Global and regional burden of hospital admissions for pneumonia in older adults:

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SUPPLEMENT ARTICLE

Global and Regional Burden of Hospital Admissions for Pneumonia in Older Adults: A Systematic Review and Meta-Analysis

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Pneumonia constitutes a substantial disease burden among adults overall and those who are elderly. We aimed to identify all studies investigating the disease burden among older adults (age, ≥65 years) admitted to the hospital with pneumonia. We estimated the hospital admission rate and in-hospital case-fatality ratio (CFR) of pneumonia in older adults, stratified by age and economic status (industrialized vs developing), with data from a systematic review of studies published from 1996 through 2017 and from 8 unpublished population-based studies. We applied these rate estimates to population estimates for 2015 to calculate the global and regional burden in older adults who would have been admitted to the hospital with pneumonia that year. We estimated the number of in-hospital pneumonia deaths by combining in-hospital CFRs with hospital admission estimates from hospital-based studies. We identified 109 eligible studies; 73 used clinical pneumonia as the case definition, and 36 used radiologically confirmed pneumonia as the case definition. We estimated that, in 2015, 6.8 million episodes (uncertainty range [UR], 5.8–8.0 episodes) of clinical pneumonia resulted in hospital admissions of older adults worldwide. The hospital admission rate increased with advancing age and was higher in men. The total disease burden was likely underestimated when using the definition of radiologically confirmed pneumonia. Based on data from 52 hospital studies reporting data on pneumonia mortality, we estimated that about 1.1 million in-hospital deaths (UR, 0.9–1.4 in-hospital deaths) occurred among older adults. The burden of pneumonia requiring hospitalization among older adults is substantial. Appropriate prevention and management strategies should be developed to reduce its impact.

Keywords. Pneumonia; older adults; disease burden.

Pneumonia constitutes a substantial disease burden among adults overall and those who are elderly. The Global Burden of Disease (GBD), Injuries, and Risk Factors Study 2015 estimated that, in 2015, lower respiratory tract infections (LRIs) caused 1.2 million deaths (uncertainty range [UR], 1.0–1.3) and 13.5 million disability-adjusted life-years (UR, 11.7–14.4) among adults aged ≥65 years [1]. A prospective population-based study across multiple centers in the United States described the causes and rates of hospitalized community-acquired pneumonia (CAP). This study estimated that the hospital admission rate for CAP among adults aged ≥18 years was 2.5 cases/1000 persons per year and that the highest rates occurred in older adults aged 65–79 years (6.3 cases/1000 persons per year) and those aged ≥80 years (16.4 cases/1000 persons per year) [2]. The hospital admission rate increased with age. Currently, there are no systematically established global estimates of the hospitalization rate for pneumonia or acute respiratory tract infection (ARI) in older adults aged ≥65 years. However, there is a substantial quantity of high-quality data on hospitalizations and in-hospital mortality from pneumonia among adults worldwide. Therefore, we aim to estimate the rate of hospital admissions and in-hospital deaths due to pneumonia in older adults aged ≥65 years in 2015, worldwide and stratified by age and economic status (industrialized versus developing). Furthermore, we examined how these estimates varied by case definition and sex.

METHODS

Search Strategy and Selection Criteria

We conducted a systematic review across 9 databases (including 3 Chinese-language databases), following the approach detailed in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [3]. Tailored search strategies were developed and used to search Medline, Embase,

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Global Health, CINAHL, Web of Science, LILACS, China National Knowledge Infrastructure (CNKI), Wanfang Data, and Chongqing VIP databases (Supplementary Table 1). All searches were limited to literature between January 1996 and September 2017. No publication status criteria or language restrictions were applied. We included studies that fulfilled the selection criteria in Supplementary Panel 1.

Three investigators (T. S., A. D., and A. T.) conducted the search in English-language databases and extracted data by using standardized data-extraction templates. Any disagreements were resolved after discussion. One investigator (T. S.) whose first language is Chinese performed searches and data extraction from Chinese-language databases (CNKI, Wanfang, and Chongqing VIP). Based on the published studies and our knowledge of previously funded/currently ongoing studies, we contacted investigators who led studies in the past 15 years on hospitalization for pneumonia in older adults, and we identified unpublished data from 8 studies. The investigator group (of collaborators sharing unpublished data with us) agreed on a common approach for data analysis and interpretation and formulated common case definitions. They used these case definitions to reanalyze data from their already published work, or they shared hitherto unpublished data from ongoing studies. This method resulted in analysis of additional unpublished data, which supplemented and substantially enriched data from the review of published studies.

