Assessing the mortality, morbidity, and hospitalisations due to influenza lower respiratory infections from 1990 to 2017: an analysis from the Global Burden of Disease Study 2017

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Abstract

Background. While the burden of influenza is often considered in the context of historical pandemics and the threat of a future pandemic, every year a substantial burden occurs due to lower respiratory infections (LRIs), other respiratory conditions (like chronic obstructive pulmonary disease), and cardiovascular conditions that are attributable to seasonal influenza. The Global Burden of Disease Study 2017 (GBD 2017) is a systematic, scientific effort to quantify the health-loss associated with a comprehensive set of diseases and disabilities. This paper focuses on LRIs which can be attributed to influenza.

Methods. We modelled the LRI incidence, hospitalisations, and mortality attributable to influenza for every country and select subnational locations by age and year from 1990-2017 as part of GBD 2017. We used a counterfactual approach that first estimated the LRI incidence, hospitalisations, and mortality and then attributed a fraction of those outcomes to influenza.

Findings. Influenza LRI was responsible for an estimated 144,505 deaths among all ages in 2017 (95% Uncertainty Interval [UI] 98,922-200,205). The influenza LRI mortality rate was highest among adults over 70 (16.4 deaths per 100,000, 95% UI 11.6-21.9) and the highest rate among all ages was in Eastern Europe (5·0 per 100,000, 95% UI 3·6-6.5). We estimated that influenza LRI accounted for 9,458,902 LRI hospitalisations (95% UI 3,708,873-22,934,779) and 81,535,737 hospital-days (95% UI 24,330,208-259,851,048). We estimated that 11.5% of LRI episodes were attributable to influenza (95% UI 10.0-12.9%), accounting for 54,480,725 LRI episodes (95% UI 38,465,002-73,864,037), and 8,172,109 severe LRI episodes (5,000,450-13,295,527).

Conclusion. This comprehensive assessment of the burden of influenza LRI highlights the substantial annual impact on global health. While preparedness planning will be important for potential pandemics, it is important to not overlook the ongoing health-loss due to seasonal influenza LRI, including vaccine use. Efforts to improve influenza prevention measures are needed.

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Research in context

Evidence before the study. The burden of influenza has frequently been described in geographic[1] or age-specific[2] subpopulations with a number of studies reporting on pandemic H1N1[3] or syndromic definitions of influenza, such as among influenza-like illness.[4] There have been several studies that sought to describe mortality and morbidity associated with influenza, including a recent publication led by the United States Centers for Disease Control and the World Health Organization that estimated 298,243-645,832 seasonal influenza-associated respiratory deaths globally in 2015.[5] Previous iterations of the Global Burden of Disease study (GBD) reported influenza-attributable lower respiratory infection (LRI) mortality focusing on the global level and most recently estimated 58,193 deaths (95% Uncertainty Interval 43,953-74,175) in 2016.[6,7] An analysis for a comprehensive description of influenza LRIs that covers a spectrum of disease for every age, geography, and over time has not been previously undertaken.

Added value of this study. This study sought to build on previous GBD results to produce estimates of the influenza-attributable LRI burden spanning incidence, hospitalisations, and deaths for every country globally, for both sexes, for all ages, and between 1990-2017. To the best of our knowledge, no other study has produced estimates at such specific demographic categories. We leverage the statistical methodology developed for the GBD to produce internally consistent estimates of LRI morbidity and mortality, and applied a counterfactual strategy to determine the fraction of LRI burden that is directly caused by influenza. The strength of this methodology is that the results are interpretable as a preventable burden if influenza transmission were reduced or eliminated. Such findings provide detailed evidence about where influenza LRI burden is greatest by age and geography and about the potential health impact of efforts to reduce influenza transmission.

Implications. Our estimates of influenza LRI suggest that the burden is not uniform across space or by age and that locations or age groups with the highest underlying rate of LRI have the highest influenza LRI burden. Interventions that affect influenza transmission, such as vaccination, should be combined with interventions that reduce LRI risk, such as improving air quality, to reduce the overall burden of influenza LRI.

Introduction

One hundred years ago, in 1918, an influenza pandemic killed an estimated 20-50 million people,[8–10] more than the number that died in World War 1. Today, seasonal influenza remains a substantial contributor to the growing number of lower respiratory infection (LRI) cases across the globe. [6] There is ongoing interest and research in understanding the pandemic potential of influenza.[11–13] Such efforts have focused on understanding risk factors predictive of pandemic potential, modelling disease transmission to inform preparedness,[12] and identifying strategies to interrupt or mitigate pandemics.[14] Still, the sum of seasonal influenza deaths in the last 100 years likely exceeds deaths due to influenza pandemics, and seasonal influenza is responsible for substantial mortality, disability, and economic disruption. Appropriate steps to decrease this burden requires timely and reliable estimates of the full spectrum of disease.

The construction of an influenza disease burden pyramid would include metrics describing the spectrum of disease from incidence of moderate and severe LRIs, hospitalisations, and deaths (**Figure 1**). In contrast, a transmission pyramid may also include asymptomatic infections, which, by definition, do not have a disease burden but may be crucial to understand influenza transmission dynamics. This conceptualisation may allow public health officials, health care providers, and policy-makers to use available data to focus on any point of the pyramid and develop a comprehensive sense of influenza burden. Yet determining the burden of influenza LRI is difficult in many settings for a number of reasons including diagnosis of LRI, detection of influenza, and data availability. Further, there is a relative dearth of information available on the burden of influenza as an aetiology of LRI,[15] and a full perspective of the health-loss associated with influenza LRI at the population level is important for understanding burden and developing surveillance and intervention programs.

The Global Burden of Disease study 2017 (GBD) is a systematic, scientific effort to produce comprehensive and comparable estimates of the burden of disease across causes of death and disability. Here, we seek to quantify the influenza LRI burden and overcome some of these challenges using a counterfactual approach to estimating LRIs caused by influenza and build on previous descriptions of LRI in the GBD.[16,6] LRIs are the leading cause of infectious disease mortality, responsible for more deaths globally than tuberculosis and HIV combined. They were responsible for more than 2,500,000 deaths, and were the 5th leading incident infectious disease (336,461,645 episodes [95% Uncertainty Interval 313,084,637-361,621,709]) in 2016.[6] Within the GBD framework, influenza is considered a causal aetiology only for LRIs and it is estimated as a subset of the overall LRI burden. In this manuscript, we describe the global influenza LRI incidence, influenza LRI hospitalisation rates, and number of deaths due to influenza LRI across time, geography, and by age group.

Methods

Influenza in the GBD is considered as one of the causative aetiologies of LRI. A comprehensive description of LRI modelling has been described elsewhere, and so these methods focus on specific methodology for influenza attribution in GBD 2017.[6] This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement[17] (appendix table 1).

LRIs were defined as clinician-diagnosed pneumonia or bronchiolitis.[6] There is evidence of a causal association between influenza and LRIs among children under 5 when it is detected by RT-PCR from respiratory samples.[18] Based on these data[18] we estimated a population attributable fraction (PAF) of LRI episodes, hospitalisations, and deaths that were caused by influenza. This approach is a counterfactual analysis to determine the contribution of influenza to LRI. In this analysis, the counterfactual that is being estimated is the burden of LRI that would exist in the absence of influenza, in other words, the burden of LRI causally attributable to influenza. The attribution was based on the exposure and the risk of the outcome.

We updated a systematic review of scientific literature for the proportion of LRI that tested positive for influenza to include all data from GBD 2016 and from studies published between January 1, 1990 and May 26, 2017. The search string is provided in the **Appendix** (**Appendix page 2**). Inclusion criteria were studies that had a sample size of at least 100 people to avoid potential biases associated with having small denominators (consistent with other aetiologies in GBD 2017), studies that were at least one year in duration to limit seasonal detection bias, and studies that used a case definition of LRI, pneumonia, or bronchiolitis. During our new literature review we identified 595 studies, of which 75 met our inclusion criteria and were extracted which were added to the 153 existing data sources that were used in GBD 2016 and extracted using the same inclusion and exclusion criteria. We excluded studies that described 2009 pandemic H1N1 influenza solely and studies that used influenza-like illness as the outcome definition. We did not include surveillance or administrative data because they do not typically report the proportion of LRI positive for influenza and because they are prone to reporting and testing biases.

Specifically, we sought to model the frequency of detection of influenza in LRI episodes based on a reverse transcription polymerase chain reaction (RT-PCR) reference case definition. The frequency of detection is a modeled value with variation in age, sex, year, and geography from our model and based on the distributions of the input data. In this model, we estimated the relative frequency of detection in hospitalised compared to non-hospitalised populations and assumed that this was a proxy for fatal LRI episodes. In contrast to a categorical approach, which would stop at this point, the counterfactual approach required quantifying the relative risk of LRI given the evidence of influenza in the nasal or oropharynx for which we used odds ratios from a systematic review and meta-analysis among children under 5.[18] In the absence of available and reliable results in older children and adults, we assumed that this association was constant across age groups.

We estimated three related PAFs for non-mutually exclusive influenza LRI categories: a non-fatal PAF, a hospitalisation PAF, and a fatal PAF. The non-fatal attribution is the simplest and was defined as

$$PAF = \boldsymbol{Frequency}\ (\boldsymbol{proportion}) * \left(\mathbf{1} - \frac{\mathbf{1}}{\boldsymbol{OR}}\right)$$

Where $Frequency$ is the modeled proportion of LRI episodes that test positive for influenza by PCR and varies by age, sex, year, and geography and *OR* is the odds ratio of an LRI episode given the presence of influenza in a respiratory tract sample (5.10, 95% Confidence Interval 3.19 to 8.14). [18] To account for the previously described frequency of influenza detection in hospitalised compared to non-hospitalised LRI episodes, we applied a constant scalar to determine the PAF for LRI hospitalisations which was determined by comparing the mean frequency of influenza detection in hospitalised compared to non-hospitalised sample populations in the proportion data from our literature review *(Hospital scalar).*

$$\text{PAF Hospitalisations} = \boldsymbol{Frequency\ (proportion)} * \left(\boldsymbol{1 - \frac{1}{OR}}\right) * \boldsymbol{Hospital\ scalar}$$

Finally, to account for the relative difference in the risk of mortality between bacterial and viral causes of LRIs, we modelled the ratio in case fatality of viral-to-bacterial ICD-coded hospital admissions (**Appendix page 22**). Hospital data from high and low-income countries were used in this analysis and we estimated an age-specific curve for this relationship (**Appendix Table 3**). This scalar was applied to determine the attribution of influenza for fatal LRI outcomes (*Fatality scalar*).

$$\text{PAF Fatal} = \boldsymbol{Frequency\ (proportion)} * \left(\boldsymbol{1 - \frac{1}{OR}}\right) * \boldsymbol{Hospital\ Scalar} * \boldsymbol{Fatality\ Scalar}$$

The final number of LRI episodes, hospitalisations, and deaths attributable to influenza was the product of the relevant PAF and the overall number of episodes, hospitalisations, and deaths for each country, year, age, and sex. A description of the modeling strategy for LRI mortality, episodes, and hospitalisations follows and were modeled independently of influenza attributable fractions.

The mortality due to LRIs was modelled using a Bayesian predictive ensemble modelling tool developed for the GBD study called the Cause of Death Ensemble Model (CODEm) which is described in detail elsewhere.[7,19] In brief, CODEm uses a covariate selection algorithm to produce a wide array of sub-models which are evaluated based on their out-of-sample predictive validity. The best performing models then contribute relatively more to a final ensemble model of LRI mortality. The input data for this model are vital registration data, verbal autopsy studies, and surveillance system records (**GHDx**). The predictive validity of this model was evaluated using out-of-sample statistics and we identified the best performing model as the one with the best out-of-sample values.

