PROMISE
Preparing for RSV Immunisation and Surveillance in Europe

innovative medicines initiative

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Preparing for RSV Immunisation and Surveillance in Europe

WP1 – RSV epidemiology and impact of COVID-19

D1.5 Report on understanding the disease burden of respiratory syncytial virus in young children after the start of the COVID-19 pandemic

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Definitions

- **Participants** of the PROMISE Consortium are referred to herein according to the following codes:
  1. **UEDIN**. The University of Edinburgh (United Kingdom)
  2. **UMCU**. Universitair Medisch Centrum Utrecht (Netherlands)
  3. **UA**. Universiteit Antwerpen (Belgium)
  4. **Imperial**. Imperial College of Science, Technology and Medicine (United Kingdom)
  5. **UOXF**. The Chancellor, Masters and Scholars of the University of Oxford (United Kingdom)
  6. **THL**. Terveyden Ja Hyvinvoinnin Laitos (Finland)
  7. **RIVM**. Rijksinstituut voor Volksgezondheid en Milieu (Netherlands)
  8. **NIVEL**. Stichting Nedelands Instituut voor Onderzoek van de Gezondheidzorg (Netherlands)
  9. **TUCH**. Varsinais-Suomen Sairaanhoitopiirin Kuntayhtymä (Finland)
  10. **TEAMIT**. TEAM IT Research, S.L. (Spain)
  11. **ReSViNET**. Stichting Resvinet (Netherlands)
  12. **SSI**. Statens Serum Institut (Denmark)
  13. **SERGAS**. Servizo Galego de Saúde (Spain)
  14. **PENTA**. Fondazione PENTA - For the treatment and care of children with HIV and related diseases - ONLUS (Italy)
  15. **FISABIO**. Fundación para el Fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana (Spain)
  16. **MLU**. Martin-Luther-Universitaet Halle-Wittenberg (Germany)
  17. **SP**. Sanofi Pasteur, S.A. (France)
  18. **GSK**. GlaxoSmithKline Biologicals, S.A. (Belgium)
  19. **JANSSEN**. Janssen Pharmaceutica, N.V (Belgium)
  20. **Novavax**. Novavax Inc. (United States)
  21. **Pfizer**. Pfizer Limited (United Kingdom)
  22. **AZ**. Astrazeneca AB (Sweden)

- **Grant Agreement**. (Including its annexes and any amendments) The agreement signed between the beneficiaries of the action and the IMI2 JU for the undertaking of the PROMISE project (Grant Agreement No. 101034339).
- **Project**. The sum of all activities carried out in the framework of the Grant Agreement.
- **Work plan**. Schedule of tasks, deliverables, efforts, dates and responsibilities corresponding to the work to be carried out, as specified in Annex I to the Grant Agreement.
- **Consortium**. The PROMISE Consortium, comprising the above-mentioned participants.
- **Consortium Agreement**. The agreement concluded amongst PROMISE participants for the implementation of the Grant Agreement. The agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

Abbreviations

Acronym / Abbreviation	Meaning
RSV	Respiratory syncytial virus
ALRI	Acute lower respiratory infection
UNICEF	The United Nations Children's Fund
CFR	Case fatality ratio
ICU	Intensive care unit
OxCGRT	The Oxford COVID-19 Government Response Tracker
NPIs	Non-pharmaceutical interventions
RSV GEN	Respiratory Virus Global Epidemiology Network
GLMM	Generalised linear mixed-effects model
UR	Uncertainty range
PRISMA	The Preferred Reporting Items for Systematic Reviews and Meta-Analyses
GATHER	The Guidelines for Accurate and Transparent Health Estimates Reporting

Abstract

Background The ongoing COVID-19 pandemic was reported to have impacted the RSV epidemiology and could have important implications for RSV prevention and control strategy. We aimed to understand RSV-associated ALRI hospitalisation burden in children younger than 5 years during the COVID-19 period and the possible changes in RSV epidemiology from a global perspective.

Methods We conducted a systematic literature review to identify and include published data on RSV-associated ALRI hospitalisation burden in children younger than 5 years during the COVID-19 period; we supplemented the published data by further including more granular unpublished RSV epidemiology data shared by RSV GEN collaborators. We conducted a series of generalised linear mixed-effects meta-analyses to compare age-specific annualised RSV-associated ALRI hospitalisation rates, age distribution and disease severity between pre-pandemic and pandemic periods, separately by country income region.