The protocol of this review was published in the PROSPERO database (registration CRD42018091423).

Definitions

The definition of pneumonia or ARI in older adults aged ≥65 years was adapted from the World Health Organization (WHO) Integrated Management of Adolescent and Adult Illness definitions [4]. The details of the definitions are displayed in Supplementary Table 2. Few studies used the ARI or LRI definition; therefore, in this article we used the term "clinical pneumonia" to include ARI, LRI, CAP, pneumonia, and severe acute respiratory infection (SARI). We categorized countries as broadly within either industrialized or developing regions on the basis of the United Nations Children's Fund's 2015 classification and used this to report our results [5, 6]. The adult population estimates for 2015 were taken from the United Nations Population Division's database [7].

Statistical Analysis

For all included studies, we expressed the hospital admission rate as the number of admissions per 1000 persons per year and the in-hospital case-fatality rate (hCFR) as a percentage with an accompanying 95% confidence interval (CI), to facilitate interpretation and comparison. We applied a continuity correction of 0.0005 if the number of cases or deaths was 0 [8]. This allowed calculation of a hospital admission rate or hCFR for these instances and enabled their inclusion in subsequent meta-analyses.

We performed meta-analyses by region (classified into industrialized versus developing countries) and narrow age groups (65–74 years, 75–84 years, and ≥85 years), for the hospital admission rate and hCFR of pneumonia, and reported pooled estimates (with 95% CIs). We used the random effects model (DerSimonian-Laird method) because in-study and between-study data heterogeneity was anticipated and, thus, different effect sizes were assumed [9]. The hospital admission rate meta-estimate for pneumonia was applied to the regional population estimate for individuals aged ≥65 years (by narrow age band) to yield estimates for individuals with new episodes of pneumonia who were admitted to hospitals in 2015. We estimated in-hospital pneumonia deaths by applying the regional hCFR meta-estimate to the regional number of pneumonia-associated hospital admissions (by narrow age bands). We estimated URs for in-hospital deaths by using Monte Carlo simulation (calculating estimates from 10 000 samples from log-normal distributions, with 2.5th and 97.5th centiles defining the UR). Similar simulations were performed to generate the global estimate (from regional estimates) and to estimate the overall burden for older adults aged ≥65 years (by summing the age-specific estimates) [10].

Data were analyzed using Stata, version 13.0, and R, version 3.0.2.

RESULTS

We identified 9963 records from the literature search; of these, 92 articles (101 studies) fulfilled our selection criteria (Figure 1). Additionally, we identified 8 unpublished studies from the investigator group (Supplementary Table 3). Overall, 109 studies with data on hospital admission and mortality were included for further analysis (Supplementary Figure 1). Among them, 73 studies used the definition of clinical pneumonia confirmed by physicians. Of the 73, 49 reported the hospital admission rate among older adults aged ≥65 years, and 52 reported mortality data. Fifty-seven studies came from industrialized countries, and 16 came from developing countries. Thirty-three studies (46%) were from the WHO Region of the Americas, and 26 (36%) were from the WHO European Region. Analyses by WHO region could not be conducted, owing to a lack of data. Twenty studies were from urban areas, 7 were from rural areas, and 46 were from a mixed population.

Another 36 studies used the definition of radiologically confirmed pneumonia. Of those, 11 reported the hospital admission rate among older adults, and 31 reported mortality data. Most studies (n = 27) came from industrialized countries, and 9 studies were from developing countries. Twenty-five studies were in urban populations, 1 was in a rural population, and 10 were in mixed populations. For our article, the estimates were derived from studies using the clinical pneumonia case definition. We

