has stalled in the past decade.12–14 The number of countries that have implemented at least one key intervention of the WHO Framework Convention on Tobacco Control has increased over time; however, only 62 countries had a complete ban on smoking in public and workplace settings, and only 23 countries provided comprehensive support for smokers seeking assistance in quitting smoking, as of 2018.15

Results showed that PAFs attributable to alcohol use were much higher in males than females across all adult age categories. Alcohol use increases the risk of microbe aspiration and weakens the host immune system.16 Although alcohol use is generally higher among men than women, it is increasing among women in different parts of the world, including some countries in sub-Saharan Africa.16–18 Increased government support and engagement are essential for adopting and enforcing effective alcohol policies in sub-Saharan Africa, which is a target region for alcohol companies to expand their market.20

We found that the male-to-female ratio in global age-standardised LRI mortality rates decreased from 1·31 to 1·22 after removing the combined effects of all evaluated risk factors. Despite the smaller ratio, males still had a higher mortality rate than females, suggesting that other factors such as genetics and hormones could have a role in differential regulation of the immune system and the greater risk of mortality among males than females.19

Our results suggest that reducing the LRI burden and targeting the key risk factors that are different across age–sex groups will help in achieving multiple SDG targets, including SDG 3 (ensuring healthy lives and promoting wellbeing for all ages), SDG 7 (affordable and clean energy), and SDG-10 (reducing inequalities).21 The remarkable progress made in children younger than 5 years was a result of the scale-up of proven interventions, including vaccination and reducing exposure to known risk factors.22 Similar interventions for other age groups could contribute to the achievement of the SDG targets. Pneumococcal conjugate vaccines have been shown to have a direct protective effect on young children and an indirect protective effect on unvaccinated adults.23 The global pneumococcal conjugate vaccine coverage (third dose) among young children was estimated to be 47·9% (95% UI 47·0–48·9) in 2019.24 The gap in childhood immunisation coverage has become wider as the COVID-19 pandemic disrupted routine immunisation services worldwide, indicating an urgent need for catch-up and expansion of immunisation.25–27 Studies published since 2019 have shown that direct immunisation of older adults with PCV13 significantly reduced the disease burden.28–30 Immunisation of older adults, as well as addressing key leading risk factors such as child wasting, smoking, ambient particulate matter pollution, and household air pollution, could help reduce the burden of LRIs across all age groups. Additionally, supportive care, such as oxygen therapy, is a key part of the management of severe LRIs, and interventions to strengthen oxygen systems in low-resource settings could further help reduce LRI mortality.31

This study has several limitations. One of the key limitations is the availability of data. In the absence of data for a particular country, estimates were dependent on the regional patterns, covariates, and out-of-sample predictive validity assessment. The absence of data in a given country translated into wide intervals of uncertainty. Even in countries with data, delays in data reporting prevented their timely integration into the GBD estimation. The most recent years for which cause of death data were available were 2016 and 2017. We were able to validate our estimation method by comparing two sets of estimates produced for a particular year with and without using any data for that year. For example, GBD 2016 produced LRI mortality estimates for 2016 using data available up to 2013 and 2014; these estimates were compared with GBD 2019 estimates for the same year that were informed by empirical data for 2016. GBD 2016 estimated a mortality rate per 100 000 population of 37·0 (95% UI 34·1–40·0) and GBD 2019 estimated 37·9 (32·5–40·8) for all ages and both sexes combined for the high-income super-region in 2016. Although the estimates are not identical, they are sufficiently close enough to support the validity of our approach. In this study, we were unable to evaluate the contribution of individual causes to the LRI burden. We plan to do a comprehensive assessment of the burden attributable to various pathogens in our future GBD estimation. Additionally, we have not assessed the LRI burden attributable to some potentially important risk factors such as overcrowding and incomplete immunisation.30 Current risk–outcome pairs were included on the basis of the World Cancer Research Fund criteria for convincing or probable evidence. We could evaluate
whether additional risk factors are eligible for inclusion in future GBD iterations. Lastly, our current estimates of risk-attributable burden are limited by the quality of the primary data underlying the analysis. For example, data on some risk factors such as smoking and second-hand smoke were self-reported. Studies have indicated that self-reported smoking prevalence data might be prone to underestimation depending on respondents’ perception of the social acceptance of smoking.\textsuperscript{52,53} Second-hand smoke exposure data might also be prone to recall bias.\textsuperscript{51} Biomarker-based exposure assessment such as cotinine could help improve the accuracy of smoking and second-hand smoke data.\textsuperscript{52,53}

Although our results represent the LRI burden before the COVID-19 pandemic, the effect of the pandemic on LRI needs to be investigated further. The pandemic was linked to a reduction of influenza and respiratory syncytial virus infections, probably as a result of COVID-19 pandemic on the burden and causes of LRIs. The pandemic was linked to a reduction of influenza and respiratory syncytial virus infections, probably as a result of COVID-19 pandemic on the burden and causes of LRIs.