Results We included 61 studies, 14 from published literatures and 47 from RSV GEN; of these studies, 51, 9 and 1 were from high-income, upper-middle-income and lower-middle-income regions, respectively. The total number of RSV-associated ALRI hospitalisation in 0–<60 months in 2020 was about 36% (121,000/338,000), 18% (106,000/581,000) and 67% (942,000/1,396,000) of that in 2019 for high-income, upper-middle-income and lower-middle income countries, respectively. However, the changes in hospitalisation burden in 2021 started to vary by income region; in high-income countries, the annualised RSV-associated ALRI hospitalisation rate returned to a comparable level to 2019 by March 2022 whereas the hospitalisation rate remained lower in middle-income regions, despite higher population mobility than the pre-pandemic period in these countries. Across all time periods and all income regions, RSV-associated ALRI hospitalisation rate peaked at the age of 0–<3 months and declined substantially with increased age, although there was a significantly increased proportion of RSV-associated ALRI hospitalisation in those aged 12–<24 months during the pandemic period in both high-income and upper-middle-income regions. No substantial changes in disease severity were observed.

Conclusions Our study provides a comprehensive global overview of the changes of RSV-associated ALRI hospitalisation burden in children under five years during the COVID-19 pandemic. Despite the observed age-shift to older children in the hospitalisation burden, RSV passive immunisation strategy is expected to remain impactful in targeting protection for infants in their first 6 months of life (especially for 0–<3 months) that had the highest hospitalisation burden. While the hospitalisation rate of RSV has returned to the pre-pandemic level in high-income region, the consistently lower hospitalisation rate in middle-income regions than the pre-pandemic period might be a result of the negative impact of COVID-19 pandemic on health-care system and health-care accessibility.

1. Introduction

Human respiratory syncytial virus (RSV) is a leading cause of acute lower respiratory infection (ALRI) in infants and young children [1,2]. We previously estimated that globally in 2019, there were 33.0 million RSV-associated ALRI episodes, 3.6 million RSV-associated ALRI hospital admissions, 26,300 RSV-associated ALRI in-hospital deaths and approximately 101,000 overall deaths in children under five years [2]. Novel RSV prophylactic products targeting protection at infants have shown promises in being administered to the general infant population — the monoclonal antibody nirsevimab was approved by the European Medicines Agency to protect all infants during their first RSV season [3]; moreover, a maternal RSV bivalent vaccine reported favourable efficacy results from a phase-3 trial for protecting infants through the first 90 days of life [4].

Following the onset of the COVID-19 pandemic, low RSV activity was observed across the globe as a result of the large-scale implementation of non-pharmaceutical interventions against COVID-19 [5–7]. RSV epidemics resurged as these non-pharmaceutical interventions were lifted. However, several studies reported that RSV epidemiology might have been reshaped by the COVID-19 pandemic with regard to age distribution and disease severity although the reported changes in the RSV epidemiological characteristics were not consistent from existing local reports. Studies from France [6], Denmark [8] and Australia [9] showed that children hospitalised for RSV diseases after the COVID-19 pandemic tended to be older than those hospitalised during the pre-pandemic period whereas a study from Croatia [10] did not observe any shifts in the age distribution of hospitalised RSV cases. There were also studies on the change of disease severity showing mixed results; some reported that the proportion of severe RSV cases during the pandemic period was higher than the pre-pandemic period [10,11] while others reported no differences in disease severity [9,12]. While reports were not consistent across different locations, these possible changes in RSV epidemiology following the onset of the COVID-19 pandemic could have important implications for the RSV immunisation strategy in the upcoming RSV seasons and a comprehensive overview of the RSV disease burden during the COVID-19 pandemic in young children is needed to help inform public health decisions for the prevention and control of RSV.

In this study, we aimed to assess the burden of RSV-associated ALRI hospitalisation in children under five years during the COVID-19 pandemic period and to understand the possible changes in RSV epidemiology from a global perspective.