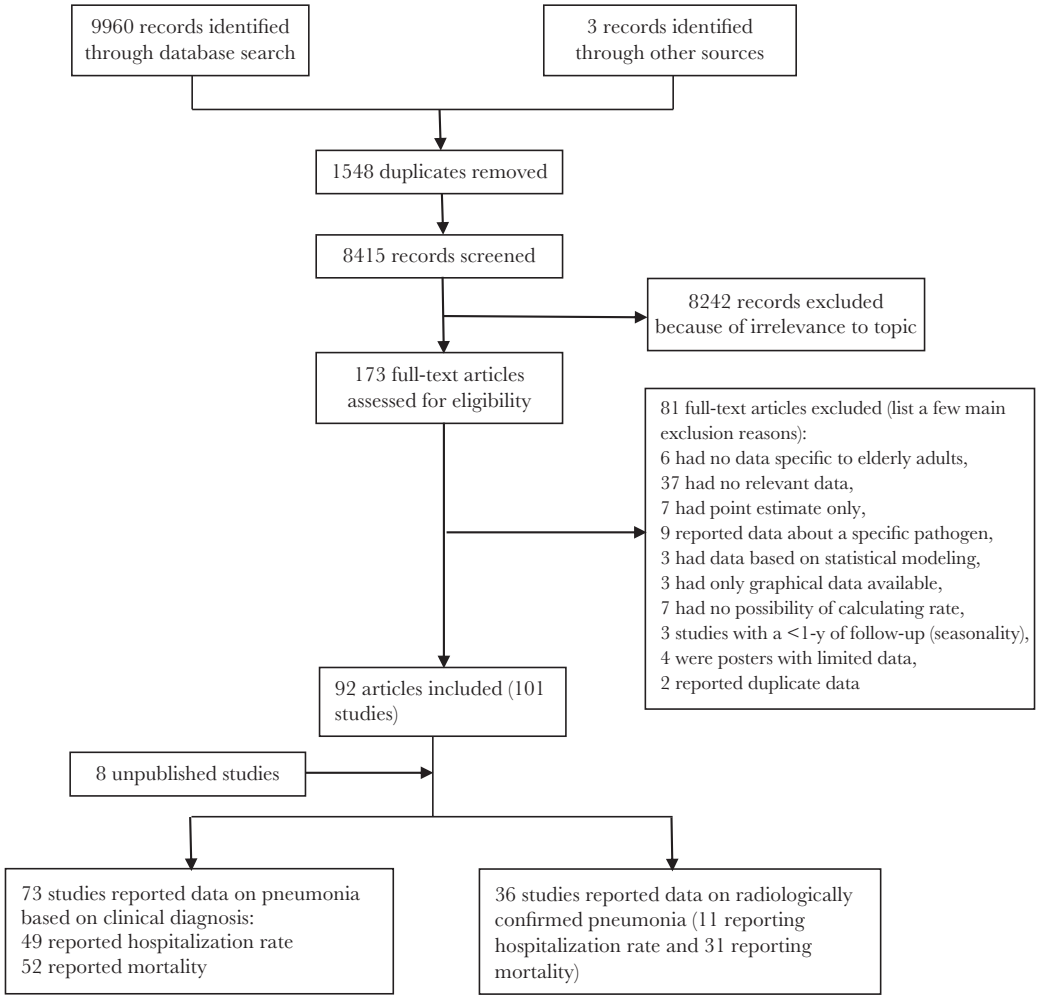

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of the literature search.

used the estimates based on studies with radiologically confirmed pneumonia case definition as a comparison group.

For 49 studies reporting the hospital admission rate with clinical pneumonia as the definition (Supplementary Table 4), the full description of study characteristics and reported data are available in Supplementary Table 5. The rate of pneumonia hospitalization in industrialized countries was estimated to be 6.8 episodes/1000 persons per year (95% CI, 4.4–10.6) in older adults aged 65–74 years, 16.4 episodes/1000 persons per year (95% CI, 10.1–26.7) in those 75–84 years, and 34.6 episodes/1000 persons per year (95% CI, 21.1–56.9) in those aged ≥85 years. For developing countries, the rate of hospital admission was estimated to be 4.9 episodes/1000 persons per year (95% CI, 3.5–6.7) in older adults aged 65–74 years with pneumonia, 14.6 episodes/1000 persons per year (95% CI, 11.2–19.0) in those aged 75–84 years, and 45.6 episodes/1000 persons per year (95% CI, 32.9–63.1) in those aged ≥85 years. The rate of hospital admission increased with age in both industrialized and developing countries. The overall number of older adults aged ≥65 years with pneumonia who were admitted to the hospital was 6.8 million (UR, 5.8 million–8.0 million), with 3.1 million (UR, 2.3 million–4.1 million) in industrialized countries and 3.7 million (UR, 3.1 million–4.5 million) in developing countries. Seven studies provided data stratified by sex, which showed that the rate of hospital admission due to pneumonia in older adults aged ≥65 years from industrialized countries was 17.3 episodes/1000 persons per year (14.5–20.7) in men and 12.9 episodes/1000 persons per year (10.1–16.4) in women. Considering that only 1 study reported sex-specific data from developing countries, a meta-analysis was not performed.