In conclusion, our results showed that despite an overall global decline in LRI incidence and mortality rates between 1990 and 2019, the pace of decline has been unequal across age groups. The observed progress in children younger than 5 years was clearly a result of targeted interventions, including improving vaccination and reducing exposure to risk factors. Similar interventions for other age groups could contribute to the achievement of multiple SDG targets, including promoting well-being at all ages and reducing health inequalities.
(B Tessa M PhD), University of Gondar, Gondar, Ethiopia; Pharmacoeconomics and Health Outcomes Research Department, Florida A&M University, Tallahassee, FL, USA (T M Asegaz MSc); Department of Laboratory Technology Sciences Department (H Abdi PhD), Department of Nursing (M Zolalad PhD), Yasuy University of Medical Sciences, Yasuy, Iran; Department of Family and Community Health, School of Public Health, University of Health and Allied Sciences, Hooroe, Gha (R A Asegay MPH); Research Center for Immunodeficiencies (H Alhassan PHD), Department of Epidemiology and Biostatistics (Y Almohamadi PhD), Non-Communicable Diseases Research Center (A Azajnajafabad MD, M Azangou-Khayy MD, S Ghamari MD, M Keyhkaei MD, S Montazmashz MD, M Rashidi MD), National Institute for Health Research (E Ehsani-Chimeh PhD), School of Medicine (A Fallahzadeh MD, S Montazmashz MD, A Nowroz BMedSci), The Institute of Pharmaceutical Sciences (TIPS) Tehran University of Medical Sciences (S Hassani PhD), Students' Scientific Research Center (M Keykhue MD), Children's Medical Center (F Kompani MD), Pediatrics Department-Pediatric Cardiology (Prof E Malakan Rad MD), Tehran Heart Center (E Mehrabani Nasab MD), Faculty of Medicine (E Mohammedi MD, E Shaker MD, P Shobeiri MD), Genomics and Biometrics Research Center (F Rahim PhD), Sina Trauma and Surgery Research Center (Prof V Rahimi-Moghadar MD), Department of Cardiology and Human Rights Nursing (Y D Abhev MSc, B B A Bodicha MSc, T K Kanko MSc), Department of Public Health (Z G Argaw MPH), School of Nursing (T M Ayana MSc, B Demisse MSc), School of Public Health (A Belachew MSc), Department of Midwifery (F W Demisse MSc, G Temesgen MSc), Department of Anatomy (S Demisse MSc), Department of Comprehensive Nursing (E Diges MSc), Department of Epidemiology and Biostatistics (A Ghereimach MPh), Medical Laboratory (A Tesfaye MSc), Arba Minch University, Arba Minch, Ethiopia; University of Human Development (Prof H Abolhassani MD), School of Health and Allied Sciences, Ho, Ghana; Erbil Technical Health College, Erbil, Iraq (T M Ayana MSc, B A Alhaj MD, F Taki PhD), Drug Applied Research Center (H Samadi Kafil MSc), Connective Tissue Diseases Research Center (F Montazeri MD, S Nejadghaderi MD, M Zangiabadian MD), Chronic Respiratory Disease Research Center, National Research Institute of Tuberculosis and Lung Diseases (M M Tazari MD), Medical Ethics and Law Research Center (M Taheri PhD), Shahid Beheshti University of Medical Sciences, Tehran, Iran; Department of Biosciences, COMSATS Institute of Information Technology, Islamabad, Pakistan (H Ahmad PhD); Department of Pathology and Microbiology (J Q Ahmad MSc, M A Yahya MSc), Department of Pharmacology, College of Pharmacy (B A Zaman MSc), University of Duhok, Duhok, Iraq; Department of Medical and Computer Science and Engineering, University of Kurdistan Hewler, Erbil, Iraq (T Ahmad Rashid PhD); Liver and Gastrointestinal Diseases Research Center (M Akbarzadeh-Khayi PhD), School of Nursing and Midwifery (H Hassankhani PhD), Student Research Committee (M Hosseini MD), Department of Parasitology (A Javadi Mamaghani PhD), Department of Medical Surgical Nursing (M Lotfi PhD), Medical Education Research Center (M Lotfi PhD), Anesthesiology and Critical Care (Prof A Mahmoodpoor MD), Department of Radiology (M Mirza-Aghazadeh-Attari MD, A Zarrintan MD), Tuberculosis and Lung Diseases Research Center (S Mousavi-Aghdas MSc), Cardiovascular Research Center (M Rahimi MD), Connective Tissues Disease Research Center (A Safary PhD), Drug Applied Research Center (H Samadi Kafil PhD), Department of Immunology (M Soltani-Zangbar MSc), Tabriz University of Medical Sciences, Tabriz, Iran; Geriastic and Long Term Care Department (H Al Hamad MD, B Sathian PhD), Rumlalil Hospital (H Al Hamad MD), Hamad Medical Corporation, Doha, Qatar; Department of Experimental Medicine, University of Campania Luigi Vanvitelli, Naples, Italy (L Albano PhD); Department of Pharmacy, University of Huddersfield, Huddersfield, UK (M A Aldeyva PhD), Faculty of Health Sciences (A A Alene MPH), School of Public Health (E K Chowdhury PhD), Curtin University, Perth, WA, Australia; Westermers Centre of Vaccines and Infectious Diseases, Teleton Kids Institute, Perth, WA, Australia (K A Alene MPH); Department of Bacteriology, Immunology, and Mycology, Suez Canal University, Ismailia, Egypt (Prof A A Alganam PhD); Faculty of Nursing, Philadelphia University, Amman, Jordan (F A N Alhallaq PhD, Prof A M Batha PhD); Psychological Sciences Association/Jordan, Amman, Jordan (F A N Alhallaq PhD); Institute of Health Research (K A Alhasan PhD, M Immurana PhD), Department of Health Policy Planning and Management (M A Ayaneore PhD), University of Health and Allied Sciences, Ho, Ghana; Erbil Technical Health College, Erbil Polytechnic University, Erbil, Iraq (B A Ali PhD); Department of Biological Sciences, National University of Medical Sciences, Rawalpindi, Pakistan (I Ali PhD); School of Medical Laboratory, Module of Microbiology and Parasitology, Hawaii University, Hawaii, USA (M A Ali PhD), Center for Biotechnology and Microbiology, University of Swat, Swat, KPK, Pakistan (I S Ali MD), Pars Advanced and Minimally Invasive Medical Manners Research Center (Y Almohamadi PHD), Health Management and Economics Research Center (V Alipour PhD, J Arabloo PhD), Department of Health
UK (S Gaihre PhD); Department of Surgical Technology, Lorestan University of Medical Sciences, Khorramabad, Iran (N Galehdar PhD); Department of Tuberculosis, Masun Health Research Center, Manušica Mozambique (A L Garcia-Basteiro PhD); Viral and Bacterial Infections Research Program, Barcelona Institute for Global Health, Barcelona, Spain (A L Garcia-Basteiro PhD); Department of Radiology, King Edward Memorial Hospital, Mumbai, India (T Garg MBBS); Department of Nursing, Debre Berhan University, Debre Birhan, Ethiopia (B N B Gemeda MSc); Pfizer Vaccines, Collegeville, PA, USA (B D Gessner MD); Agency of Preventive Medicine, Paris, France (B D Gessner MD); Department of Emergency and Critical Care Medicine (M Getachew MD), Department of Nursing (G F W Mijena MSc), Haramaya University, Harer, Ethiopia; School of Nursing, Arba Minch University, Arba Minch, Ethiopia (A Getie MSc); E-Learning Center, Faculty of Health (M Ghasemi Nour MD), Applied Biomedical Research Center (A Sahebkar PhD), Biotechnology Research Center (A Sahebkar PhD), Social Determinants of Health Research Center (M Sarkhosh PhD), Mashhad University of Medical Sciences, Mashhad, Iran; School of Public Health (A Ghashgheaei BS), Institute for Prevention of Non-communicable Diseases (R Kalhor PhD), Health Services Management Department (R Kalhor PhD), Department of Food Hygiene and Safety and Medical Microbiology Research Center (Prof R Mahmondi PhD), Qazvin University of Medical Sciences, Qazvin, Iran; Department of Environmental Health Engineering, North Khorasan University of Medical Sciences, Bojnurd, Iran (A Gholizadeh PhD); Institute for Global Health Sciences (R Ghosh PhD), Department of Bioengineering and Therapeutic Sciences (Prof M S Zastrozhin PhD), University of California San Francisco, San Francisco, CA, USA; Department of Radiology (S Ghoby MD), Division of Infectious Diseases (Prof I I Tleyeh MD), Mayo Clinic, Rochester, MN, USA; Department of Genetics, Sana Institute of Higher Education, Sari, Iran (P Goleij MSc); Department of Nursing, Arak University of Medical Sciences, Arak, Iran (M Golitaleb PhD, M Harorani MSc); Oncological Network, Prevention and Research Institute, Institute for Cancer Research, Prevention and Clinical Network, Florence, Italy (G Gorini MD); Center for Clinical and Epidemiological Research (A C Goulart PhD), Department of Internal Medicine (A C Goulart PhD), University of São Paulo, São Paulo, Brazil; Public Health Department, Salale University, Fitche, Ethiopia (G G Groomo MPH); College of Science, Jigjiga University, Jigjiga, Ethiopia (R A Gululed PhD); Toxicology Department, Shirram Institute for Industrial Research, Delhi, Delhi, India (S Gupta MSc); School of Medicine, Deakin University, Geelong, VIC, Australia (V Gupta PhD); Department of Clinical Medicine (Prof V K Gupta PhD), School of Engineering (N Rahbe PhD); Macquarie University, Sydney, NSW, Australia; Department of Midwifery, Dire Dawa University, Dire Dawa, Ethiopia (A Guta MSc); School of Health and Environmental Studies, Hamdan Bin Mohammed Smart University, Dubai, United Arab Emirates (Prof S Hamidi DrPH); Department of Biochemistry and Molecular Biology, Bangladesh Agricultural University, Mymensingh, Bangladesh (Prof M Hannan PhD); Department of Anatomy, Dongguk University, Gyeonggi, South Korea (Prof M Hannan PhD); Department of Zoology and Entomology, Al Azhar University, Cairo, Egypt (A I Hashaballah PhD); Department of Ophthalmology, IUMS, Karaj, Iran (H Hasani MD); Department of Plastic Surgery, The University of Texas MD Anderson Cancer Center, University of Texas, Houston, TX, USA (A M Hassan MD); Chapter of Addiction Medicine (Prof H Hassanian-Moghaddam MD), Save Sight Institute (H Kandel PhD), School of Public Health (D L Knibbs PhD), University of Sydney, Sydney, NSW, Australia: Independent Consultant, Tehran, Iran (H Hassanikhani PhD); Institute of Pharmaceutical Sciences, University of Veterinary and Animal Sciences, Lahore, Pakistan (K Hayat MS); Department of Pharmacy Administration and Clinical Pharmacy, Xian Jiaotong