2. Methods

2.1. Definitions

As previously [2], ALRI was defined based on physician-confirmed diagnosis of pneumonia or bronchiolitis for studies based on hospital settings. RSV-associated ALRI was defined as ALRI with laboratory-confirmed RSV infection in upper respiratory specimens. We categorised countries into high, upper-middle, lower-middle, and low income based on the World Bank classification [13] (for consistency, the classification for the year of 2019 was applied to all analyses regardless of time period), and industrialised and developing country designations followed UNICEF categories [14]. Although the exact date of COVID-19 epidemics varied across the globe, for ease of comparison, we applied a uniform definition of the onset of the COVID-19 pandemic, the beginning of 2020.

2.2. Systematic literature review

We conducted a systematic literature review (PROSPERO registration number: CRD42022303344) to identify and include studies that reported the burden of RSV-associated hospitalisation in children under five years following the onset of COVID-19 pandemic. We searched a total of 11 electronic databases, including MEDLINE (Ovid), EMBASE (Ovid), Web of Science, Global Health (Ovid), the WHO COVID-19 Global literature on coronavirus disease database, CINAHL, LILACS, grey literature (OpenGrey) databases, China National Knowledge Infrastructure (CNKI), WanFang and CqVip for relevant studies published between January 1, 2020 and June 30, 2022 using a tailored search strategy similar to our previous reviews (Text S1).

We included studies reporting data for RSV associated ALRI necessitating hospital admission in children under five years as primary infection; reporting hospital admission rates or at least of one of the following severity measures: in-hospital case fatality ratio (CFR), proportion of hospitalised ALRI cases that needed supplemental oxygen, and proportion of hospitalised ALRI that needed mechanical ventilation or ICU admission. We only included studies reporting data for at least 12 consecutive months except for those reporting severity measures. Studies were excluded if case definition was not clearly defined or not consistently applied; or RSV infection was not laboratory-confirmed or was confirmed solely from serology; or no data were available after the onset of the COVID-19 pandemic.

Two reviewers (BC and UK) screened the literature search results with no language restrictions and extracted data independently using a tailored data extraction template. The data extraction template collected study-level information, such as location or country, study period, eligibility criteria, age group, case definition, clinical specimen and diagnostic tests, and the reported hospitalisation and mortality estimates. Any discrepancies between the two reviewers during data screening and extraction stages were arbitrated by a senior member of the review team (HN or YL).

2.3. Unpublished RSV data

To supplement data extracted from the systematic literature review, we included more granular unpublished data shared by members of the Respiratory Virus Global Epidemiology Network (RSV GEN) — we collected monthly aggregated data on RSV-associated ALRI hospitalisation between January 2019 and May 2022, by each of the following age groups: 0–<3 months, 3–<6 months, 6–<9 months, 9–<12 months, 12–<18 months, 18–<24 months and 24–<60 months. This level of granularity allowed us to analyse how the RSV hospitalisation burden might have changed over time during the

course of the pandemic and how the changes might vary by different age groups. The complete list of unpublished datasets is in appendix Table S1.

2.4. Quality assessment

For both published and unpublished RSV data, two reviewers (BC and UK) assessed the study quality using a quality scoring form identical to that used in our previous review [2,15]. Briefly, the quality scoring form assessed study quality and risk of bias based on study design, subjects, case definition, sampling strategy (for RSV testing), and diagnostic tests; for studies reporting hospitalisation rate, adjustment for health-care utilisation was also assessed. We calculated the overall score for each study after assessing each criterion as listed above; based on the individual assessment questions above, an overall quality score was calculated for each study, ranging between 0 (lowest quality) and 1 (highest quality). Regardless of the scores, all studies were included in main analysis; studies with quality scores <0.6 were excluded in sensitivity analysis.

2.5. Population mobility and COVID-19 NPI stringency data

As transmission risk of RSV was shown to be affected by population behaviours in response to the implementation and relaxation of non-pharmaceutical interventions, we decided to include country-level population mobility data and policies on non-pharmaceutical interventions (NPIs) from the Oxford COVID-19 Government Response Tracker (OxCGRT) to compare the population behaviours between different time periods of the pandemic and the pre-pandemic period. We downloaded the Google community mobility data that documented the population mobility changes compared to a pre-pandemic reference [16], and Stringency Index of COVID-19 NPIs (a composite measure ranging from 0, no interventions, to 100, strictest interventions) [17]. For Google community mobility data, we selected the mobility metric of visits to retail and recreation places as the proxy of population mobility; the mobility metric was expressed as the percentage of changes in the number of visits to retail and recreation places compared to the pre-pandemic reference period. For each country, the metric was arbitrarily set to 0 for the entire pre-pandemic period and could theoretically range between –100% (i.e., zero absolute mobility) to infinity during the pandemic period.