Commented [CT1]: Current link, will need to be updated following November 5 public release of GBD 2017. http://ghdx.healthdata.org/gbd-2016/data-input-sources?components=4&causes=322

The incidence of all LRI episodes was modelled in a Bayesian meta-regression tool developed for the GBD study called DisMod-MR 2·1 (DisMod).[20] DisMod is designed to incorporate all available epidemiological data, standardise them so that they are comparable, and develop age, sex, year, and geography specific estimates of disease burden. Data for this model primarily come from population-representative surveys, inpatient and outpatient healthcare utilisation records, and scientific literature. LRIs in GBD are defined as either moderate or severe and the proportion of severe LRI episodes was determined by a meta-analysis of the incidence of severe, defined as either requiring inpatient admission, requiring oxygen therapy, or meeting the Integrated Management of Childhood Infections definition of severe pneumonia, compared to non-severe LRI from studies that reported the incidence of both.[6] Severe influenza LRI and hsopitalised influenza LRI were not modeled using the same data and so are not independent in this analysis.

The incidence of LRI hospitalisations was also modelled using DisMod. For this model, only inpatient utilisation data were used which were primarily from high-income countries such as the United States and in Western Europe, but data from Brazil, India, Indonesia, Kenya, Mexico, Nepal, the Philippines, Qatar, and Vietnam were also used (**Appendix Table 3, Appendix page 31**). Covariates such as the total inpatient visits per person and the healthcare access and quality index[21] were used to help account for variation in healthcare availability and access. The duration in days of hospitalisation for viral LRI episodes was determined by a meta-analysis of studies that reported this duration.[6]

All modelled estimates for the GBD study, including influenza attributable fractions, influenza LRI incidence, hospitalisations, and deaths, were estimated for every country and some subnational locations, by sex, for each age group, from 1990 to 2017. The results presented below are the mean values from a distribution of one thousand estimated observations (draws) for each modelled value or input parameter. Uncertainty intervals (UI) are reported as the 2.5^{th} and 97.5^{th} percentiles of the posterior distributions.

Role of the Funding Source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

We estimated the quantifiable burden of disease due to influenza LRI including deaths, hospitalisations, and moderate and severe episodes (**Figure 1**). We estimated that 5·6% of LRI deaths (95% Uncertainty interval [UI] 4·3-7·1%) were attributable to influenza in 2017, accounting for 144,505 (95% UI 98,922-202,205) deaths among all ages (**Table 1**) This corresponded to 0.26% of all deaths in 2017 (95% UI 0.2-0.32%). The attributable fraction was greater among adults over 70 years old (6·3%, 95% UI 4.8-7.8%) compared to children under 5 (2·9%, 95% UI 2·0-4·0%) (**Figure 2**). The fraction of LRI deaths that were attributable to influenza ranged from 23.7% in Ukraine (95% UI 19.1-27.6%) to 1.9% in Mozambique (95% UI 1.6-2.2%; **Appendix Figure 6C, Appendix page 35).** Most influenza LRI deaths occurred among the elderly (70,912 deaths among adults over 70, 95% UI 50,221-94,825) (**Figure 2**). Among all ages, the highest estimated influenza LRI mortality rate occurred in the Caribbean (5.5 per 100,000, 95% UI 3.6-7.7) and Eastern Europe (5·2 per 100,000, 95% UI 3.5-7.2) regions while the highest mortality rate overall occurred in Taiwan (12·1 per 100,000, 95% UI 7.8-17.6) (**Table 1, Figure 3**). The estimated influenza LRI mortality rate was lowest in the Australasia region (0·9 per 100,000, 95% UI 0.5-1·27) and the country with the lowest influenza LRI mortality rate was Qatar (0·3 per 100,000, 95% UI 0·1-0·4) (**Table 1, Figure 3**). Nearly a third of all influenza LRI deaths occurred in India (25,517 deaths, 95% UI 16,211-37,037), China (10,772, 95% UI 7,245-15,000), and Russia (7,979, 95% UI 5,422-11,083) (**Table 1**). Between 1990 and 2017, the influenza LRI mortality rate decreased by 29.5% among all ages (from 2·68 to 1·89 per 100,000). The rate of decline in this period was fastest among children under 5 (67.8%) and slowest among adults over 70 years (10.2%).

Influenza was more frequently associated with non-fatal and non-severe LRI episodes. In fact, we estimated that influenza was present in hospitalised LRI episodes 23% less frequently than in non-hospitalised LRI episodes (95% UI 9-33%). This is also reflected in the proportionally greater attribution of influenza to non-fatal LRI (**Figure 2**). Among all ages, an estimated 8·5% of LRI hospitalisations were attributable to influenza (95% UI 5.4-13.5%) (**Figure 2**). Influenza was responsible for 9,458,902LRI hospitalisations (95% UI 3,708,873-22,934,779), a rate of 123.8 per 100,000 (95% UI 48.5-300.2) (**Table 1, Figure 2**) in 2017 and corresponding with an estimated 81,535,737 hospital-days (95% UI 24,330,208-259,851,048) due to influenza LRI. The greatest number of influenza LRI episodes and hospitalisations occurred among childhood age groups under 10 years old (**Figure 2**). We estimated that there were 2,223,923 LRI hospitalisations due to influenza (95% UI 737,701-5,979,075) among children younger than 5 years in 2017. However, the incidence of non-hospitalised and hospitalised influenza LRI followed a U-shaped curve, increasing in children and elderly adults (**Figure 2**). The incidence of hospitalisation due to influenza LRI was greatest in Eastern Europe (488.7 hospitalisations per 100,000, 95% UI 185.9-1204.6) and Central Asia (303.1, 95% UI 120.5-721.6) (**Table 1**, **Figure 4).** The countries with the highest estimated influenza LRI hospitalisation rates were Lithuania (560.7 per 100,000, 95% UI 227.2-

1351.7) and Russia (494.4 per 100,000, 95% UI 183.6-1241.6) while the lowest were in Nepal (9.4 per 100,000, 95% UI 3.2-25.7) and Bangladesh (11.9 per 100,000, 95% UI 3.7-33.8) (**Figure 3**). Globally, 17.4% (95% UI 9.6-31.0) of influenza LRI cases were hospitalised among all ages in 2017 (**Appendix Figure 6B, Appendix page 34**); the proportion hospitalised was highest in adults over 70 (45.8%, 95% UI 27.5-72.1) (**Appendix Figure 8, Appendix page 36**). The Maldives (1·3%, 95% UI 0·6-2·6) and Indonesia (1·2%, 95% UI 0·6-2.3) had the lowest estimated proportions of influenza LRI episodes that were hospitalised while Brunei (59.1%, 95% UI 29.6-100.0) and Singapore (59.0%, 95% UI 31.8-100.0) had the highest proportions (**Appendix Figure 7, Appendix page 35**). Although the number of influenza LRI hospitalisations increased between 1990 and 2017 (14.0% increase, from 8,300,111 to 9,458,902), the hospitalisation rate declined over this time (19.6% decrease, from 153.9 to 123.8 per 100,000).

Among all ages, we estimated that 11.5% of LRI episodes were attributable to influenza (95% UI 10.0-12.9%) (**Figure 2**). This attributable fraction was highest among middle age adult age groups and was responsible for 9·2% (95% UI 8·0-10·2%) of LRI episodes among children under 5 and 10·8% (95% UI 9·3-12.0%) of LRI episodes among adults over 70 (**Figure 2**). We estimated that influenza was responsible for 54,480,725 LRI episodes among all ages in 2017 (95% UI 38,465,002-73,864,037; **Table 1**), including 8,172,109 severe LRI episodes (5,000,450-13,295,527). Influenza episodes were most common in Eastern Europe (2,399.3 episodes per 100,000, 95% UI 1,717.2-3,205.6) and Southeast Asia (1,591.2 per 100,000, 95% UI 1,118.1-2160.2) (**Table 1, Figure 5**). The highest overall incidence occurred in Vietnam (3710.5 per 100,000, 95% UI 2,537.3-5,141.6) and in Lithuania (2,489.6 per 100,000, 95% UI 1,728.2-3,469.3) while the lowest incidence occurred in Italy (63.7 per 100,000, 95% UI 44.5-85.1) and in Israel (83.2 per 100,000, 95% UI 57.3-117.2). The incidence of influenza LRI decreased between 1990 and 2017 (9.7% decrease, from 789.9 to 713.1 per 100,000), but increased in young adults 15-49 years (12.1% increase, from 566.1 to 634.6 per 100,000).

Discussion

Summary. This manuscript provides the most thorough and comprehensive analysis of the burden of lower respiratory infections attributable to influenza to date, covering incidence, severe incidence, hospitalisations, and mortality for each age group, annually from 1990 to 2017, and geography. We estimated that influenza LRI caused 144,505 deaths (95% UI 98,922-200,205), 54,480,725 LRI episodes (95% UI 38,465,002-73,864,037), 8,172,109 severe LRI episodes (5,000,450-13,295,527), and 9,458,902 LRI hospitalisations (95% UI 3,708,873-22,934,779).

Influenza pyramid. A full picture of lower and upper respiratory tract infections (including the non-respiratory infections), either symptomatic or inapparent, hospitalisations, and deaths is necessary to quantify the entire spectrum of influenza illness (**Figure 1**). This study has captured many, but not all of those components. Inapparent, or asymptomatic influenza virus infection is crucial for modelling the transmission of influenza spread. The Global Burden of Disease study does not typically estimate asymptomatic infections for causes of disease. There is evidence that influenza virus infection may be a risk factor for cardiovascular mortality,[22] renal failure, and other systemic outcomes, perhaps by exacerbation of underlying or comorbid diseases. These outcomes may begin with a respiratory infection and might be captured in time-series analyses of influenza burden or determined through influenza vaccine probe studies with severe illness endpoints to measure vaccine-preventable disease incidence.[23] Our study quantified the remaining aspects of influenza disease burden, focusing exclusively on LRIs attributable to influenza. We have shown that a moderate amount of LRIs are attributable to influenza. The attributable fraction is highest in adolescents and adults but because of the greater overall risk of LRIs in young children and elderly adults, our results suggest that the greatest number of LRI episodes, severe episodes, hospitalisations, and deaths occur in young children and elderly adults.

Appreciating age patterns in rates and counts is important in developing appropriate responses and interventions. Global estimates of seasonal influenza vaccine coverage were not available for this study and could provide additional evidence of disease burden. Although our study did not account for influenza vaccine coverage, our results help to show where the greatest impact of a seasonal or universal influenza vaccine could occur. Modelling studies have indicated that vaccinating targeted populations could reduce seasonal influenza outbreaks,[24] and may help to prevent episodes and hospitalisations in elderly adults.[25] Our results support the potential impact on the burden of influenza LRI by reducing severe and non-severe episodes and deaths and suggest that targeting specific age groups, particularly the elderly, and locations such as Eastern Europe and Southeast Asia could dramatically reduce the global burden of influenza LRI. The counterfactual strategy used in our model allow for a quantification of the avertable burden through vaccination or other interventions.

Diagnostic tools. To estimate the attributable fraction of LRI that is due to influenza, we made several important analytic decisions and assumptions. Based on our analysis of the available data that reflected the frequency of influenza isolation among respiratory samples from pneumonia or bronchiolitis episodes (definition of LRI in GBD 2017), we found that RT-PCR is significantly more sensitive in detecting acute influenza infection than ELISA-based methods. The mean frequency of influenza positive samples was about 25% greater when using RT-PCR than using non-RT-PCR diagnostics (**Appendix page 4**), a result that is consistent with the general body of knowledge regarding molecular diagnostic methods.[26] Another systematic review of influenza detection among acute LRI episodes in children found that PCR diagnostics detected influenza more than 2 times more frequently than in immunofluorescence tests.[27] One of the reasons for this finding could be due to the anatomical site where samples are collected, which may affect the frequency of influenza detection. Most studies use nasopharyngeal swabs due to the relative ease of collection and non-invasiveness,[28] and the data from our systematic review were nearly exclusively from nasopharyngeal or oropharyngeal swabs. Studies have shown varying levels of specificity and sensitivity in the relationship between detection in nasopharyngeal samples and LRIs.[28,29] The time period between infection, symptoms onset, geographic regions, and sample collection could also play critical roles in influenza virus detection with or without molecular diagnostics.