University, Xian, China (K Hayat MS); Public Health, Environmental Health, Epidemiology and Health Education Department (Z D Heyi MPH), Department of Midwifery (D G Testaye MSc), Madda Walabu University, Robe, Ethiopia; Department of Applied Microbiology, Taiz University, Taiz, Yemen (K Hezam PhD); Department of Microbiology, Nankai University, Tianjin, China (K Hezam PhD); Kasturba Medical College, Mangalore (R Holla MD, A Kamath MD), Department of Physiotherapy (Prof V K PhD); Forensic Medicine and Toxicology, Kasturba Medical College Mangalore (J Padubidri MD), Manipal Manipal Hospital, Manipal, India (J Padubidri MD); Research Department, Electronic Medical Records for the Developing World, York, UK (S Hong MD); Department of Pulmonology, Yokohama City University, Yokohama, Japan (N Horita PhD); National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, USA (N Horita PhD); Department of Dermatology (N Hostiuc PhD), Department of Dermatology (C N Matei PhD, M Tampa PhD), Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; College of Science and Engineering, Hamad Bin Khalifa University, Doha, Qatar (Prof M Housh PhD); Burn Research Center (S Hovedrælanshmidt MD), Shahid Motahari Hospital, Tehran, Iran; Department of Biomedical Sciences, University of Zilko, Zilko, Iraq (N R Hussein PhD); Department of Public Health, University of Naples Federico II, Naples, Italy (Prof I Iavicoli PhD); Department of Community Medicine, University College Hospital, Ibadan, Nigeria (O S Ilesanmi PhD); Department of Epidemiology, University of Kragujevac, Kragujevac, Serbia (Prof M D Ilic PhD); Department of Clinical Pharmacy, MAHSA University, Bandar Saujana Putra, Malaysia (Prof N Ismail PhD); Department of Health Services Research, University of Tsukuba, Tsukuba, Japan (M Iwagami PhD); Department of Non-communicable Disease Epidemiology (M Iwagami PhD), Medical Statistics Department (S Shivalli MD), London School of Hygiene & Tropical Medicine, London, UK; Department of Environmental Health Engineering (J Jaafari PhD), Gastrointestinal and Liver Diseases Research Center (F Joukar PhD), Caspian Digestive Disease Research Center (F Joukar PhD), Department of Medical-Gastroenterological Sciences (S Kakhkh MSc), Guilan University of Medical Sciences, Rasht, Iran; Division of Pulmonary Medicine, Lausanne University Hospital, Lausanne, Switzerland (E Jamshidi PharmD); Department of Preventive Medicine, Yonsei University, Seodaemun-gu, South Korea (Prof S Jang PhD); Health Informatic Lab (T Javaheri PhD), Department of Computer Science (R Rawassizadeh PhD), Boston University, Boston, MA, USA; Department of Medical Myology (J Javidnia PhD), Department of Immunology (Prof A Rafiei PhD), Molecular and Cell Biology Research Center (Prof A Rafiei PhD), Mazandaran University of Medical Sciences, Sari, Iran; Centre of Studies and Research, Ministry of Health, Muscat, Oman (S Javyaraj MD), Postgraduate Institute of Medicine (U Y Javyaraj MD), Department of Pharmacology (P Ransange PhD), University of Colombo, Colombo, Sri Lanka; Department of Surgery, National Hospital, Colombo, Colombo, Sri Lanka (U Y Javyaraj MD); Department of Biochemistry, Government Medical College, Mysuru, India (Prof S Jayaraman PhD); Institute of Molecular and Clinical Ophthalmology Basel, Basel, Switzerland (Prof B B Jonas PhD); Department of Ophthalmology, Heidelberg University, Mannheim, Germany (Prof J B Jonas MD); Department of Family Medicine and Public Health, University of Opole, Opole, Poland (J J Jozwiak PhD); School of Public Health, University College Cork, Cork, Ireland (Z Kahir PhD); Department of Medicine, Faculty of Medicine, University of Tlemcen, Tlemcen, Algeria (S O Kacimi MD); Social Determinants of Health Research Center (L R Kalankesh PhD), Department of Anatomy (J Majidpoor PhD), Department of Nutrition (S Talaatmehzadeh PhD), Gonabad University of Medical Sciences, Gonabad, Iran; Department of Community Medicine and Family Medicine, All India Institute of Medical Sciences, Hyderabad, India (B D Kamble MD); Department of Community Medicine, Banaras Hindu University, Varanasi, India (B D Kamble MD); Sydney Eye Hospital, South Eastern Sydney Local Health District, Sydney, NSW, Australia (H Kandel PhD); School of Health Professions and Human Services, Hofstra University, Hempstead, NY, USA (I M Karyae MD); Institute for Epidemiology and Social Medicine, University of Munster, Munster, Germany (A Karch MD); Centre for Tropical Diseases and Global Health, Catholic University of Bukavu, Bukavu, Democratic Republic of the Congo (P D Katoko PhD); Department of Medical-Surgical Nursing, King Edward Memorial Hospital, Cape Town, South Africa (P D Katoko PhD); Department of Healthcare Services Management, School of Health, Allzuor University of Medical Sciences, Karaj, Iran (L Keikavoosi-Arani PhD); Department of Public Health, Jordan University of Science and Technology, Irbid, Jordan (Prof Y S Khader PhD); Department of Epidemiology and
Articles