2.6. Data analysis

For all data analyses, we used the year of 2019 as the pre-pandemic reference; we also presented our previously published RSV disease burden estimate for the year of 2019 for comparison that was based exclusively on pre-pandemic data up to and including 2019 [2]. As RSV epidemiology could change during the course of the pandemic, we further divided the COVID-19 pandemic period into the following three 12-month periods where data allow: the year of 2020, the year of 2021, and the latest available period, between April 2021 and March 2022 (unless stated otherwise).

2.6.1. Hospitalisation rate

We conducted generalised linear mixed-effects model (GLMM) meta-analysis [18] to synthesise RSV-associated ALRI hospitalisation rate by region (income classification and country development status), age group and time period (i.e., 2019, 2020, 2021 and latest available period). Similar to our previous work [2], to account for under-testing of RSV, the RSV-associated hospitalisation rate was adjusted upwards by applying the RSV positive proportion among ALRI cases tested for RSV to the total number of tested and untested ALRI cases for each age group, if it was not done already in the

individual studies. The number of RSV-associated ALRI hospitalisation was calculated based on the population estimates for the corresponding years from World Population Prospects [19]. We calculated the median and interquartile range, across the study sites, of the average mobility metrics for each of the time periods above to accompany the rate estimates to help better interpret these rate estimates. The same analysis was repeated to obtain the hospitalisation rate of RSV-associated ALRI that required mechanical ventilation or intensive care unit (ICU) admission.

For a subset of individual studies that had monthly aggregated data on RSV-associated ALRI hospitalisation, we calculated the 12-month moving RSV-associated ALRI hospitalisation rate between January 2019 and May 2022 for each study and conducted GLMM meta-analysis similarly to above. The selection of 12-month window could account for the typical annual seasonality of RSV while allowing us to understand how the hospitalisation rate of RSV had changed in a finer time scale (i.e., the 12-month interval moved month by month). We further calculated the 12-month moving average population mobility for each study site and conducted cross-correlation analysis between the 12-month hospitalisation rate and the 12-month moving average population mobility, with a range of time lags between 0 and 11 months. For each country, we identified the time lag with the highest correlation coefficient (which needed to be over 0.5) as the optimal time lag between population mobility and hospitalisation rate. This would help understand the temporal association between changes in population mobility and rebound in hospitalisation rate.

2.6.2. Age distribution

We selected the age group of 0–<3 months as the reference, considering that this age band was available in most studies included and could be used to test out whether older age bands accounted for more RSV-associated ALRI hospitalisations relative to this youngest age band. We calculated the odds ratio (OR) for observing RSV-associated ALRI hospitalisation cases in older age groups (i.e., 3–<6 months, 6–<9 months, 9–<12 months, and 12–<24 months) during the pandemic period for each study, and then conducted GLMM meta-analysis to obtain the pooled OR separately by region, age group, and time period (i.e., 2020, 2021 and latest available period). In addition, we restricted the analysis to RSV-associated ALRI hospitalisation cases that required mechanical ventilation or ICU admission to examine whether the age distribution had changed specifically among severe cases.

2.6.3. Proportion of severe outcomes and in-hospital mortality

We considered two severe outcomes: RSV-associated ALRI hospitalisation that required supplemental oxygen, and RSV-associated ALRI hospitalisation that required mechanical ventilation or ICU admission. For each study, we calculated the OR for observing severe outcomes among all RSV-associated ALRI hospitalisation cases during the pandemic period, and then conducted GLMM meta-analysis to obtain the pooled OR separately by outcome (i.e., those requiring supplemental oxygen, and those requiring mechanical ventilation or ICU admission), age group, and time period (i.e., 2020, 2021 and latest available period).

For studies reporting in-hospital CFR, we obtained pooled meta-estimates of CFR for RSV-associated ALRI hospital admission by region, age groups and time period (here being 2019 and 2020 onwards; no further stratification due to data scarcity) using GLMM**.**

2.6.4. Uncertainty range

For estimates that were generated from single meta-analysis, the uncertainty range (UR) was derived from the coefficient and its standard error of that meta-analysis. For estimates that were generated through results from multiple meta-analyses, the UR of the estimates were generated using the Monte Carlo simulation to avoid inflation of the UR, based on 1000 samples of each of the meta-estimates from log-normal distributions, with 2.5th percentile and 97.5th percentile defining the lower and upper bounds [20].