An increasing trend in the hospitalization rate with advancing age was also observed in 11 studies in which the definition of radiologically confirmed pneumonia was used. Overall, the estimated number of radiologically confirmed pneumonia cases among older adults aged ≥65 years admitted to hospitals from industrialized countries was 2.6 million (UR, 1.3 million–6.0 million). Similarly, in industrialized countries, the hospitalization rate was higher in men than in women, based on only 2

studies (13.8 episodes/1000 persons per year [95% CI, 12.0–16.0] vs 7.8 episodes/1000 persons per year [95% CI, 6.6–9.1]). There were insufficient data to develop an estimate for developing countries (0–1 study for narrow age bands) based on radiologically confirmed pneumonia.

Of 52 studies reporting mortality data using clinical pneumonia as the case definition, 45 reported hCFR, 15 reported 30-day mortality after admission, and 5 reported 12-month mortality after admission. For 45 studies with hCFR data (Supplementary Table 6), a full description of the study characteristics and their data are available in Supplementary Table 7. In industrialized countries, the meta-estimate of hCFR for older adults admitted to hospitals with pneumonia was 9.0% (95% CI, 7.0%–11.6%) for those aged 65–74 years, 12.1% (95% CI, 9.5%–15.4%) for those aged 75–84 years, and 17.5% (95% CI, 13.4%–22.7%) for those aged ≥85 years. Similarly, the hCFR increased with age in developing countries, with values of 13.0% (95% CI, 9.7%–17.4%) in the group aged 65–74 years, 17.1% (95% CI, 11.8%–24.9%) in the group aged 75–84 years, and 22.9% (95% CI, 14.7%–35.7%) in the group aged ≥85 years. Across all age bands, the hCFR in developing countries was higher than that in industrialized countries, with overlapping 95% CIs. The overall number of in-hospital deaths in older adults aged ≥65 years generated from regional and age-specific estimates was 1.1 million (UR, 0.9 million–1.4 million) in 2015, with 0.4 million deaths (UR, 0.3 million–0.6 million) in industrialized countries and 0.7 million deaths (UR, 0.5 million–1.0 million) in developing countries. Only 2 studies provided sex-specific data, resulting in hCFRs of 11.6%–11.9% in men and 9.8%–10.2% in women. The meta-estimate of 30-day mortality after admission for older adults aged ≥65 years with pneumonia was 15.9% (95% CI, 13.0%–19.3%) in industrialized countries (11 studies; there were no data for developing countries). In addition, the meta-estimate of the 12-month mortality after admission was 37.7% (95% CI, 25.3%–56.3%) among those aged ≥65 years in industrialized countries (3 studies).

There were 31 studies reporting mortality data based on radiologically confirmed pneumonia as the case definition; 19 reported hCFRs, 14 reported 30-day mortality after admission, and only 1 reported 12-month mortality after admission. Most studies only reported the data for the group aged ≥65 years without providing narrow age band–specific estimates. Therefore, overall in-hospital deaths for older adults with radiologically confirmed pneumonia were not calculated, owing to missing data in narrow age bands. The meta-estimate of hCFR for older adults aged ≥65 years was 9.1% (95% CI, 7.5%–11.1%) in industrialized countries and 10.9% (95% CI, 7.3%–16.2%) in developing countries. A sex-specific meta-estimate was only available in industrialized countries, with a value of 14.3% (95% CI, 8.7%–23.7%) in men and 8.5% (95% CI, 5.5%–13.0%) in women. The 30-day mortality after admission was 9.1% (95% CI, 6.5%–12.7%) in industrialized countries and 8.4% (95% CI, 3.7%–19.4%) in developing countries.

DISCUSSION

This is the first systematic review to evaluate and summarize the available literature and unpublished data on the burden of hospitalized pneumonia in older adults aged ≥65 years. Our review summarized data from about 17 million cases of pneumonia-related hospitalizations in older adults from 101 studies reported in 92 articles and 8 unpublished studies. We estimated that, in 2015, there were about 6.8 million hospital admissions involving in older adults with pneumonia. We further estimated that there were about 1.1 million pneumonia-related hospital deaths.