PAF data and assumptions. These results are based on approximately 650 data points from 100 sources in 40 countries (**Appendix Figure 2; Appendix Table 2, Appendix pages 5-26).** The predictive modelling tools used in the GBD study use space-time information and covariates to help make estimates for every geography, year, age. In areas with sparse data, the uncertainty around the estimates is greater. The modelled frequency of influenza attributable LRI episodes is a component of the counterfactual attribution strategy used in GBD 2017. The second component of the PAF model, the odds ratio, reflects how likely a sample that tests positive for influenza identifies the etiology of LRI. The source that we used to quantify this relationship is a systematic review among children under 5. Because of a lack of data on this relationship in older age groups, we assume that it is constant across ages, an assumption that may not hold because of a variety of immunological or biological differences between young children and adults. If adults are more likely than children under 5 to have an LRI episode given influenza detection, our estimates in adults may be an underestimate and inversely may be an over-estimate if adults are less likely to have an LRI episode given influenza detection than children under 5. Results from a study in South Africa found that the odds of severe acute respiratory illness given influenza was lower among 5-65 years than under-5 and over-65,[30] suggesting that, despite being a single study with a different case definition than used in this study, our results may be overestimates of influenza attribution in these age groups.

There is evidence of a potentially important role in influenza co-infection with *Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae* type B, and other bacterial pneumonias.[31–33] The interpretation of the counterfactual attribution used in the GBD, while estimated independently for each pathogen, allows for overlap in the attribution of LRI episodes or deaths due to multiple pathogens. However, our estimation does not explicitly account for influenza infection as a risk factor for subsequent bacterial infections, a potentially important burden.

Comparisons. The GBD 2017 estimates of LRI deaths attributable to influenza are about two times greater than the estimates from GBD 2016. This change is largely due to an important adjustment scalar in determining how frequently viral causes of LRI are associated with mortality compared to bacterial causes of LRI. Our analysis found that bacterial aetiologies are more likely to lead to death than viral aetiologies.[6] For previous GBD studies, this relationship was quantified using data from a small subset of countries. We reproduced this analysis for GBD 2017 using a much larger dataset of hospitalisation records that were coded specifically to viral or bacterial causes of LRI and where the outcome, discharge or death, was known. The ICD codes used in this step are unlikely to capture any interaction between influenza and bacterial aetiologies of LRI and the risk of death in viral-bacterial coinfections is probably higher than in viral infections alone.[34] This reanalysis substantially reduced the uncertainty around this adjustment while also decreasing the magnitude of the scalar used to adjust the fatal influenza attributable fraction. A detailed description of these changes can be found in the **Appendix (p 29-32, 37-39).**

The number of LRI deaths attributable to influenza remain much lower than a recently published report from Iuliano et al. 2018 that found an estimated 290,000-650,000 seasonal influenza-associated respiratory deaths.[5] Differences in the modelling strategy account for a large amount of the variation in the estimates and have been explored as part of a modeling workshop between these research groups. Where the approach by Iuliano et al. was designed to estimate any deaths that may be considered *associated* with influenza, the GBD 2017 approach estimates the proportion of LRI deaths that are *attributable* to (caused by) influenza in our counter-factual framework. The GBD 2017 estimation strategy starts with an overall number of LRI deaths and counterfactually attributes a fraction of these deaths to influenza. In contrast, Iuliano et al. use a time-series analysis to determine excess mortality among all respiratory-coded deaths (ICD 10 codes J00-J99) during the influenza season and uses these estimates to model annual influenza-associated respiratory deaths. While the strategy used by Iuliano allows for variation in burden by year and season, the approach used in GBD 2017 is robust to influenza occurrence, association with LRI episodes, and consistency between other causes of death, and estimates that were produced for every year, age, sex, and geography. The estimates produced by Iuliano and GBD 2017 follow fundamentally different premises. Our approach has the major advantage of quantifying the potentially avertable influenza burden and our results can be used to estimate the vaccine preventable burden and the burden preventable by other interventions.

A study by Lafond and colleagues[27] estimated the global pediatric influenza-associated hospitalisations. Using a similar approach to ours, starting with a systematic review of the proportion of hospitalised respiratory infections among children younger than 18 and finding the product of that proportion and the number of acute LRI episodes hospitalized in 2010, they estimated 870,000 (610,000-1,237,000) influenza-associated hospitalisations among children younger than 5.[27] This value is lower than ours (2,223,923, 95% UI 737,701-5,979,075 in 2017) but our estimates of the fraction of hospitalized LRI due to influenza are nearly identical (7.4% in Lafond et al,[27] 6.9% in our study) and suggests that the main difference is in the overall estimates of LRI hospitalisations among children younger than 5. Indeed, our estimate of 32,211,143 (95% UI 18,072,832-52,111,555) is much larger than the value used in the Lafond study (11,751,000).[27,35] This is an example of the impact of multiple estimated values in both studies and that the rates of hospitalisations depends on not only on the attributable fraction of LRI due to influenza but also on the overall availability and usage of healthcare.

Limitations. Our study has a number of limitations. The availability and quality of data are very important in any predictive regression model. In particular, there are a scarcity of data in several geographic regions such as South Asia and sub-Saharan Africa for several of our models in this analysis, particularly the models for LRI mortality and hospitalisation. In contrast, there is good data coverage for LRI incidence globally because of population representative surveys. The data that inform the attributable fraction of influenza are also sparse in some parts of the world, such as Central Europe and Central Asia. Strengthening the capacity for detecting influenza has been a priority among global health organisations largely to improve early detection systems but expanding routine surveillance may also help improve global burden estimates.[36] Our systematic review identified a number of sources from central-latitude locations which identified substantial proportion of influenza in LRI episodes.[37] This suggests that influenza may be an important cause of LRIs in tropical climates,[38] an area of some current debate that argues if environmental suitability is necessary for seasonal influenza burden.

As mentioned, due to a lack of available data we assume that the presence of influenza in a respiratory sample has the same risk of contributing to an LRI episode among children under 5 as for older children and adults. There are a number of reasons that this may not be a consistent assumption including immunology, biology, and circulating influenza strains. Changes in circulating influenza virus strains over time and space has been studied extensively in order to predict strains for seasonal vaccine development and for assessing the risk of a pandemic.[39] Our study attempted to combine all strains of influenza into a single burden estimate and it is possible that stratification by sub-type, including influenza A, B, and pandemic H1N1 (H1N1pdm09), might reveal additional trends in influenza burden. However, it is well known that influenza burden has the potential to change dramatically from year to year and from season to season.[40] We deliberately chose to include only studies that were conducted over the period of a full year in order to avoid biasing our estimates from studies conducted during the peak influenza season. We also chose to exclude studies that tested for H1N1pdm09 exclusively because we believed this would bias our estimates but did include studies that tested for H1N1pdm09 concurrently with seasonal influenza. These decisions contributed to relative stability over time in our estimates of the attributable fraction of influenza. While our model likely failed to capture significant year-to-year variation in influenza burden, the purpose of this modelling approach was to minimise the effect of such variation in determining the attributable burden of influenza LRI.

Call to action, reflection. While much of the public attention on influenza has centered around the global threat of a pandemic, rightly emphasizing its potential impact on an increasingly interconnected global community, our results show that ongoing seasonal influenza contributes to a substantial burden of lower respiratory tract infections. The best way to prevent influenza-specific LRI is through vaccination or through targeted prophylaxis and we have previously demonstrated that reducing exposure to air pollution and tobacco smoke could have major impacts on all LRI risk.[6] As the highest burden of influenza-LRI is seen in low and middle income countries, additional data on influenza epidemiology in LMICs are needed to guide decisions on development of vaccines and appropriate vaccination strategies to prevent severe influenza illnesses in LMICs.[41] Efforts to develop improved influenza vaccines that could avert a large annual burden of disease ranging from LRI episodes, hospitalisations, and mortality are needed.[42,43] A full understanding of the burden of seasonal influenza could contribute to a better understanding of the epidemiology of the virus and preparedness in case of another influenza pandemic.

Conflicts of Interest

We declare that we have no conflicts of interest.

Tables and Figures

Table 1. Influenza LRI episodes, hospitalisations, and deaths from influenza LRI among all ages in 2017 by GBD country, region, and super-region.

Location	Deaths (95% UI)	Deaths per 100,000 (95% UI)	Hospitalisations (95% UI)	Hospitalisations per 100,000 (95% UI)	Episodes (95% UI)	Incidence per 100,000 (95% UI)
Global	144,505 (98,922-200,205)	1.9 (1.3-2.6)	9,458,902 (3,708,873-22,934,779)	123.8 (48.5-300.2)	54,480,725 (38,465,002-73,864,037)	713.1 (503.4-966.7)
Southeast Asia, East Asia, and Oceania	26,846 (18,499-37,226)	1.2 (0.9-1.7)	2,330,052 (919,244-5,591,636)	107.9 (42.6-259.0)	13,255,832 (9,342,350-17,963,170)	614.0 (432.8-832.1)
East Asia	14,465 (9,848-20,453)	1.0 (0.7-1.4)	883,669 (336,420-2,168,000)	59.5 (22.6-145.9)	2,571,276 (1,786,685-3,510,115)	173.1 (120.3-236.3)
China	10,772 (7,245-15,500)	0.8 (0.5-1.1)	739,467 (279,032-1,825,566)	52.4 (19.8-129.2)	2,144,719 (1,481,039-2,940,786)	151.8 (104.9-208.2)
North Korea	602 (311-1,046)	2.3 (1.2-4.1)	50,461 (16,367-140,181)	196.2 (63.6-545.1)	156,175 (106,251-217,302)	607.3 (413.2-845.0)
Taiwan	2,858 (1,835-4,157)	12.1 (7.8-17.6)	79,906 (28,218-206,210)	338.8 (119.7-874.4)	230,314 (160,695-310,342)	976.6 (681.4-1,315.9)
Southeast Asia	11,890 (7,960-16,598)	1.8 (1.2-2.5)	204,588 (76,581-517,869)	31.0 (11.6-78.4)	10,509,349 (7,384,864-14,267,957)	1,591.2 (1,118.1-2,160.2)
Cambodia	221 (120-370)	1.4 (0.7-2.3)	2,377 (747-6,882)	14.7 (4.6-42.7)	132,014 (87,892-188,081)	818.8 (545.2-1,166.6)
Indonesia	2,994 (1,920-4,373)	1.2 (0.7-1.7)	40,440 (14,378-107,946)	15.7 (5.6-41.8)	3,316,987 (2,261,372-4,618,922)	1,285.0 (876.0-1,789.3)
Laos	292 (143-518)	4.2 (2.1-7.4)	2,642 (828-7,514)	37.9 (11.9-107.8)	152,649 (104,873-210,256)	2,190.0 (1,504.6-3,016.5)
Malaysia	795 (404-1,255)	2.6 (1.3-4.1)	6,192 (2,023-17,425)	20.2 (6.6-56.9)	342,172 (230,466-480,177)	1,116.8 (752.2-1,567.2)
Maldives	1 (1-2)	0.3 (0.2-0.5)	84 (26-244)	18.4 (5.7-53.2)	6,706 (4,627-9,257)	1,462.2 (1,008.8-2,018.4)
Mauritius	16 (10-24)	1.3 (0.8-1.9)	267 (91-714)	21.0 (7.2-56.1)	14,291 (9,874-19,691)	1,123.4 (776.2-1,547.9)
Myanmar	1,091 (600-1,826)	2.1 (1.1-3.5)	10,992 (3,615-30,390)	20.8 (6.8-57.6)	609,181 (418,457-844,597)	1,153.9 (792.6-1,599.8)