Sciences, Hamadan, Nahavand, Iran (A Sharifi PhD); Department of Medical Oncology, Kent Hospital, Warwick, RI, USA (P Sharma MD); Department of Microbiology, Kasar College, Mangalore, Manipal Academy of Higher Education, Manipal, Mangalore, India (S M Shenoy MD); Public Health Dentistry Department, Krishna Institute of Medical Sciences Deemed to be University, Karad, India (Prof K M Shivalakumar PhD); School of Health, Victoria University of Wellington, Wellington, New Zealand (Prof C R Simpson PhD); Institute of Medical Sciences Deemed to be University, Ho Chi Minh City, Vietnam (B Vo PhD); Department of Pulmonary and Critical Care Medicine, Medical College of Wisconsin, Milwaukee, WI, USA (H Singh MD); School of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA (Prof A Singh MD); Medicine Service, US Department of Veterans Affairs, Birmingham, AL, USA (Prof A Singh MD); Department of Chemistry, Maharishi Markandeshwar (Deemed to be University), Mullana, India (S S Siwal PhD); Department Number 16, Moscow Research and Development Center, Moscow, Russia (V Y Skryabin MD); Taub Institute for Research on Alzheimer’s Disease and Epidemiology, Pirogov Russian National Research Medical University, Moscow, Russia (A A Skryabina MD); Taub Institute for Research on Alzheimer’s Disease and the Aging Brain, Columbia University Medical Center, New York, NY, USA (S Song PhD); Department of Land Surveying and Geomatics, Hong Kong Polytechnic University, Hong Kong, China (Y Song PhD); Department of Microbiology, All India Institute of Medical Sciences, Bilaspur, India (P Sood PhD); Division of Community Medicine, International Medical University, Kuala Lumpur, Malaysia (C T Sreearameddy MD); Department of Medicine, Democracy University, Alexandria, Egypt (S Sharafeldin MD); Center for Biotechnology and Microbiology, University of Swat, Mingora, Swat, Pakistan (M Suleman PhD); Department of Life Sciences, Xi’an Jiaotong University, Xi’an, China (M Suleman PhD); Department of Biostatistics and Epidemiology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran (M Taheri Soodejani PhD); Department of Dermato-Venereology, Dr Victor Babes Clinical Hospital of Infectious Diseases and Tropical Diseases, Bucharest, Romania (M Tampa PhD); Department of Science, Technology and Natural Resources, Policy Research Institute, Kathmandu, Nepal (S Tandukar PhD); Department of Economics, Rice University, Houston, TX, USA (N Y Tat MS); Research and Innovation Department, Ervement Medical Innovation, Houston, TX, USA (N Y Tat MS); Department of Pathology, University of Texas, Galveston, TX, USA (Y Tat BS); Department of Public Health, Dire Dawa university, Dire Dawa, Ethiopia (Y M Tefera MPH); Pediatric Intensive Care Unit, King Saud University, Riyadh, Saudi Arabia (M Tensah MD); Faculty of Public Health, Universitas Sam Ratulangi, Manado, Indonesia (J H V Ticoula MPH); Department of Epidemiology and Biostatistics, Birjand University of Medical Sciences, Birjand, Iran (A A Valadan Tahbaz PhD, S Yahzadeh Jabbari PhD); Department of Biotechnology, Islamic Azad University, Tehran, Iran (S Valadan Tahbaz PhD, S Yahzadeh Jabbari PhD); Department of Biotechnology, International Medical University, Jinhong, China (X Xu PhD); Department of Clinical Microbiology, Imam Reza University of Medicine, Isfahan, Iran (S Yaghoubi PhD); Department of Pediatrics, Konyung Hee University, Seoul, South Korea (D Yon MD); Department of Neuropsychopharmacology, National Center of Neurology and Psychiatry, Kodaira, Japan (N Yonemoto PhD); Department of Public Health, Juntendo University, Tokyo, Japan (N Yonemoto PhD); Department of Radiology, Children’s Hospital of Philadelphia, Philadelphia, PA, USA (A Zandifar MD); Unit on Child & Adolescent Health, Medical Research Council South Africa, Cape Town, South Africa (Prof H J Zar PhD); Research and Development Department, Sina Medical Biochemistry Technologies, Shiraz, Iran (I Zare BSc); Addictology Department, Russian Medical Academy of Continuous Professional Education, Moscow, Russia (Prof M S Zastrozhin PhD); Department of International Health, Georgetown University, Washington, DC, USA (Prof W Zeng PhD); Department of Nutrition and Health Science, Ball State University, Muncie, IN, USA (M Zhang PhD); Department of Infection, University College London, London, UK (Prof A Zumla PhD).