2.7. Statistical software and checklists

All statistical analyses were done using R (version 4.1.2). This study was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (appendix pp 45–48) and in accordance with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) recommendations (appendix pp 43–44).

3. Results

We identified 2,490 records from the systematic literature search after removing duplicates and included a total of 14 studies. For unpublished data, we included data from 47 study sites from 14 countries. This brought the total number of included studies to 61 (**Figure 1**). Of the 61 studies, 15 studies contributed to the estimate of RSV-associated ALRI hospitalisation rate with the rest contributing only to the proportion of severe cases or in-hospital case fatality ratio. Among studies contributing to hospitalisation rates, 3, 3, 4 and 5 studies were from Africa, Western Pacific, North America and European region, respectively (**Figure 2**). The basic characteristics of the included studies are available in Table S2 and S3.

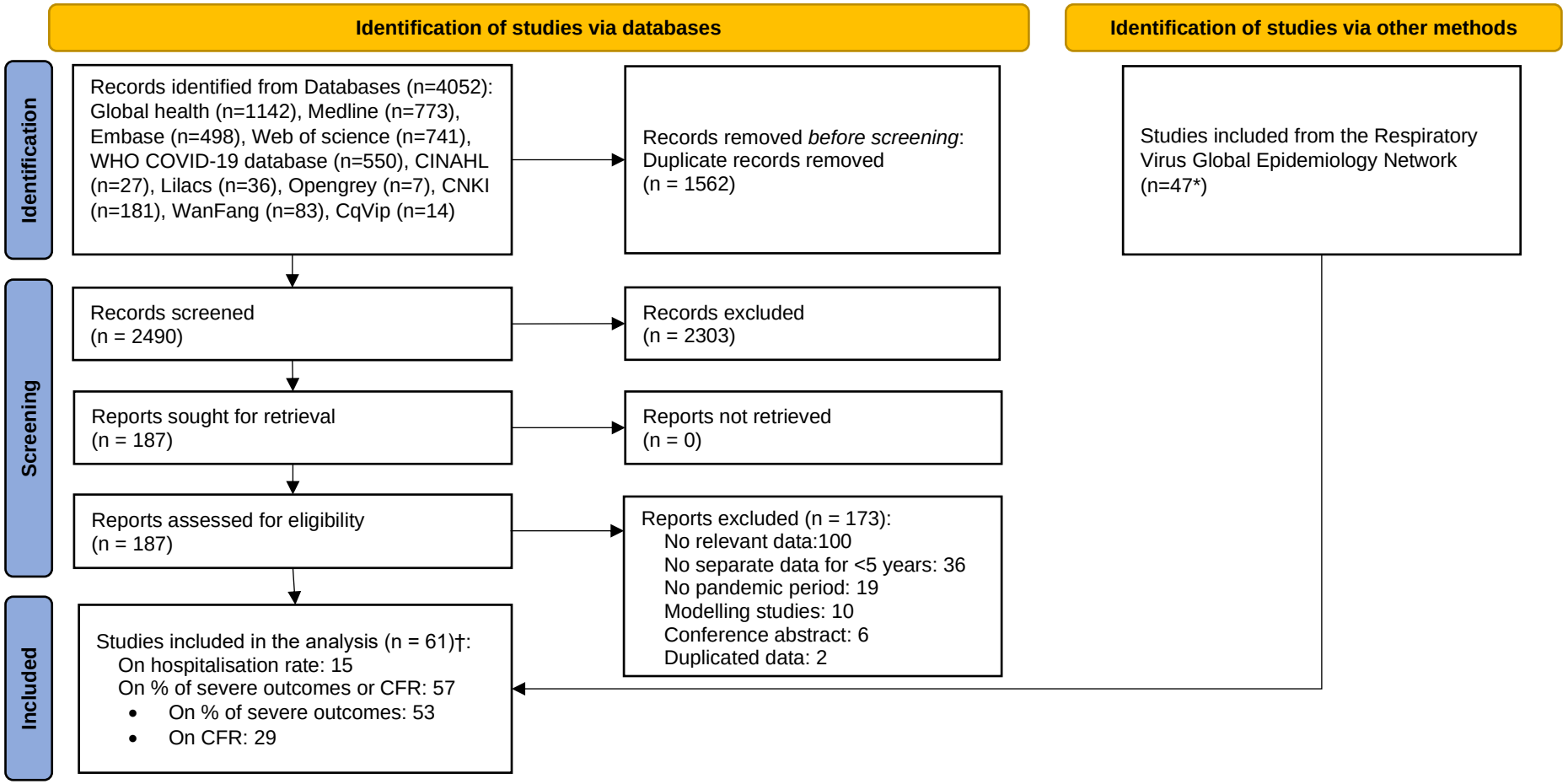

Figure 1. PRISMA diagram showing selection of studies.