Location	Deaths (95% UI)	Deaths per 100,000 (95% UI)	Hospitalisations (95% UI)	Hospitalisations per 100,000 (95% UI)	Episodes (95% UI)	Incidence per 100,000 (95% UI)
Philippines	2,037 (1,246-3,121)	2.0 (1.2-3.0)	21,624 (7,560-57,858)	20.9 (7.3-55.9)	1,168,776 (798,033-1,615,665)	1,129.6 (771.3-1,561.5)
Sri Lanka	268 (141-465)	1.2 (0.7-2.2)	5,521 (1,829-15,243)	25.6 (8.5-70.6)	297,364 (204,983-411,292)	1,376.9 (949.2-1,904.4)
Seychelles	4 (2-6)	3.7 (2.2-5.7)	32 (11-87)	32.2 (11.0-86.6)	1,606 (1,110-2,212)	1,591.2 (1,099.7-2,191.8)
Thailand	2,096 (1,051-3,284)	3.0 (1.5-4.7)	20,091 (7,112-52,926)	28.4 (10.1-74.9)	869,446 (608,384-1,188,505)	1,231.1 (861.4-1,682.8)
Timor-Leste	22 (9-38)	1.7 (0.7-3.0)	353 (109-1,023)	27.4 (8.5-79.4)	18,923 (12,868-26,528)	1,469.8 (999.5-2,060.4)
Vietnam	2,038 (1,114-3,464)	2.1 (1.2-3.6)	134,531 (47,748-356,052)	139.9 (49.7-370.3)	3,567,264 (2,439,338-4,943,211)	3,710.5 (2,537.3-5,141.6)
Oceania	491 (272-830)	3.9 (2.2-6.6)	19,193 (6,295-54,351)	152.3 (49.9-431.3)	192,464 (134,370-264,357)	1,527.2 (1,066.2-2,097.6)
American Samoa	1 (1-2)	1.7 (1.0-2.9)	60 (19-171)	107.5 (34.8-307.9)	618 (424-860)	1,110.5 (762.2-1,545.2)
Federated States of Micronesia	2 (1-4)	2.2 (1.0-3.9)	121 (39-346)	116.7 (37.6-333.0)	1,255 (863-1,743)	1,207.7 (830.6-1,676.9)
Fiji	21 (11-35)	2.3 (1.3-3.8)	1,033 (338-2,900)	113.9 (37.3-319.8)	10,167 (7,010-14,094)	1,121.0 (773.0-1,554.0)
Guam	3 (2-5)	2.0 (1.2-3.3)	179 (60-498)	106.8 (35.7-297.0)	1,752 (1,210-2,422)	1,043.7 (721.0-1,443.4)
Kiribati	2 (1-4)	1.8 (0.9-3.2)	121 (37-374)	102.4 (31.0-316.5)	1,170 (776-1,695)	989.9 (656.3-1,433.4)
Marshall Islands	1 (1-3)	2.6 (1.3-4.6)	66 (21-189)	118.0 (38.1-335.7)	703 (484-976)	1,249.0 (860.2-1,733.6)
Northern Mariana Islands	1 (0-1)	1.7 (1.0-2.8)	45 (15-125)	101.1 (34.4-278.1)	448 (310-618)	998.2 (690.9-1,376.9)
Papua New Guinea	394 (201-697)	4.3 (2.2-7.6)	15,016 (4,749-43,851)	162.7 (51.5-475.2)	150,922 (103,374-210,300)	1,635.6 (1,120.3-2,279.0)
Samoa	3 (2-6)	1.7 (0.9-3.0)	239 (75-696)	120.1 (37.9-350.0)	2,279 (1,560-3,177)	1,145.5 (784.3-1,597.3)
Solomon Islands	25 (14-42)	3.9 (2.1-6.6)	841 (257-2,555)	132.0 (40.3-400.8)	8,350 (5,544-12,081)	1,309.6 (869.6-1,894.7)

Location	Deaths (95% UI)	Deaths per 100,000 (95% UI)	Hospitalisations (95% UI)	Hospitalisations per 100,000 (95% UI)	Episodes (95% UI)	Incidence per 100,000 (95% UI)
Tonga	2 (1-3)	1.7 (0.9-2.9)	97 (30-293)	94.2 (29.5-285.1)	948 (629-1,369)	921.7 (612.1-1,331.6)
Vanuatu	8 (4-14)	2.6 (1.3-4.9)	352 (110-1,025)	122.6 (38.2-356.5)	3,297 (2,256-4,602)	1,146.5 (784.5-1,600.2)
Central Europe, Eastern Europe, and Central Asia	16,423 (11,299-22,546)	3.9 (2.7-5.4)	1,609,003 (659,834-3,730,806)	386.8 (158.6-897.0)	6,624,018 (4,795,541-8,752,473)	1,592.6 (1,153.0-2,104.3)
Central Asia	2,779 (1,847-3,961)	3.1 (2.0-4.4)	275,567 (109,605-656,085)	303.1 (120.5-721.6)	1,175,062 (866,816-1,530,700)	1,292.3 (953.3-1,683.5)
Armenia	80 (51-118)	2.6 (1.7-3.9)	11,051 (4,073-27,308)	365.0 (134.5-902.1)	40,298 (28,311-54,453)	1,331.2 (935.2-1,798.8)
Azerbaijan	245 (130-416)	2.4 (1.3-4.1)	25,862 (8,999-70,393)	252.9 (88.0-688.4)	109,026 (75,003-153,985)	1,066.3 (733.5-1,506.0)
Georgia	133 (82-201)	3.6 (2.2-5.4)	10,785 (4,446-24,827)	292.2 (120.5-672.6)	46,625 (32,832-62,891)	1,263.1 (889.4-1,703.7)
Kazakhstan	632 (391-959)	3.5 (2.2-5.4)	61,161 (22,213-156,157)	341.6 (124.1-872.2)	242,644 (169,914-329,837)	1,355.2 (949.0-1,842.2)
Kyrgyzstan	101 (58-160)	1.6 (0.9-2.5)	25,372 (9,231-65,363)	398.4 (144.9-1,026.3)	87,714 (60,568-120,523)	1,377.3 (951.0-1,892.5)
Mongolia	66 (35-113)	2.0 (1.1-3.5)	7,881 (2,750-20,650)	242.4 (84.6-635.1)	34,725 (24,268-46,945)	1,068.0 (746.4-1,443.8)
Tajikistan	380 (201-650)	4.1 (2.2-7.0)	24,533 (8,204-69,208)	265.4 (88.7-748.7)	111,940 (75,705-160,521)	1,211.0 (819.0-1,736.5)
Turkmenistan	104 (57-175)	2.1 (1.2-3.5)	10,370 (3,555-28,562)	208.4 (71.4-573.9)	46,887 (31,933-66,875)	942.1 (641.6-1,343.7)
Uzbekistan	1,039 (604-1,635)	3.2 (1.9-5.1)	98,978 (34,506-262,244)	307.0 (107.0-813.5)	455,541 (314,931-625,682)	1,413.1 (976.9-1,940.9)
Central Europe	2,773 (1,902-3,824)	2.4 (1.7-3.3)	139,412 (59,860-312,317)	121.4 (52.1-272.0)	410,948 (289,084-560,444)	358.0 (251.8-488.2)
Albania	32 (17-56)	1.2 (0.6-2.0)	3,209 (1,103-8,550)	116.0 (39.9-309.1)	10,108 (6,967-13,926)	365.4 (251.8-503.4)
Bosnia and Herzegovina	33 (19-56)	1.0 (0.6-1.7)	3,612 (1,260-9,478)	106.3 (37.1-278.8)	11,494 (7,957-15,764)	338.1 (234.1-463.7)
Bulgaria	149 (93-225)	2.1 (1.3-3.2)	8,202 (2,969-20,708)	116.3 (42.1-293.6)	23,660 (16,533-32,203)	335.5 (234.4-456.6)
Croatia	59 (38-88)	1.4 (0.9-2.1)	4,106 (1,802-9,138)	96.0 (42.1-213.7)	10,742 (7,484-14,957)	251.3 (175.1-349.8)

Location	Deaths (95% UI)	Deaths per 100,000 (95% UI)	Hospitalisations (95% UI)	Hospitalisations per 100,000 (95% UI)	Episodes (95% UI)	Incidence per 100,000 (95% UI)
Czech Republic	303 (195-444)	2.9 (1.8-4.2)	10,901 (4,541-24,963)	102.9 (42.9-235.7)	32,151 (22,494-43,698)	303.5 (212.4-412.5)
Hungary	95 (61-140)	1.0 (0.6-1.4)	9,314 (3,262-24,639)	95.7 (33.5-253.3)	30,434 (20,975-41,863)	312.9 (215.6-430.4)
Macedonia	15 (8-26)	0.7 (0.4-1.2)	2,438 (825-6,794)	112.1 (37.9-312.4)	8,304 (5,645-11,874)	381.8 (259.6-546.0)
Montenegro	7 (4-12)	1.2 (0.6-1.9)	789 (267-2,182)	126.1 (42.7-348.3)	2,562 (1,735-3,672)	409.0 (277.0-586.3)
Poland	532 (338-781)	1.4 (0.9-2.0)	21,385 (8,755-49,068)	55.7 (22.8-127.8)	56,508 (39,028-77,050)	147.2 (101.7-200.7)
Romania	1,191 (769-1,732)	6.1 (4.0-8.9)	65,108 (27,568-147,024)	335.0 (141.9-756.5)	173,656 (121,356-235,007)	893.6 (624.5-1,209.3)
Serbia	142 (83-222)	1.6 (0.9-2.5)	5,841 (2,252-14,325)	65.8 (25.4-161.4)	24,288 (16,809-33,320)	273.7 (189.4-375.5)
Slovakia	159 (95-246)	2.9 (1.8-4.5)	5,485 (2,165-13,237)	101.2 (40.0-244.3)	17,362 (12,062-23,734)	320.4 (222.6-438.0)
Slovenia	55 (34-81)	2.6 (1.7-3.9)	2,548 (1,019-5,857)	123.2 (49.2-283.1)	6,162 (4,285-8,402)	297.9 (207.1-406.1)
Eastern Europe	10,871 (7,420-15,091)	5.2 (3.5-7.2)	1,027,209 (390,825-2,532,133)	488.7 (185.9-1,204.6)	5,043,230 (3,609,558-6,738,064)	2,399.3 (1,717.2-3,205.6)
Belarus	245 (147-385)	2.6 (1.5-4.1)	45,704 (15,287-127,316)	481.5 (161.1-1,341.4)	231,642 (158,083-328,479)	2,440.6 (1,665.6-3,460.9)
Estonia	43 (26-67)	3.3 (2.0-5.1)	6,134 (2,195-15,841)	466.6 (166.9-1,205.1)	28,280 (19,885-38,252)	2,151.3 (1,512.7-2,909.9)
Latvia	78 (47-119)	4.0 (2.4-6.1)	8,272 (3,265-19,880)	425.2 (167.8-1,021.9)	43,527 (30,659-58,788)	2,237.4 (1,576.0-3,021.9)
Lithuania	141 (88-211)	4.9 (3.1-7.4)	15,966 (6,469-38,491)	560.7 (227.2-1,351.7)	70,896 (49,212-98,794)	2,489.6 (1,728.2-3,469.3)
Moldova	198 (127-294)	5.3 (3.4-7.9)	16,813 (5,999-44,364)	451.7 (161.2-1,192.0)	89,159 (62,815-120,612)	2,395.6 (1,687.7-3,240.7)