Contributors
Please see appendix 1 for more detailed information about individual author contributions to the research, divided into the following categories: managing the overall research enterprise; writing the first draft of the manuscript; primary responsibility for applying analytical methods to produce estimates; primary responsibility for seeking, cataloging, extracting, or cleaning data; designing or coding figures and tables; providing data or critical feedback on data sources; developing methods or computational machinery; providing critical feedback on methods or results; drafting the manuscript or revising it critically for important intellectual content; and managing the estimation or publications process. Members of the core research team (HHK, AV, SBS, AN, CET, MCD, RGB, JRL, MHB, SBA, KB, FBB, JTZ, WMG, JH, DB, RVD, MN, MB, and CJLM) for this topic area had full access to the underlying data used to generate the estimates presented in the article. All other authors had access to and reviewed the estimates as part of the research evaluation process, which included additional formal stages of review. The corresponding author had final responsibility for the decision to submit for publication.

Declaration of interests
V Abedi reports grants or contracts from Genentech/ROCHE Biotech company and the National Institutes of Health (NIH) (2R56HL136812-04) ending in 2021, outside the submitted work. S Afzal reports leadership or fiduciary roles in board, society, committee, or advocacy groups, paid or unpaid, as a member of the Corona Expert Advisory Group, a member of the Medical Microbiology and Infectious Diseases Society of Pakistan, and as secretary of the task force for integrated management of childhood illnesses, all outside the submitted work. F Ata reports grants or contracts from the NIH and National Heart, Lung, and Blood Institute (K23 HL096938) and participation on a data safety monitoring board for effectiveness of low-dose theophylline for biomass-associated chronic obstructive pulmonary disease study, all outside the submitted work. D Bryazka reports grants or contracts from Bloomberg beyond the submitted work. B D Gesnner is an employee of Pfizer Vaccines and holds stock options in Pfizer. J Jozwik reports personal fees for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Teva, Aragen, Synexus, Boehringer Ingelheim, Zentiva, and Sanofi, all outside the submitted work. K Krishan reports non-financial support from the UGC Centre of Advanced Study, CAS II, Department of Anthropology, Panjab University, Chandigarh, India, all outside the submitted work. J A Loureiro reports support for the present manuscript from Scientific Employment Stimulus (CRIEINGT000049/2018). A F A Ments reports grants or contracts from MilkSafe: a novel pipeline to enrich formula milk using omics technologies, a research co-financed by the European Regional Development Fund of the European Union and Greek national funds through the operational programme competitiveness, entrepreneurship and innovation, under the call research, create, innovate (T2EDK-02222), as well as from ELIDEK (Hellenic Foundation
for Research and Innovation, MIMS-860); stock or stock options in a family winery; support from BGI Group as a scientific officer. L. Monasta and L. Ronzani report support for the present manuscript from the Italian Ministry of Health on project Ricerca Corrente 34/2017 and payments made to Institute for Maternal and Child Health IRCCS Burlo Garofolo. O. Odukoya reports support from the present manuscript from the Fogarty International Center of the National Institutes of Health (F43TW020704) for protected time. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. M Postma reports stock or stock options from Pharmacoeconomics Advice Groningen and Health-Ecore, outside the submitted work. M Raad reports consulting fees from Fondation Mérieux, support for attending meetings from Fondation Mérieux, and is the CEO of an antibiotic prescription assistance company SMARTBIOTIC, all outside the submitted work. K E Rudd reports grants or contracts from the NIH National Institute of General Medical Sciences (IK2GM141463), outside the submitted work. C R Simpson reports grants or contracts from New Zealand Ministry of Business, Innovation and Employment; Health Research Council of New Zealand, UK Medical Research Council, and UK Chief Scientist Office, as research grants paid to their institution, outside the submitted work. J A Singh reports consulting fees from Cretaia Horizon, Medisys, Fidia, PK Med, Two Labo, Adept Field Solutions. Clinical Care Options, Cleargreen Healthcare Partners, Potnrun Associates, Focus Forward, Navi­gant Consulting, Spherix, MediQ, Jupiter Life Science, UBIO, Trio Health, Medscape, WebMD, and Practice Point Communications, the National Institutes of Health, and the American College of Rheumatology; payment or honoraria for lectures, presentations, speakers’ bureaus, manuscript writing or educational events from Simply Speaking; support for attending meetings or travel from the steering committee of OMERACT; participation on a data safety monitoring board or advisory board with the US Food and Drug Administration Arthritis Advisory Committee; leadership or fiduciary role in board, society, committee or advocacy group, paid or unpaid, with OMERACT as a steering committee member, with the Veterans Affairs Rheumatology Field Advisory Committee as Chair (unpaid), and with the UAB Cochrane Musculoskeletal Group Satellite Center on Network Meta-analysis and editor and director (unpaid); stock or stock options in TT­F Global Tech, Vaxart Pharmaceuticals, Ayu Biopharma, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics, Seres Therapeutics, Tonix Pharmaceuticals and Charlotte’s Web Holdings, and previously owned stock options in Aamarin, Viking, and Moderna Pharmaceuticals; all outside the submitted work. E Upadhyay reports patents published for a system and method of reusable filters for anti-pollution mask and a system and method for electricity generation through crop stubble by using microbial fuel cells and filed for a system for disposed personal protection equipment (PPE) into biofuel through pyrolysis and method and a novel herbal pharmaceutical aid for formulation of gel and method thereof and a leadership or fiduciary role as part of the Joint Secretary of Indian Meteorological Society, Jaipur Chapter (India). A Zuma reports grants or contracts from Pan-African Network on Emerging and Re-Emerging Infections (https://www.pandora-id.net/) funded by the European and developing countries clinical trials partnership the EU horizon 2020 framework programme. Acknowledge support from EDCTP-Central Africa and East African Clinical Research Networks (CANTAM-3, EACCR-3) and unpaid membership of the Scientific Advisory Committee of the EC-EDCTP-3 global health programme, Brussels with effect from March, 2022, all outside the submitted work. All other authors declare no competing interests.