Severe outcomes = hospitalised ALRI that needed supplemental oxygen or that needed mechanical ventilation or ICU admission.
RSV=respiratory syncytial virus, CFR= case fatality ratio, O2= supplemental oxygen, ICU=intensive care unit, MV=mechanical ventilation
*Details in appendix Table S1. †Studies could have contributed data to more than one category.

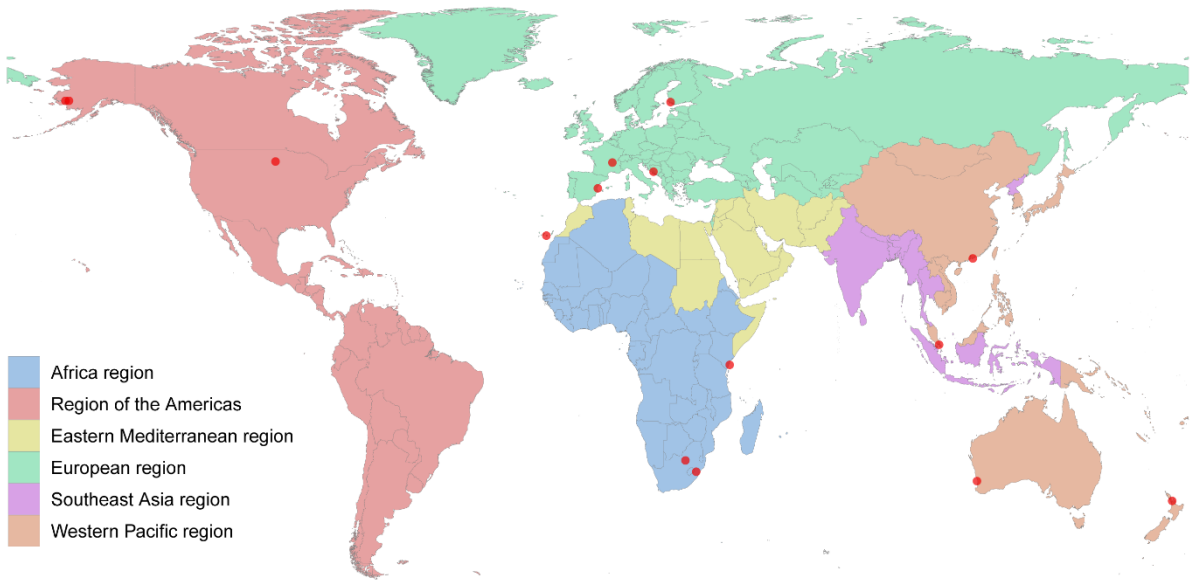

Figure 2. Geographical distribution of included studies reporting RSV-associated hospitalisation rates

3.1. Hospitalisation rates

The median of population mobility as measured by the Google mobility metric of visits to retail and recreation places decreased by 16%, 24% and 14% across high-income, upper-middle-income and lower-middle-income regions in 2020, respectively. The mobility increased in 2021 and in latest available period in all three regions; in high-income countries, the mobility had not yet returned to the pre-pandemic level by March 2022, which was 8% lower than the pre-pandemic level whereas the mobility in lower-middle-income and upper-middle-income countries included in this study had increased to above the pre-pandemic level by March 2022 (**Table 1**).