Location	Deaths (95% UI)	Deaths per 100,000 (95% UI)	Hospitalisations (95% UI)	Hospitalisations per 100,000 (95% UI)	Episodes (95% UI)	Incidence per 100,000 (95% UI)
Russian Federation	7,979 (5,422-11,083)	5.5 (3.7-7.6)	722,750 (268,439-1,815,081)	494.4 (183.6-1,241.6)	3,504,184 (2,454,367-4,756,911)	2,397.0 (1,678.9-3,253.9)
Ukraine	2,186 (1,368-3,272)	4.9 (3.1-7.3)	211,171 (75,486-549,558)	472.5 (168.9-1,229.7)	1,075,834 (755,918-1,455,967)	2,407.4 (1,691.5-3,258.0)
High-income	23,542 (16,580-31,589)	2.2 (1.5-2.9)	821,039 (366,083-1,725,106)	76.4 (34.1-160.5)	2,269,080 (1,667,513-2,962,557)	211.1 (155.1-275.6)
High-income Asia Pacific	7,546 (5,129-10,388)	4.0 (2.7-5.6)	157,103 (64,431-357,083)	84.0 (34.4-190.9)	273,087 (192,215-369,645)	146.0 (102.8-197.6)
Brunei	6 (3-9)	1.3 (0.8-2.1)	444 (151-1,134)	102.6 (35.0-262.2)	751 (512-1,045)	173.7 (118.3-241.6)
Japan	6,543 (4,438-9,039)	5.1 (3.5-7.0)	103,804 (43,013-236,360)	80.9 (33.5-184.1)	181,588 (126,697-247,752)	141.5 (98.7-193.0)
South Korea	830 (535-1,208)	1.6 (1.0-2.3)	43,774 (15,744-108,486)	83.1 (29.9-206.0)	74,586 (52,291-101,379)	141.6 (99.3-192.5)
Singapore	167 (111-237)	3.0 (2.0-4.3)	9,521 (3,629-22,095)	171.0 (65.2-396.8)	16,148 (11,406-21,742)	290.0 (204.8-390.4)
Australasia	243 (152-361)	0.9 (0.5-1.3)	11,315 (4,276-27,229)	39.9 (15.1-95.9)	38,585 (26,752-52,710)	135.9 (94.2-185.7)
Australia	208 (127-314)	0.9 (0.5-1.3)	9,166 (3,353-22,541)	38.3 (14.0-94.1)	29,982 (20,725-41,117)	125.2 (86.6-171.7)
New Zealand	35 (21-52)	0.8 (0.5-1.2)	2,098 (835-4,981)	47.2 (18.8-112.0)	8,591 (5,880-11,884)	193.1 (132.2-267.2)
Western Europe	9,208 (6,564-12,296)	2.1 (1.5-2.8)	259,545 (119,111-528,501)	59.9 (27.5-122.1)	595,260 (453,391-754,998)	137.5 (104.7-174.4)
Andorra	2 (1-3)	2.4 (1.3-4.0)	42 (16-104)	52.5 (19.6-129.7)	106 (75-144)	132.4 (94.3-180.6)
Austria	63 (41-93)	0.7 (0.5-1.1)	4,960 (2,062-10,882)	56.4 (23.4-123.8)	10,984 (7,760-14,875)	124.9 (88.2-169.2)
Belgium	367 (231-543)	3.2 (2.0-4.8)	9,803 (4,157-21,579)	86.6 (36.7-190.6)	19,427 (13,631-26,588)	171.6 (120.4-234.9)
Cyprus	12 (7-20)	0.9 (0.5-1.6)	348 (141-821)	27.6 (11.2-65.0)	1,138 (806-1,537)	90.1 (63.9-121.7)
Denmark	155 (98-227)	2.7 (1.7-4.0)	3,577 (1,411-8,227)	62.4 (24.6-143.5)	7,872 (5,595-10,560)	137.3 (97.6-184.2)

Location	Deaths (95% UI)	Deaths per 100,000 (95% UI)	Hospitalisations (95% UI)	Hospitalisations per 100,000 (95% UI)	Episodes (95% UI)	Incidence per 100,000 (95% UI)
Finland	74 (46-110)	1.3 (0.8-2.0)	5,021 (2,019-11,292)	91.0 (36.6-204.6)	10,529 (7,413-14,306)	190.8 (134.3-259.3)
France	1,453 (892-2,181)	2.2 (1.4-3.3)	36,243 (13,656-87,943)	55.2 (20.8-133.8)	88,423 (62,479-119,622)	134.6 (95.1-182.0)
Germany	1,376 (862-2,068)	1.7 (1.0-2.5)	48,637 (19,705-111,643)	58.4 (23.7-134.0)	101,297 (72,025-137,386)	121.6 (86.5-164.9)
Greece	280 (175-411)	2.7 (1.7-4.0)	6,339 (2,433-14,982)	60.9 (23.4-144.0)	14,844 (10,601-19,801)	142.7 (101.9-190.4)
Iceland	6 (4-9)	1.8 (1.2-2.8)	163 (64-387)	48.3 (19.0-114.7)	421 (297-569)	124.7 (88.0-168.7)
Ireland	89 (56-131)	1.8 (1.1-2.7)	2,063 (772-5,056)	42.4 (15.9-104.0)	5,517 (3,896-7,456)	113.5 (80.2-153.4)
Israel	115 (71-175)	1.3 (0.8-2.0)	2,837 (1,047-7,241)	31.7 (11.7-80.9)	7,450 (5,126-10,486)	83.2 (57.3-117.2)
Italy	472 (292-703)	0.8 (0.5-1.2)	17,108 (7,108-37,363)	28.2 (11.7-61.7)	38,402 (26,972-51,561)	63.4 (44.5-85.1)
Luxembourg	10 (6-15)	1.6 (1.0-2.5)	287 (114-658)	48.6 (19.4-111.5)	713 (505-961)	120.7 (85.6-162.7)
Malta	11 (7-17)	2.6 (1.7-3.9)	256 (103-593)	59.0 (23.6-136.6)	624 (445-837)	143.7 (102.4-192.8)
Netherlands	388 (249-576)	2.3 (1.5-3.4)	8,193 (3,176-19,528)	48.1 (18.7-114.7)	19,494 (13,912-26,452)	114.5 (81.7-155.3)
Norway	192 (128-270)	3.6 (2.4-5.1)	9,075 (3,809-19,935)	172.4 (72.4-378.8)	25,777 (17,981-35,171)	489.8 (341.6-668.2)
Portugal	470 (301-685)	4.4 (2.8-6.4)	4,747 (1,871-11,184)	44.4 (17.5-104.7)	16,582 (11,860-22,083)	155.2 (111.0-206.7)
Spain	729 (463-1,065)	1.6 (1.0-2.3)	17,490 (6,685-41,401)	37.7 (14.4-89.2)	42,283 (30,137-55,992)	91.1 (65.0-120.7)
Sweden	228 (145-338)	2.3 (1.4-3.4)	7,430 (2,789-18,059)	74.0 (27.8-179.8)	16,812 (11,725-23,015)	167.4 (116.7-229.1)
Switzerland	208 (128-312)	2.4 (1.5-3.6)	7,575 (3,128-17,044)	88.2 (36.4-198.4)	17,756 (12,528-24,192)	206.6 (145.8-281.5)
United Kingdom	2,499 (1,680-3,464)	3.7 (2.5-5.2)	67,089 (30,367-138,355)	100.7 (45.6-207.6)	148,172 (105,331-198,511)	222.4 (158.1-297.9)
England	2,103 (1,409-2,929)	3.8 (2.5-5.2)	60,961 (27,793-124,775)	108.8 (49.6-222.6)	133,030 (94,272-178,953)	237.4 (168.2-319.3)
Northern Ireland	65 (40-97)	3.4 (2.1-5.1)	1,092 (418-2,624)	57.0 (21.8-137.1)	2,679 (1,901-3,599)	139.9 (99.3-188.0)

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Scotland	187 (116-280)	3.4 (2.1-5.1)	3,083 (1,186-7,323)	56.0 (21.6-133.1)	7,290 (5,203-9,739)	132.5 (94.6-177.0)
Wales	144 (91-214)	4.5 (2.9-6.7)	2,258 (873-5,286)	71.1 (27.5-166.4)	5,178 (3,692-6,916)	163.0 (116.2-217.7)
Southern Latin America	2,582 (1,759-3,631)	3.9 (2.7-5.5)	78,320 (31,961-181,785)	119.4 (48.7-277.1)	340,895 (250,568-447,727)	519.6 (381.9-682.4)
Argentina	1,932 (1,222-2,853)	4.4 (2.8-6.4)	45,876 (16,689-116,857)	103.6 (37.7-264.0)	185,768 (127,496-257,640)	419.7 (288.0-582.0)
Chile	523 (324-785)	2.9 (1.8-4.4)	27,567 (10,883-67,548)	153.8 (60.7-377.0)	137,706 (92,797-197,509)	768.5 (517.9-1,102.3)
Uruguay	127 (80-190)	3.7 (2.3-5.6)	4,292 (1,587-10,528)	125.4 (46.4-307.7)	16,808 (11,701-22,980)	491.3 (342.0-671.6)
High-income North America	3,962 (2,665-5,516)	1.1 (0.7-1.5)	195,031 (79,949-444,280)	54.0 (22.2-123.1)	1,013,619 (711,497-1,375,719)	280.9 (197.2-381.2)
Canada	285 (174-427)	0.8 (0.5-1.2)	15,898 (5,976-38,379)	44.2 (16.6-106.7)	78,005 (54,184-106,510)	216.8 (150.6-296.0)
Greenland	1 (0-1)	0.9 (0.5-1.5)	27 (10-68)	48.5 (17.6-121.5)	156 (108-213)	277.6 (192.5-378.8)
United States	3,676 (2,470-5,135)	1.1 (0.8-1.6)	178,522 (73,122-407,443)	55.0 (22.5-125.4)	935,170 (655,596-1,272,353)	287.9 (201.8-391.7)
Latin America and Caribbean	13,366 (9,166-18,419)	2.3 (1.6-3.2)	434,058 (177,361-1,028,775)	74.6 (30.5-176.8)	2,663,821 (1,871,378-3,628,127)	457.7 (321.6-623.4)
Caribbean	2,523 (1,688-3,583)	5.5 (3.6-7.7)	74,991 (28,488-188,074)	162.1 (61.6-406.5)	480,812 (350,216-631,423)	1,039.3 (757.0-1,364.8)
Antigua and Barbuda	6 (3-9)	6.3 (3.9-9.7)	146 (51-388)	163.9 (56.8-436.1)	955 (660-1,298)	1,074.1 (742.4-1,459.3)
The Bahamas	13 (8-20)	3.4 (2.0-5.3)	380 (131-1,049)	101.1 (34.8-279.5)	2,515 (1,727-3,536)	669.9 (460.0-941.9)
Barbados	32 (20-48)	10.8 (6.7-16.2)	692 (251-1,780)	233.8 (84.9-601.7)	3,940 (2,759-5,296)	1,331.8 (932.4-1,789.8)
Belize	19 (11-29)	4.7 (2.8-7.3)	491 (164-1,357)	124.4 (41.4-343.6)	3,684 (2,515-5,057)	932.7 (636.7-1,280.5)
Bermuda	3 (2-4)	4.5 (2.7-6.8)	103 (37-267)	156.7 (56.3-405.9)	612 (428-824)	929.2 (649.9-1,250.9)
Cuba	699 (444-1,029)	6.1 (3.9-9.0)	15,881 (5,816-41,605)	139.6 (51.1-365.7)	84,501 (59,549-115,471)	742.8 (523.4-1,015.0)