Only 25 (23%) of 109 studies reported data from developing countries. Estimates from developing countries were missing for some WHO regions (the Eastern Mediterranean Region, the South-East Asia Region, and much of the African Region), as well as for narrower age bands. This is expected because, in general, the health information systems in developing countries do not provide accurate information about the regional and national burden of pneumonia on hospital services [11]. The hospital admission estimates of pneumonia from developing countries largely came from studies where the catchment population had relatively good access to care and good healthcare-seeking behavior. We expect that many adults with pneumonia in developing countries do not receive hospital care [12]. Therefore, our global and regional estimates likely underestimate the true burden of pneumonia that should be treated in hospitals. Moreover, only 1 study provided a hospital admission rate, and 2 reported hCFRs for older adults with very severe pneumonia. More studies are needed to better understand the burden of very severe pneumonia in older adults. Although our results suggested that men had higher a hospital admission rate and hCFR, the number of available studies was limited, and conclusions can be drawn only for the entire group of adults aged ≥65 years. More studies with sex-specific data are required to provide robust evidence regarding sex-based differences.

Our estimates vary widely among regions and study sites. Comparisons among studies should be interpreted with caution because several factors may affect the estimates: differences in enrollment criteria, case definitions, demographic characteristics, geographical location of the study sites, surveillance methods, temporal variability in pneumonia incidence, cultural factors, and healthcare-seeking behavior of the underlying population. Therefore, the true uncertainties around these estimates may be larger than those expressed in the standard 95% CIs that we report.

Our findings suggest that the number of hospital admissions among individuals aged ≥65 years in industrialized countries was comparable to the number of admissions in developing countries (ie, 3.1 million and 3.7 million, respectively). This

may be partially explained by the high proportion of older adults and low thresholds for hospital admission in industrialized countries and poor care-seeking behavior in developing countries. However, the hCFR in industrialized countries was lower than that reported for developing countries (although with overlapping 95% CIs). These findings suggest that patients in industrialized countries have better access to high-quality healthcare facilities.

GBD 2015 studies estimate that the overall number of cases and deaths from LRIs in older adults aged ≥65 years were 78.8 million (95% uncertainty interval [UI], 72.5 million–84.8 million) and 1.2 million (95% UI, 1.0 million–1.3 million), respectively [1, 13]. We, however, estimated that, in 2015, there were 6.8 million pneumonia hospitalizations (UR, 5.8 million–8.0 million) and 1.1 million in-hospital deaths (UR, 0.9 million–1.4 million). Although these data are not strictly comparable owing to the different modeling methods used, they may be consistent with the interpretation that a majority of pneumonia cases (approximately 91%) were not hospitalized, while most deaths associated with pneumonia (approximately 92%) occurred in hospitals. This result is probably due to the large difference in CFR between hospital-based and outside-hospital pneumonia cases, the fact that most older adults with pneumonia from developing countries are not admitted, and possible underestimation of mortality from GBD estimates.

Developing standardized pneumonia definitions for epidemiological research and clinical trials is challenging. Among the included 109 studies, 73 reported data on an outcome that we included as clinical pneumonia (including CAP, ARI [in 3 studies], LRI [in 2], and SARI [in 1]), which was based on symptoms and signs, *International Classification Diseases, Ninth Revision, Clinical Modification* (ICD-9CM) discharge codes 480–486, or ICD-10 discharge codes J10–J18. Another 36 studies reported radiologically confirmed pneumonia. Our final estimates for all-cause pneumonia were based on the 73 studies using clinical pneumonia as the case definition, because we found substantial differences in estimates between the clinical pneumonia and radiologically confirmed pneumonia case definitions. Both the hospitalization rate and the number of hospitalized cases of radiologically confirmed pneumonia were smaller than those using the definition of all-cause clinical pneumonia. This is consistent across all age groups, indicating that, by using the definition of radiologically confirmed pneumonia, the burden of pneumonia in hospitals was likely substantially underestimated. Therefore, when limiting the analysis to older adults with radiologically confirmed pneumonia, we may have underestimated the disease burden because only a proportion of adults with clinical pneumonia had chest radiographs (eg, 50% in the study by Prapasiri et al and 60% in the study by Watt et al) [14, 15]. One study in our review presented the hospital admission data for both clinical and radiologically confirmed pneumonia [15]. This study observed that the hospitalization rate in older adults aged ≥65 years was substantially lower when radiologically confirmed CAP was used as the case definition (30.3 vs 62.2 episodes/1000 persons per year). This difference may be because some pneumonia cases do not have radiographic findings. The presence of chronic lung disease, including tuberculosis, can complicate the radiographic diagnosis of pneumonia. Significant variability also exists between reviewers in interpreting chest radiography findings [15]. In addition, since the definition of pneumonia was based on clinical and radiological criteria, the features could overlap with those from other conditions (eg, chronic lung disease and congestive heart failure). Finally, the percentage of diagnosed cases in which pathogen isolation was performed was usually low; thus, there is a possibility of misclassification of pneumonia.