All three income regions saw substantial decreases in the hospitalisation rate of RSV-associated ALRI consistently across all age groups in 2020. The total number of RSV-associated ALRI hospitalisation in 0–<60 months in 2020 was about 36% (121,000/338,000), 18% (106,000/581,000) and 67% (942,000/1,396,000) of that in 2019 for high-income, upper-middle-income and lower-middle income countries, respectively. However, the changes in hospitalisation rate in 2021 started to vary by income region. In high-income countries, the annualised RSV-associated ALRI hospitalisation rate returned to a comparable level to 2019 by March 2022; the hospitalisation rate in children aged 0–<60 months was 5.7/1000 (95% UR: 5.0–6.6) for April 2021 to March 2022, similar to 5.2/1000 (3.7–7.1) in 2019 estimated in this study and 6.0/1000 (4.7–7.7) estimated by our previous analysis [2]; notably, the hospitalisation rate in children aged 12–<60 months was even higher in the latest available period than in 2019 despite overlapping uncertainty ranges. By contrast, the annualised RSV-associated ALRI hospitalisation rate generally remained substantially lower in 2021 and the latest available period compared to 2019 in upper-middle-income and lower-middle-income countries; the only exception was for lower-middle-income region (i.e., data from Kenya) where the hospitalisation rate for 12–<60 months returned to the pre-pandemic level (1.0/1000 [0.6–1.6] in 2021 vs 0.7/1000 [0.4–1.2] in 2019 from this study and 1.6/1000 [1.0–2.7] from our previous analysis [2]). Across all time periods and all income regions, RSV-associated ALRI hospitalisation rate peaked at the age of 0–<3 months and declined substantially with increased age (**Table 1** and Table S4). Regional estimates stratified by country development status showed similar trends; when extrapolating to global estimates, we

estimated that there were 1.0 million (0.6–2.0) and 1.8 million (1.0–3.5) RSV-associated ALRI hospitalisations in children aged 0–<60 months in 2020 and 2021, respectively, which was substantially lower than the estimates [3.3 million (1.8–6.4)] for 2019 in this analysis with fewer studies, and that in our previously analysis [3.6 million (2.9–4.6)] [2] (Table S5). Similar trends were observed when restricting to RSV-associated ALRI hospitalisation requiring mechanical ventilation or ICU admission (Table S6).

Table 1. Estimates of RSV-associated ALRI hospitalisation burden (hospitalisation rate per 1000 and number in thousands) in children younger than 5 years by World Bank income region in different time periods

	2019 (from this study)	2019 (from Li Lancet 2022)[2]	2020	2021‡	Latest (Apr 2021 to Mar 2022)
High-income Countries					
Median of stringency index (IQR)*	0	0	63.5 (50.7, 71.2)	43.1 (40.4, 46.2)	36.0 (26.4, 39.5)
Median changes in mobility (IQR)	0	0	-16.1 (-20.9, -14.9)	-9.4 (-12.3, -7.6)	-7.8 (-9.3, -6.3)
0–<3m					
Studies	7	19	9	9	8
Hospital admission rate (95% UR)	42.2 (24.7, 72.2)	34.7 (21.5, 56.2)	16.6 (5.6, 49.2)	23.7 (14.2, 39.6)	37.5 (23.2, 60.7)
Number of episodes (95% UR)	133 (78, 226)	116 (72, 188)	51 (17, 151)	72 (43, 120)	114 (70, 184)
3–<6m					
Studies	7	21	9	9	8
Hospital admission rate (95% UR)	24.7 (13.3, 45.9)	20.7 (13.5, 31.6)	11.4 (3.5, 37.6)	13.4 (8.8, 20.4)	20.7 (13.7, 31.3)
Number of episodes (95% UR)	78 (42, 144)	69 (45, 106)	35 (11, 115)	41 (27, 62)	63 (41, 95)
0–<6m†					
Studies	7	27	10	9	8
Hospital admission rate (95% UR)	34.6 (19.8, 60.4)	28.4 (20.2, 40.0)	12.0 (3.8, 37.7)	18.0 (11.2, 29.0)	29.1 (17.8, 47.4)
Number of episodes (95% UR)	217 (124, 379)	190 (135, 267)	74 (23, 232)	109 (68, 176)	177 (108, 288)
6–<12m					
Studies	7	27	10	9	8
Hospital admission rate (95% UR)	10.5 (4.7, 23.2)	11.2 (7.5, 16.7)	4.0 (1.1, 14.8)	7.2 (4.3, 12.1)	10.2 (5.9, 17.6)
Number of episodes (95% UR)	66 (30, 145)	75 (50, 112)	25 (7, 91)	44 (26, 73)	62 (36, 107)
0–<12m†					
Studies	7	41	11	9	8
Hospital admission rate (95% UR)	23.8 (13.4, 42.2)	22.0 (17.1, 28.4)	8.2 (2.7, 25.2)	13.1 (8.3, 20.8)	20.4 (12.8, 32.6)
Number of episodes (95% UR)	299 (168, 530)	294 (228, 380)	101 (33, 310)	159 (100, 252)	248 (155, 396)
12–<60m					
Studies	6	17	9	8	7
Hospital admission rate (95% UR)	1.8 (1.0, 3.1)	1.6 (1.2, 2.1)	0.8 (0.2, 2.8)	1.7 (1.0, 3.0)	2.3 (1.5, 3.4)