Location	Deaths (95% UI)	Deaths per 100,000 (95% UI)	Hospitalisations (95% UI)	Hospitalisations per 100,000 (95% UI)	Episodes (95% UI)	Incidence per 100,000 (95% UI)
Dominica	5 (3-8)	7.8 (4.7-11.9)	130 (46-343)	188.9 (66.2-497.4)	792 (550-1,072)	1,148.9 (797.6-1,555.4)
Dominican Republic	384 (211-622)	3.7 (2.0-5.9)	17,553 (5,804-47,989)	167.9 (55.5-459.1)	121,309 (82,770-166,707)	1,160.7 (791.9-1,595.0)
Grenada	10 (6-15)	9.1 (5.7-13.7)	205 (73-543)	184.5 (65.5-489.6)	1,086 (758-1,504)	979.4 (683.6-1,356.0)
Guyana	43 (26-67)	5.8 (3.4-9.0)	976 (327-2,647)	131.4 (44.1-356.6)	6,831 (4,675-9,355)	920.3 (629.8-1,260.3)
Haiti	737 (372-1,300)	6.2 (3.2-11.0)	21,624 (7,024-60,135)	182.9 (59.4-508.5)	146,372 (99,856-200,810)	1,237.8 (844.5-1,698.2)
Jamaica	88 (50-142)	3.2 (1.8-5.1)	3,557 (1,210-9,606)	128.0 (43.5-345.6)	24,844 (17,079-33,892)	893.9 (614.5-1,219.5)
Puerto Rico	285 (179-422)	7.8 (4.9-11.5)	7,602 (2,745-19,711)	207.4 (74.9-537.7)	43,293 (30,302-58,178)	1,181.0 (826.6-1,587.0)
Saint Lucia	10 (6-15)	5.7 (3.4-8.6)	296 (103-786)	167.6 (58.4-445.6)	1,949 (1,349-2,644)	1,104.3 (764.7-1,498.1)
Saint Vincent and the Grenadines	8 (5-12)	6.9 (4.2-10.5)	202 (71-530)	177.0 (62.3-464.8)	1,269 (880-1,719)	1,112.0 (771.5-1,506.6)
Suriname	31 (19-48)	5.4 (3.2-8.3)	746 (256-1,978)	130.3 (44.8-345.5)	4,947 (3,417-6,729)	864.2 (597.0-1,175.5)
Trinidad and Tobago	55 (31-90)	4.0 (2.2-6.5)	1,973 (686-5,290)	141.8 (49.3-380.1)	13,336 (9,229-18,119)	958.2 (663.1-1,301.8)
Virgin Islands, U.S.	6 (3-9)	5.4 (3.2-8.5)	175 (63-450)	166.6 (59.7-428.7)	1,045 (731-1,409)	995.9 (696.1-1,342.3)
Andean Latin America	1,460 (932-2,146)	2.4 (1.5-3.5)	21,874 (8,264-54,678)	35.6 (13.4-89.0)	426,838 (293,165-590,776)	694.6 (477.1-961.4)
Bolivia	268 (140-448)	2.3 (1.2-3.9)	3,537 (1,175-9,740)	30.6 (10.2-84.4)	71,806 (49,200-99,623)	622.1 (426.2-863.1)
Ecuador	278 (173-417)	1.7 (1.0-2.5)	6,085 (2,428-14,671)	36.5 (14.6-87.9)	124,849 (85,523-173,128)	748.2 (512.5-1,037.6)
Peru	914 (547-1,408)	2.8 (1.6-4.2)	12,232 (4,313-32,093)	36.8 (13.0-96.6)	230,183 (158,442-318,024)	692.9 (477.0-957.3)
Central Latin America	3,315 (2,244-4,625)	1.3 (0.9-1.8)	113,267 (40,984-295,085)	44.3 (16.0-115.5)	1,133,837 (776,479-1,573,322)	443.8 (303.9-615.8)
Colombia	594 (364-902)	1.2 (0.7-1.8)	27,854 (8,978-79,128)	55.0 (17.7-156.4)	272,841 (182,846-385,512)	539.1 (361.3-761.8)
Costa Rica	30 (18-46)	0.6 (0.4-1.0)	1,793 (570-5,115)	38.5 (12.2-109.9)	19,199 (12,912-27,052)	412.6 (277.5-581.3)

Location	Deaths (95% UI)	Deaths per 100,000 (95% UI)	Hospitalisations (95% UI)	Hospitalisations per 100,000 (95% UI)	Episodes (95% UI)	Incidence per 100,000 (95% UI)
El Salvador	81 (43-132)	1.3 (0.7-2.2)	1,980 (645-5,562)	32.5 (10.6-91.4)	18,253 (12,250-25,523)	299.9 (201.3-419.3)
Guatemala	539 (330-814)	3.2 (1.9-4.8)	12,878 (4,182-36,330)	76.1 (24.7-214.7)	115,992 (77,048-166,390)	685.4 (455.3-983.1)
Honduras	63 (32-115)	0.7 (0.3-1.2)	6,284 (1,896-18,785)	66.2 (20.0-197.8)	61,352 (40,931-87,911)	645.9 (430.9-925.5)
Mexico	1,662 (1,112-2,347)	1.3 (0.9-1.9)	49,282 (18,493-126,341)	38.9 (14.6-99.8)	502,888 (342,997-703,587)	397.3 (271.0-555.9)
Nicaragua	23 (13-37)	0.4 (0.2-0.6)	1,290 (399-3,763)	20.2 (6.2-58.8)	13,401 (8,935-18,932)	209.5 (139.7-296.0)
Panama	47 (29-72)	1.2 (0.7-1.8)	1,930 (628-5,433)	49.2 (16.0-138.6)	18,186 (12,189-25,681)	463.8 (310.8-654.9)
Venezuela	276 (162-434)	0.9 (0.5-1.4)	10,851 (3,531-30,655)	35.2 (11.5-99.4)	110,842 (74,516-156,273)	359.5 (241.7-506.9)
Tropical Latin America	6,069 (4,003-8,631)	2.8 (1.8-3.9)	176,848 (72,594-414,204)	80.8 (33.2-189.4)	620,005 (420,101-871,097)	283.4 (192.1-398.2)
Brazil	5,880 (3,875-8,392)	2.8 (1.8-4.0)	163,835 (67,495-382,496)	77.3 (31.9-180.6)	569,012 (384,199-801,950)	268.6 (181.4-378.6)
Paraguay	189 (106-308)	2.7 (1.5-4.5)	13,720 (4,460-38,661)	197.9 (64.3-557.8)	51,208 (34,557-71,672)	738.8 (498.6-1,034.1)
North Africa and Middle East	5,503 (3,569-8,101)	0.9 (0.6-1.3)	745,571 (252,545-2,026,725)	124.2 (42.1-337.7)	4,655,896 (3,180,375-6,468,301)	775.7 (529.9-1,077.7)
North Africa and Middle East	5,503 (3,569-8,101)	0.9 (0.6-1.3)	745,571 (252,545-2,026,725)	124.2 (42.1-337.7)	4,655,896 (3,180,375-6,468,301)	775.7 (529.9-1,077.7)
Afghanistan	772 (382-1,359)	2.4 (1.2-4.1)	74,237 (22,127-223,264)	226.0 (67.3-679.5)	394,684 (260,090-570,945)	1,201.3 (791.6-1,737.8)
Algeria	316 (174-532)	0.8 (0.4-1.3)	53,441 (17,366-151,712)	132.1 (42.9-374.9)	320,242 (216,542-452,477)	791.4 (535.2-1,118.2)
Bahrain	7 (4-12)	0.5 (0.3-0.8)	1,487 (472-4,330)	101.2 (32.1-294.5)	10,174 (6,930-14,305)	692.0 (471.3-972.9)
Egypt	709 (347-1,281)	0.7 (0.4-1.3)	97,542 (29,689-280,838)	101.1 (30.8-291.1)	588,112 (394,804-818,494)	609.5 (409.2-848.3)
Iran	669 (420-953)	0.8 (0.5-1.2)	84,399 (28,824-230,344)	102.7 (35.1-280.3)	482,343 (332,350-674,604)	587.0 (404.4-820.9)
Iraq	179 (98-300)	0.4 (0.2-0.7)	54,845 (16,402-165,460)	126.6 (37.9-382.1)	357,249 (237,919-511,508)	825.0 (549.4-1,181.2)

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Jordan	59 (33-96)	0.6 (0.3-0.9)	11,777 (4,076-32,241)	110.6 (38.3-302.8)	84,268 (56,507-119,922)	791.4 (530.7-1,126.2)
Kuwait	63 (39-96)	1.5 (0.9-2.2)	6,836 (2,218-19,320)	160.4 (52.1-453.3)	46,621 (31,570-65,186)	1,093.8 (740.7-1,529.4)
Lebanon	53 (29-90)	0.6 (0.3-1.1)	12,416 (3,813-37,646)	145.9 (44.8-442.3)	81,802 (54,859-116,451)	961.0 (644.5-1,368.1)
Libya	62 (33-106)	0.9 (0.5-1.5)	9,235 (2,953-27,055)	133.7 (42.7-391.6)	62,159 (42,058-87,768)	899.7 (608.8-1,270.4)
Morocco	645 (340-1,099)	1.8 (1.0-3.1)	84,116 (27,216-237,416)	237.0 (76.7-669.0)	509,409 (345,411-710,668)	1,435.4 (973.3-2,002.5)
Palestine	36 (21-60)	0.7 (0.4-1.2)	6,759 (2,080-20,038)	139.3 (42.9-413.0)	43,580 (29,098-62,273)	898.2 (599.7-1,283.4)
Oman	29 (15-50)	0.6 (0.3-1.1)	4,790 (1,529-13,948)	105.6 (33.7-307.5)	35,161 (23,963-49,409)	775.2 (528.3-1,089.3)
Qatar	7 (4-12)	0.2 (0.1-0.4)	2,821 (899-8,206)	102.7 (32.7-298.7)	18,877 (12,923-26,425)	687.1 (470.4-961.9)
Saudi Arabia	272 (145-462)	0.8 (0.4-1.3)	35,796 (11,567-104,381)	103.9 (33.6-303.0)	266,538 (181,404-374,349)	773.8 (526.7-1,086.8)
Sudan	444 (209-838)	1.1 (0.5-2.1)	63,504 (18,995-191,483)	157.8 (47.2-475.7)	354,424 (235,250-509,563)	880.4 (584.4-1,265.8)
Syria	142 (74-242)	0.8 (0.4-1.3)	21,642 (6,771-63,554)	119.4 (37.3-350.5)	148,140 (99,524-210,436)	817.0 (548.9-1,160.6)
Tunisia	120 (63-205)	1.0 (0.6-1.8)	17,808 (5,822-50,585)	155.6 (50.9-442.1)	103,327 (70,085-145,646)	903.0 (612.5-1,272.9)
Turkey	566 (332-876)	0.7 (0.4-1.1)	44,027 (16,679-109,899)	54.7 (20.7-136.6)	342,108 (238,860-465,526)	425.2 (296.9-578.6)
United Arab Emirates	46 (19-89)	0.5 (0.2-0.9)	7,457 (2,445-21,575)	76.6 (25.1-221.6)	57,936 (39,971-80,778)	595.2 (410.6-829.8)
Yemen	301 (146-554)	1.0 (0.5-1.8)	61,139 (18,499-185,628)	200.8 (60.8-609.6)	346,953 (230,410-498,728)	1,139.5 (756.7-1,637.9)
South Asia	31,382 (20,121-45,490)	1.8 (1.1-2.6)	765,451 (255,142-2,096,138)	42.9 (14.3-117.6)	18,950,286 (12,934,681-26,373,644)	1,063.0 (725.6-1,479.4)
South Asia	31,382 (20,121-45,490)	1.8 (1.1-2.6)	765,451 (255,142-2,096,138)	42.9 (14.3-117.6)	18,950,286 (12,934,681-26,373,644)	1,063.0 (725.6-1,479.4)
Bangladesh	1,000 (534-1,741)	0.6 (0.3-1.1)	18,658 (5,753-53,093)	11.9 (3.7-33.8)	718,521 (483,918-1,005,573)	457.7 (308.3-640.6)