We found that pneumonia hospitalization rates and hCFRs increased with age, as discussed in other studies [16]. This indicates that age might be a risk factor for pneumonia in adults. However, the majority of older adults included in our study had underlying medical conditions, which are associated with an increased risk of pneumonia and poor outcome. The study by McLaughlin et al [17] reported the hospital admission rate among individuals with CAP, which increased from low-risk adults (ie, those who were immunocompetent without chronic medical conditions) to moderate-risk adults (ie, those who were immunocompetent with ≥1 chronic medical condition), with the highest rate among high-risk adults (ie, those who were immunocompromised). Thus, comorbidities should be taken into consideration when evaluating the role of age in pneumonia hospitalizations. Most studies included a mixture of participants with or without comorbidities and did not report comorbidity-specific disease burdens. One study presented hCFRs for patients with and those without diabetes mellitus (18.7% and 21.3%, respectively) [18]. Further research into the high-risk profiles of older adults admitted to hospitals with severe or very severe pneumonia could help guide prevention and management strategies.

In conclusion, this study reviews the existing evidence regarding the burden of pneumonia resulting in hospitalization among older adults aged ≥65 years. Pneumonia is a common and severe disease among older adults. Appropriate preventive and therapeutic interventions should be developed to address the specific pathogens causing pneumonia, to minimize the disease burden.

STUDY GROUP MEMBERS

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Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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References

1. Global Burden of Disease 2015 Lower Respiratory Tract Infection Collaborators. Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory tract infections in 195 countries: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Infect Dis **2017**. https://www.ncbi.nlm.nih.gov/pubmed/28843578.
2. Jain S, Self WH, Wunderink RG, et al.; CDC EPIC Study Team. Community-acquired pneumonia requiring hospitalization among U.S. adults. N Engl J Med **2015**; 373:415–27.
3. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ **2009**; 339:b2535.
4. World Health Organization. Integrated management of adolescent and adult illness (IMAI). Geneva: WHO, **2004**.
5. United Nations Children's Fund (UNICEF). The state of the world's children 2015: reimagine the future: innovation for every child. New York: UNICEF, **2014**.
6. United Nations Children's Fund (UNICEF). The state of the world's children 2012. New York: UNICEF, **2012**.
7. United Nations Department of Economic and Social Affairs, Population Division. World population prospects: the 2017 revision, custom data acquired via website. Accessed 1 March 2018. https://population.un.org/wpp/Download/Standard/Population/.
8. Sweeting MJ, Sutton AJ, Lambert PC. What to add to nothing? Use and avoidance of continuity corrections in meta-analysis of sparse data. Stat Med **2004**; 23:1351–75.

9. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to meta-analysis. Chichester, U.K.: John Wiley & Sons, **2009**.
10. Shi T, McAllister DA, O'Brien KL, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. Lancet **2017**; 390:946–58.
11. Klingler C, Silva DS, Schuermann C, Reis AA, Saxena A, Strech D. Ethical issues in public health surveillance: a systematic qualitative review. BMC Public Health **2017**; 17:295.
12. Bigogo G, Audi A, Aura B, Aol G, Breiman RF, Feikin DR. Health-seeking patterns among participants of population-based morbidity surveillance in rural western Kenya: implications for calculating disease rates. Int J Infect Dis **2010**; 14:e967–73.
13. Global Burden of Disease 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet **2017**; 390:1151–210.
14. Prapasiri P, Jareinpituk S, Keawpan A, et al. Epidemiology of radiographically-confirmed and bacteremic pneumonia in rural Thailand. Southeast Asian J Trop Med Public Health **2008**; 39:706–18.
15. Watt JP, Moïsi JC, Donaldson RL, et al. Measuring the incidence of adult community-acquired pneumonia in a Native American community. Epidemiol Infect **2010**; 138:1146–54.
16. Buzzo AR, Roberts C, Mollinedo LG, Quevedo JM, Casas GL, Soldevilla JM. Morbidity and mortality of pneumonia in adults in six Latin American countries. Int J Infect Dis **2013**; 17:e673–7.
17. McLaughlin JM, Johnson MH, Kagan SA, Baer SL. Clinical and economic burden of community-acquired pneumonia in the Veterans Health Administration, 2011: a retrospective cohort study. Infection **2015**; 43:671–80.
18. Akirov A, Shimon I. The prognostic significance of admission blood glucose levels in elderly patients with pneumonia (GAP Study). J Diabetes Complications **2016**; 30:845–51.