Data sharing
To download the data used in these analyses, please visit the Global Health Data Exchange GBD 2019 website.

Editorial note: The Lancet Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

References
1. Vos T, Lim SS, Abate A, 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: 1204–22.
2. Rudd KE, Johnson SC, Agusa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. Lancet 2020; 395: 200–11.
3. WHO and UNICEF. Ending preventable child deaths from pneumonia and diarrhoea by 2025: the integrated global action plan for pneumonia and diarrhoea (GAPPD). 2013. https://apps.who.int/iris/handle/10665/79200 (accessed Feb 13, 2022).
4. Stop Pneumonia. The Stop Pneumonia Initiative. https://stoppneumonia.org/stop-pneumonia-initiative/ (accessed Feb 13, 2022).
5. WHO. IMCI integrated management of childhood illness. 2005. https://apps.who.int/iris/handle/10665/42539 (accessed April 5, 2022).
6. Falagas ME, Mourtzoukou EG, Vardakas KZ. Sex differences in the incidence and severity of respiratory tract infections. Respir Med 2007; 101: 1845–63.
7. Murray CJL, Aravkin AY, Zheng P, et al. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020; 396: 1223–49.
8. Naghavi M, Makela S, Foreman K, O’Brien J, Pourmalek F, Lozano R. Algorithms for enhancing public health utility of national causes-of-death data. Popul Health Metr 2010; 8: 9.
9. Foreman K, Lozano R, Lopez AD, Murray CJL. Modeling causes of death: an integrated approach using CODEm. Popul Health Metr 2012; 10: 1.
10. Troeger CE, Khalil IA, Blacker BF, et al. Quantifying risks and interventions that have affected the burden of lower respiratory infections among children younger than 5 years: an analysis for the Global Burden of Disease Study 2017. Lancet Infect Dis 2020; 20: 60–79.
11. Flaxman AD, Vos T, Murray CJL. An integrative metaregression framework for descriptive epidemiology. 1st edn. Seattle, WA: University of Washington Press. 2015.
12. Wang H, Abbas K, Abbasi­far M, et al. Global age–sex–specific fertility, mortality, healthy life expectancy (HALE), and population estimates in 204 countries and territories, 1950–2019: a comprehensive demographic analysis for the Global Burden of Disease Study 2019. Lancet 2020; 396: 1609–201.
13. UNICEF. Global action plan on child wasting. https://www.unicef.org/media/96991/file/Global-Action-Plan-on-Child-Wasting.pdf (accessed Feb 13, 2022).
14. Fore HH, Dongu Q, Beasley DM, Ghalebeyasu TA. Child malnutrition and COVID-19: the time to act is now. Lancet 2020; 396: 517–18.
15. Heady D, Heidkamp R, Osendarp S, et al. Impacts of COVID-19 on childhood malnutrition and nutrition-related mortality. Lancet 2020; 396: 519–21.
16. Hay SI. Maintaining progress for the most beautiful chart in the world. Int Health 2019; 11: 344–48.
17. Howie SRC, Murdoch DR. Global childhood pneumonia: the good news, the bad news, and the way ahead. Lancet Glob Health 2019; 7: e6–5.
18. Wu X, Nethery RC, Sabath MB, Braun D, Dominici F. Air pollution and COVID-19 mortality in the United States: strengths and limitations of an ecological regression analysis. Sci Adv 2020; 6: eabd4049.
19. Cole MA, Ozgen C, Strobil E. Air pollution exposure and COVID-19 in Dutch municipalities. Environ Resour Econ (Dordr) 2020; published online Aug 4. https://doi.org/10.1007%2Fs10640-020-00491-4.
20. Frontera A, Gianfanelli I, Vlachos K, Landoni G, Crenonna G. Severe air pollution links to higher mortality in COVID-19 patients: the “double-hit” hypothesis. J Infect 2020; 81: 255–39.
21. Reid CE, Maestas MM. Wildfire smoke exposure under climate change: impact on respiratory health of affected communities. Curr Opin Palm Med 2019; 25: 179–87.
22. Omidvarbournah H, Bauwain M, Al-Marmun A. Ambient air quality and exposure assessment study of the Gulf Cooperation Council countries: a critical review. Sci Total Environ 2018; 636: 437–48.
23. Mee SA, Almutairi FJ, Abukhalaf AA, Alesza OM, Al-Khaliwi T, Mee AS. Sandstorm and its effect on particulate matter PM 2.5, carbon monoxide, nitrogen dioxide, ozone pollutants and SARS-CoV-2 cases and deaths. Sci Total Environ 2021; 795: 148646.
Wang Q, Gu J, Wang X. The impact of Sahara dust on air quality and public health in European countries. Atmos Environ 2020; 241: 117771.

Yin S, Wang X, Zhang X, Guo M, Miura M, Xiao Y. Influence of biomass burning on local air pollution in mainland southeast Asia from 2001 to 2016. Environ Pollut 2019; 254: 112949.

Kutlar Joss M, Effrens M, Gintowt E, Kappeler R, Künzli N. Time to harmonize national ambient air quality standards. Int J Public Health 2017; 62: 453–62.

Corfe-Morlot J, Parks P, Ogunleye J, Ayeni F. Achieving clean energy access in sub-Saharan Africa. January, 2019. https://www.oecd.org/energy/cclimate-futures-case-study-achieving-clean-energy-access-in-sub-saharan-africa.pdf (accessed April 10, 2022).

Ministry of Environment, Forest and Climate Change, Government of India. National clean air programme. https://moef.gov.in/en/wed-2019-2/national-clean-air-programme-ncap/ (accessed April 13, 2022).

Kalli R, Jena PR, Managi S. Subsidized LPG scheme and the shift to cleaner household energy use: evidence from a tribal community of eastern India. Sustainability (Basel) 2022; 14: 2450.

Reade MC, Yende S, D’Angelo G, et al. Differences in immune response may explain lower survival among older men with pneumonia. Crit Care Med 2009; 37: 1655–62.

Klein SL, Flanagan KL. Sex differences in immune responses. Nat Rev Immunol 2016; 16: 626–38.

Jiang C, Chen Q, Xie M. Smoking increases the risk of infectious diseases: a narrative review. Tob Induc Dis 2020; 18: 60.

Reitsma MB, Kendrick PJ, Ababneh E, et al. Spatial, temporal, and demographic patterns in prevalence of smoking tobacco use and attributable disease burden in 204 countries and territories, 1990–2019: a systematic analysis from the Global Burden of Disease Study 2019. Lancet Public Health 2021; 397: 2337–60.