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Bhutan	10 (5-17)	1.0 (0.5-1.7)	199 (59-588)	20.8 (6.2-61.4)	8,734 (5,901-12,201)	912.2 (616.3-1,274.4)
India	25,517 (16,308-37,037)	1.8 (1.2-2.7)	588,160 (196,228-1,611,329)	42.6 (14.2-116.7)	13,966,155 (9,448,863-19,552,248)	1,011.6 (684.4-1,416.3)
Nepal	475 (245-811)	1.6 (0.8-2.7)	2,809 (954-7,668)	9.4 (3.2-25.7)	207,897 (140,121-292,772)	695.5 (468.8-979.4)
Pakistan	4,381 (2,164-7,838)	2.0 (1.0-3.7)	126,080 (37,625-378,217)	58.8 (17.6-176.5)	4,058,959 (2,720,607-5,746,060)	1,894.2 (1,269.6-2,681.5)
Sub-Saharan Africa	27,443 (17,380-40,491)	2.7 (1.7-3.9)	1,597,833 (555,739-4,249,918)	155.7 (54.2-414.2)	6,052,010 (4,188,778-8,317,538)	589.8 (408.2-810.6)
Central Sub-Saharan Africa	4,104 (2,330-6,712)	3.4 (1.9-5.5)	293,238 (98,081-811,775)	241.0 (80.6-667.2)	936,919 (635,980-1,310,283)	770.0 (522.7-1,076.9)
Angola	712 (371-1,220)	2.5 (1.3-4.3)	52,004 (17,253-144,533)	184.4 (61.2-512.5)	170,290 (115,655-238,370)	603.8 (410.1-845.2)
Central African Republic	240 (117-431)	5.2 (2.5-9.3)	12,268 (3,999-34,524)	265.4 (86.5-746.9)	39,246 (26,703-54,795)	849.0 (577.7-1,185.4)
Congo	137 (72-235)	2.8 (1.5-4.8)	9,784 (3,264-27,031)	199.1 (66.4-550.2)	32,457 (22,224-45,145)	660.6 (452.3-918.9)
Democratic Republic of the Congo	2,949 (1,513-5,141)	3.6 (1.9-6.4)	213,545 (69,086-607,635)	264.0 (85.4-751.2)	674,930 (454,675-953,762)	834.4 (562.1-1,179.2)
Equatorial Guinea	20 (10-37)	1.5 (0.8-2.8)	2,328 (750-6,650)	173.1 (55.7-494.4)	8,490 (5,775-11,832)	631.2 (429.3-879.6)
Gabon	45 (24-75)	2.6 (1.4-4.4)	3,484 (1,174-9,575)	204.6 (68.9-562.4)	11,536 (7,922-15,991)	677.5 (465.3-939.2)
Eastern Sub-Saharan Africa	6,629 (4,199-9,733)	1.7 (1.1-2.5)	430,037 (145,847-1,167,492)	109.4 (37.1-296.9)	2,182,660 (1,503,652-2,993,552)	555.1 (382.4-761.4)
Burundi	210 (108-366)	1.9 (1.0-3.4)	12,793 (4,039-36,528)	117.3 (37.0-335.0)	66,425 (44,795-92,741)	609.1 (410.8-850.4)
Comoros	13 (7-22)	1.8 (1.0-3.0)	739 (246-2,030)	102.8 (34.2-282.6)	3,917 (2,672-5,414)	545.3 (372.0-753.7)
Djibouti	15 (7-27)	1.3 (0.7-2.4)	996 (325-2,800)	89.5 (29.2-251.6)	5,319 (3,621-7,369)	477.9 (325.3-662.1)
Eritrea	115 (58-202)	2.0 (1.0-3.4)	6,589 (2,110-18,812)	112.5 (36.0-321.1)	36,337 (24,569-50,604)	620.2 (419.3-863.7)

Location	Deaths (95% UI)	Deaths per 100,000 (95% UI)	Hospitalisations (95% UI)	Hospitalisations per 100,000 (95% UI)	Episodes (95% UI)	Incidence per 100,000 (95% UI)
Ethiopia	993 (599-1,508)	1.0 (0.6-1.5)	69,381 (22,749-191,550)	67.4 (22.1-186.2)	338,784 (230,186-467,732)	329.3 (223.7-454.6)
Kenya	853 (537-1,291)	1.8 (1.1-2.7)	73,585 (24,190-206,358)	152.3 (50.1-427.0)	365,616 (244,861-512,372)	756.5 (506.7-1,060.2)
Madagascar	881 (449-1,545)	3.4 (1.7-5.9)	57,342 (18,563-164,401)	219.6 (71.1-629.7)	299,606 (203,824-417,080)	1,147.5 (780.7-1,597.5)
Malawi	352 (191-583)	2.0 (1.1-3.4)	21,587 (6,866-61,435)	125.6 (39.9-357.4)	110,066 (73,765-154,332)	640.2 (429.1-897.7)
Mozambique	266 (138-460)	0.9 (0.5-1.5)	16,015 (5,120-46,612)	53.3 (17.0-155.2)	89,219 (60,401-125,851)	297.0 (201.1-419.0)
Rwanda	183 (96-315)	1.5 (0.8-2.5)	13,288 (4,113-38,844)	105.8 (32.8-309.4)	67,600 (44,186-97,203)	538.5 (352.0-774.3)
Somalia	357 (176-639)	2.1 (1.0-3.8)	17,273 (5,413-50,276)	102.3 (32.1-297.8)	88,369 (59,527-123,548)	523.5 (352.6-731.9)
South Sudan	294 (146-523)	3.0 (1.5-5.3)	12,147 (3,763-35,188)	122.2 (37.9-354.0)	59,878 (40,191-83,929)	602.3 (404.3-844.3)
Tanzania	1,438 (772-2,397)	2.7 (1.4-4.4)	75,482 (24,608-212,856)	139.9 (45.6-394.4)	384,620 (261,428-533,802)	712.6 (484.4-989.0)
Uganda	468 (247-795)	1.2 (0.6-2.0)	40,106 (12,640-115,956)	102.6 (32.3-296.7)	211,795 (142,907-297,930)	542.0 (365.7-762.4)
Zambia	187 (99-314)	1.1 (0.6-1.8)	10,069 (3,264-28,327)	58.0 (18.8-163.1)	53,609 (36,587-74,788)	308.7 (210.7-430.7)
Southern Sub-Saharan Africa	2,335 (1,496-3,384)	3.0 (1.9-4.4)	155,818 (56,715-398,658)	201.4 (73.3-515.2)	532,257 (372,920-726,714)	687.9 (482.0-939.2)
Botswana	42 (23-69)	1.8 (1.0-3.0)	3,323 (1,124-8,928)	145.6 (49.3-391.3)	12,484 (8,585-17,151)	547.1 (376.2-751.6)
Lesotho	85 (43-148)	4.4 (2.2-7.6)	5,261 (1,772-14,406)	270.1 (91.0-739.7)	18,857 (12,978-26,135)	968.2 (666.4-1,341.9)
Namibia	62 (33-104)	2.6 (1.4-4.4)	5,206 (1,745-14,313)	221.2 (74.1-608.2)	18,533 (12,710-25,751)	787.5 (540.0-1,094.2)
South Africa	1,535 (990-2,224)	2.8 (1.8-4.0)	107,965 (39,505-274,607)	196.5 (71.9-499.7)	364,578 (255,788-497,377)	663.4 (465.5-905.1)
Swaziland	36 (18-63)	3.2 (1.6-5.6)	2,672 (886-7,439)	237.6 (78.8-661.6)	9,907 (6,787-13,786)	881.0 (603.6-1,226.0)
Zimbabwe	575 (298-967)	3.9 (2.0-6.6)	31,285 (10,509-85,700)	212.6 (71.4-582.5)	107,945 (73,625-150,724)	733.6 (500.4-1,024.4)

Location	Deaths (95% UI)	Deaths per 100,000 (95% UI)	Hospitalisations (95% UI)	Hospitalisations per 100,000 (95% UI)	Episodes (95% UI)	Incidence per 100,000 (95% UI)
Western Sub-Saharan Africa	14,376 (8,802-21,976)	3.3 (2.0-5.1)	736,346 (250,820-1,995,529)	169.7 (57.8-460.0)	2,408,441 (1,644,131-3,354,242)	555.2 (379.0-773.2)
Benin	370 (189-652)	3.2 (1.6-5.6)	19,861 (6,548-55,124)	171.4 (56.5-475.8)	66,264 (45,016-92,415)	572.0 (388.6-797.7)
Burkina Faso	1,021 (499-1,858)	4.8 (2.4-8.8)	47,655 (14,626-146,411)	225.6 (69.2-693.2)	150,615 (95,646-227,206)	713.1 (452.8-1,075.7)
Cameroon	852 (439-1,481)	3.1 (1.6-5.3)	50,682 (16,605-140,926)	182.5 (59.8-507.5)	171,096 (116,351-238,473)	616.1 (419.0-858.8)
Cape Verde	14 (8-23)	2.6 (1.5-4.2)	944 (327-2,508)	172.9 (60.0-459.4)	3,263 (2,254-4,483)	597.8 (412.9-821.4)
Chad	892 (459-1,519)	5.9 (3.0-10.0)	41,699 (13,153-118,824)	273.9 (86.4-780.6)	126,017 (84,702-177,330)	827.9 (556.4-1,165.0)
Cote d'Ivoire	1,709 (890-2,979)	6.8 (3.6-11.9)	98,969 (32,909-273,216)	396.4 (131.8-1,094.4)	326,632 (222,550-455,363)	1,308.3 (891.4-1,824.0)
The Gambia	51 (27-86)	2.4 (1.3-4.0)	3,089 (1,008-8,780)	144.9 (47.2-411.7)	10,287 (6,835-14,698)	482.4 (320.5-689.2)
Ghana	800 (432-1,328)	2.6 (1.4-4.4)	44,574 (14,846-124,282)	147.6 (49.1-411.5)	154,614 (104,240-218,036)	511.9 (345.1-721.8)
Guinea	588 (314-992)	5.0 (2.7-8.4)	30,089 (9,878-83,871)	254.6 (83.6-709.6)	94,097 (63,799-131,429)	796.1 (539.8-1,111.9)
Guinea-Bissau	60 (31-105)	3.3 (1.7-5.7)	3,535 (1,150-9,878)	190.5 (62.0-532.3)	11,825 (8,024-16,513)	637.3 (432.4-889.9)
Liberia	118 (60-208)	2.5 (1.3-4.4)	10,190 (3,321-28,509)	215.8 (70.3-603.7)	33,382 (22,675-46,565)	706.8 (480.1-986.0)
Mali	520 (257-933)	2.6 (1.3-4.6)	30,037 (9,530-85,857)	148.3 (47.1-423.9)	96,525 (65,376-135,684)	476.6 (322.8-669.9)
Mauritania	97 (51-168)	2.5 (1.3-4.3)	7,035 (2,302-19,768)	179.7 (58.8-505.1)	23,387 (15,914-32,561)	597.5 (406.6-831.9)
Niger	929 (467-1,642)	4.3 (2.2-7.7)	50,113 (16,111-142,342)	234.4 (75.4-665.9)	154,944 (104,361-217,665)	724.9 (488.2-1,018.3)
Nigeria	5,406 (2,800-9,481)	2.6 (1.4-4.6)	231,464 (74,522-654,841)	112.3 (36.2-317.7)	758,410 (511,634-1,063,013)	368.0 (248.3-515.8)
Sao Tome and Principe	7 (4-11)	3.4 (1.9-5.6)	459 (154-1,265)	229.1 (77.1-631.8)	1,624 (1,111-2,251)	811.2 (555.1-1,124.5)
Senegal	398 (210-682)	2.7 (1.4-4.6)	33,572 (11,066-92,896)	228.6 (75.3-632.5)	105,805 (71,735-147,803)	720.3 (488.4-1,006.3)

Location	Deaths (95% UI)	Deaths per 100,000 (95% UI)	Hospitalisations (95% UI)	Hospitalisations per 100,000 (95% UI)	Episodes (95% UI)	Incidence per 100,000 (95% UI)
Sierra Leone	346 (181-601)	4.4 (2.3-7.7)	19,618 (6,433-54,239)	250.6 (82.2-692.7)	64,288 (43,636-89,733)	821.1 (557.3-1,146.1)
Togo	198 (103-339)	2.6 (1.4-4.5)	14,298 (4,745-39,440)	190.2 (63.1-524.7)	47,955 (32,728-66,623)	638.0 (435.4-886.4)

Figure 1. Conceptual diagram of the influenza LRI burden pyramid

This diagram shows a spectrum of influenza LRI disease. This manuscript presents estimates of moderate and severe influenza LRI, of which some fraction (modeled independently) is hospitalised, and mortality due to influenza LRI. This study did not estimate inapparent infection which may be important for understanding influenza LRI transmission dynamics but does not account for a measurable burden of disease.