WHO. WHO report on the global tobacco epidemic 2019: offer help to quit tobacco use. 2019. https://www.who.int/teams/health-promotion/tobacco-control/who-report-on-the-global-tobacco-epidemic-2019 (accessed Feb 13, 2022).

Mehta AJ, Guidot DM, Weber KT. Alcohol abuse, the alveolar macrophage and pneumonia. Am J Med Sci 2012; 343: 244–47.

Martinez P, Reislien J, Naドo N, Clausen T. Alcohol abstinence and drinking among African women: data from the World Health Surveys. BMC Public Health 2011; 11: 160.

Slade T, Chapman C, Swift W, Keyes K, Tonks Z, Teesson M. Birth and cohabitation trends in the global epidemiology of alcohol use and alcohol-related harms in men and women: systematic review and meta-regression. BMJ Open 2016; 6: e011827.

Alati R, Betts KS, Williams GM, Najman JM, Hall GD. Generational increase in young women’s drinking: a prospective analysis of mother-daughter dyads. JAMA Psychiatry 2014; 71: 952–57.

Monjele NK, Dumbili EW, Olotu IS, Parry CDH. Alcohol consumption, harms and policy developments in sub-Saharan Africa: the case for stronger national and regional responses. Drug Alcohol Rev 2021; 40: 402–19.

United Nations. #Enviro3000: 17 goals to transform the world for persons with disabilities. https://www.un.org/development/desa/disabilities/enviro3000.html (accessed April 13, 2022).

Kim YK, LaFon D, Nahm MH. Indirect effects of pneumococcal conjugate vaccines in national immunization programs for children on adult pneumococcal disease. Infect Chemother 2016; 48: 257–66.

Galloles NC, Liu PY, Updike BL, et al. Measuring routine childhood vaccination coverage in 204 countries and territories, 1980–2019: a systematic analysis for the Global Burden of Disease Study 2020, Release 1. Lancet 2021; 398: 503–21.

WHO and UNICEF. Progress and challenges with sustaining and advancing immunization coverage during the COVID-19 pandemic. 2020. https://cdn.who.int/media/docs/default-source/immunization/wuenc--progress-and-challenges-15-july-2021.pdf?sfvrsn=5e9b9141_5&download=true (accessed Feb 20, 2022).

Causey K, Fullman N, Sorensen RJ, et al. Estimating global and regional disruptions to routine childhood vaccine coverage during the COVID-19 pandemic in 2020: a modelling study. Lancet 2021; 398: 522–34.

Lewnard JA, Bruxvoort KJ, Fischer H, et al. Effectiveness of 13-valent pneumococcal conjugate vaccine against medically-attended lower respiratory tract infection and pneumonia among older adults. Clin Infect Dis 2021; published online Dec 30. https://doi.org/10.1093/cid/ciab051.

Gessner BD, Jiang Q, Van Weekhoven CH, et al. A public health evaluation of 13-valent pneumococcal conjugate vaccine impact on adult disease outcomes from a randomized clinical trial in the Netherlands. Vaccine 2019; 37: 5777–87.

Kolditz M, Schmitt J, Plets MW, Tesh F. Impact of the 13-valent pneumococcal conjugate vaccine on the incidence of all-cause pneumonia in adults aged ≥60 years: a population-based, retrospective cohort study. Clin Infect Dis 2019; 68: 2117–19.

Lam F, Stegmueller A, Chou VB, Graham HR. Oxygen systems strengthening as an intervention to prevent childhood deaths due to pneumonia in low-resource settings: systematic review, meta-analysis and cost-effectiveness. BMJ Glob Health 2021; 6: e007468.

Troeger C, Blacker B, Khalil IA, et al. Estimates of the global, regional, and national morbidity, mortality, and aetologies of lower respiratory infections in 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Infect Dis 2018; 18: 1191–210.

Jackson S, Mathews KH, Pulanic D, et al. Risk factors for severe acute lower respiratory infections in children: a systematic review and meta-analysis. Curr Med J 2013; 54: 110–21.

Connor Gorber S, Schofield Hurwitz S, Hardt J, Levesque G, Tremblay M. The accuracy of self-reported smoking: a systematic review of the relationship between self-reported and cotinine-assessed smoking status. Nicotine Tob Res 2009; 11: 12–24.

Williams J, Rakocav I, Loyola E, et al. A comparison of self-reported to cotinine-detected smoking status among adults in Georgia. Eur J Public Health 2020; 30: 1007–12.

Jankowski M, Rees V, Zagliczynski WS, Kaleta D, Gujski M, Pinks J. Self-reported secondhand smoke exposure following the adoption of a national smoke-free policy in Poland: analysis of serial, cross-sectional, representative surveys, 2009–2019. BMJ Open 2020; 10: e039918.

Olsen SJ, Azizz Baumgartner E, Budd AP, et al. Decreased influenza activity during the COVID-19 pandemic—United States, Australia, Chile, and South Africa, 2020. MMWR Morb Mortal Wkly Rep 2020; 69: 1305–09.

Stamm P, Sageschen I, Weise K, et al. Influenza and RSV incidence during COVID-19 pandemic—an observational study from in-hospital point-of-care testing. Med Microbiol Immunol (Berl) 2021; 210: 277–82.

Jones N. Why easing COVID restrictions could prompt a fierce flu rebound. Nature 2021; 598: 395.

Li Y, Wang X, Cong B, Deng S, Feikin DR, Nair H. Understanding the potential drivers for respiratory syncytial virus rebound during the COVID-19 pandemic. J Infect Dis 2022; 225: 957–64.