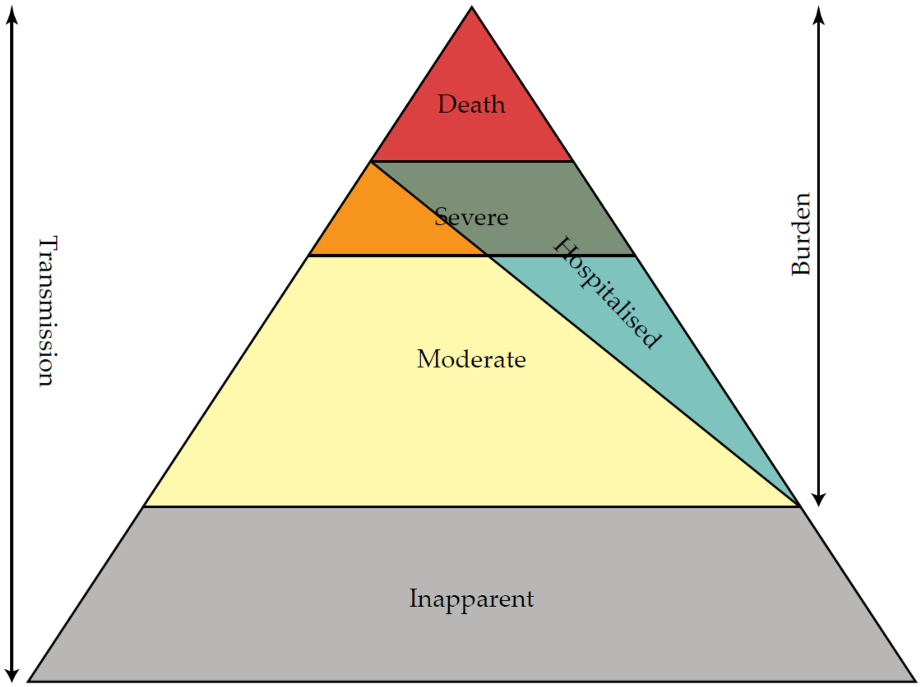


Figure *2*. Age distribution of deaths, hospitalisations, and episodes caused by influenza LRI globally in 2017

EN = early neonatal (0-6 days), LN = late neonatal (7-27 days), PN = post neonatal. Influenza is not attributed to LRI in the early or late neonatal age groups.

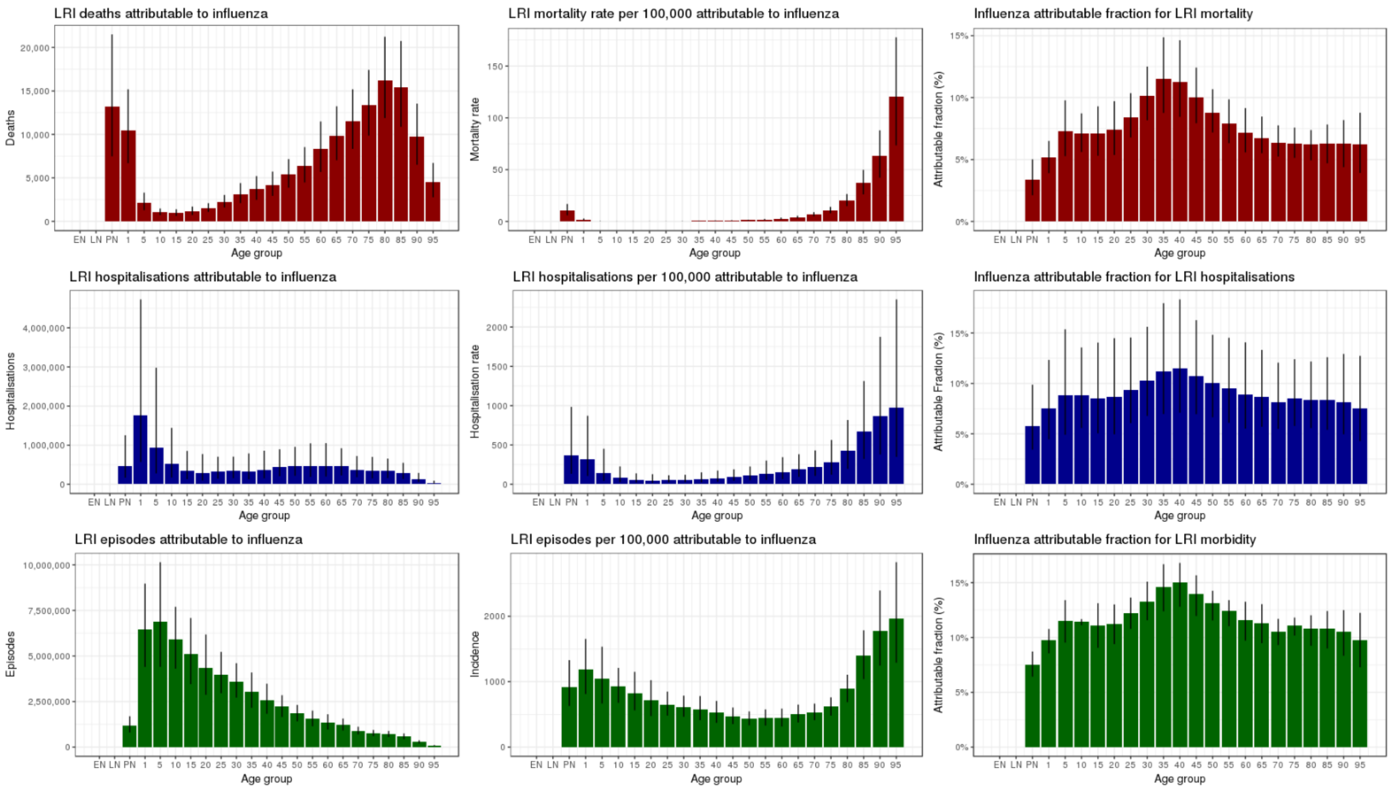


Figure 3. Influenza LRI mortality rate per 100,000 all ages in 2017

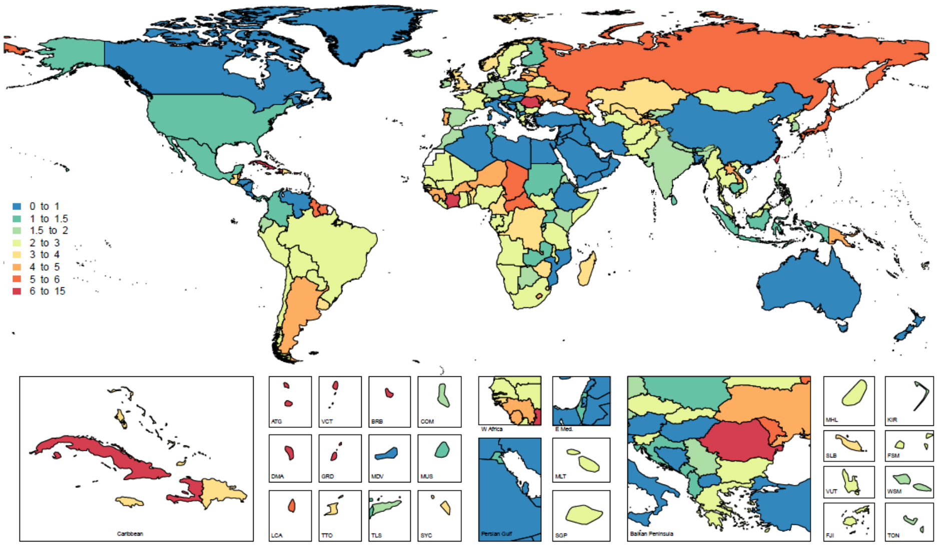


Figure 4. Influenza LRI hospitalisations per 100,000, all ages in 2017

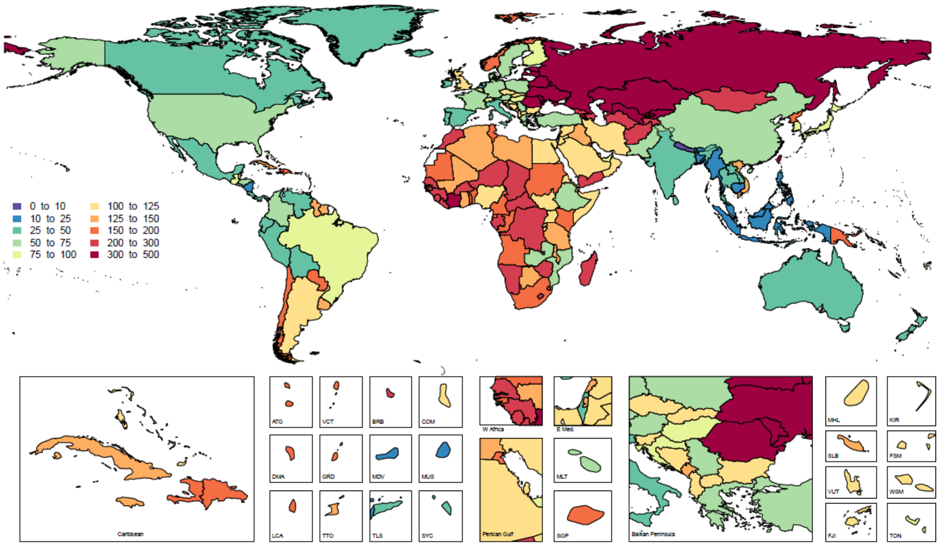
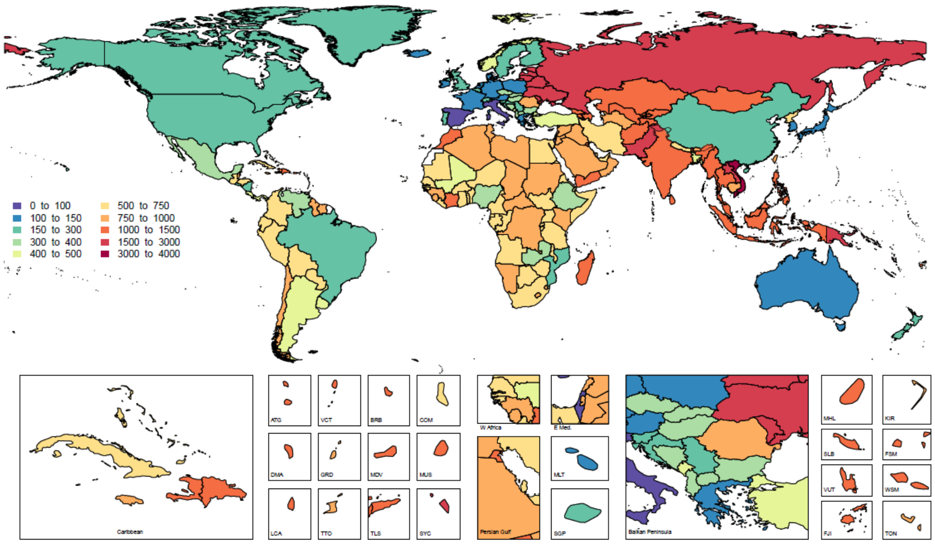


Figure 5. Influenza LRI incidence per 100,000 all ages in 2017



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