	2019 (from this study)	2019 (from Li Lancet 2022)[2]	2020	2021‡	Latest (Apr 2021 to Mar 2022)
Number of episodes (95% UR)	95 (55, 166)	88 (67, 116)	41 (12, 144)	86 (49, 152)	117 (78, 175)
0–<60m†					
Studies	6	51	9	8	7
Hospital admission rate (95% UR)	5.2 (3.7, 7.1)	6.0 (4.7, 7.7)	1.9 (0.5, 6.9)	4.0 (2.6, 6.3)	5.7 (5.0, 6.6)
Number of episodes (95% UR)	338 (244, 467)	409 (319, 524)	121 (33, 445)	253 (162, 396)	362 (314, 419)
Upper-middle-income Countries					
Median of stringency index (IQR)*	0	0	46.0 (46.0, 46.0)	56.6 (56.6, 56.6)	38.6 (38.6, 38.6)
Median changes in mobility (IQR)	0	0	-23.6 (-23.6, -23.6)	-4.6 (-4.6, -4.6)	3.4 (3.4, 3.4)
0–<3m					
Studies	2	16	2	2	2
Hospital admission rate (95% UR)	25.7 (8.7, 75.5)	26.4 (12.8, 54.5)	5.8 (3.2, 10.6)	10.9 (7.6, 15.5)	9.4 (1.8, 49.8)
Number of episodes (95% UR)	201 (68, 590)	236 (114, 486)	43 (23, 78)	74 (52, 106)	64 (12, 339)
3–<6m					
Studies	2	16	2	2	2
Hospital admission rate (95% UR)	14.8 (5.4, 40.2)	20.6 (11.8, 36.0)	2.5 (1.0, 6.7)	7.0 (4.3, 11.3)	4.2 (0.9, 20.1)
Number of episodes (95% UR)	115 (42, 314)	184 (106, 321)	19 (7, 49)	48 (30, 77)	29 (6, 137)
0–<6m†					
Studies	2	16	2	2	2
Hospital admission rate (95% UR)	20.2 (7.1, 57.6)	24.3 (13.2, 44.7)	4.1 (2.0, 8.6)	9.1 (6.8, 12.0)	6.8 (1.4, 33.9)
Number of episodes (95% UR)	316 (111, 900)	434 (236, 798)	61 (29, 126)	123 (93, 164)	93 (19, 462)
6–<12m					
Studies	2	15	2	2	2
Hospital admission rate (95% UR)	6.4 (3.2, 12.8)	12.1 (6.6, 22.1)	0.7 (0.3, 2.0)	2.4 (1.4, 4.1)	2.0 (0.4, 11.4)
Number of episodes (95% UR)	100 (50, 200)	215 (117, 394)	11 (4, 29)	33 (19, 56)	28 (5, 155)
0–<12m†					
Studies	2	15	2	2	2
Hospital admission rate (95% UR)	13.4 (5.1, 35.1)	18.7 (10.2, 34.5)	2.5 (1.3, 4.8)	5.6 (4.4, 7.3)	4.4 (0.9, 22.2)
Number of episodes (95% UR)	420 (161, 1097)	669 (363, 1232)	73 (37, 141)	154 (119, 198)	119 (23, 604)

	2019 (from this study)	2019 (from Li Lancet 2022)[2]	2020	2021‡	Latest (Apr 2021 to Mar 2022)
12–<60m					
Studies	2	8	2	2	2
Hospital admission rate (95% UR)	0.9 (0.3, 3.3)	1.5 (0.8, 2.8)	0.2 (0.1, 0.4)	0.4 (0.3, 0.7)	0.3 (0.1, 1.7)
Number of episodes (95% UR)	127 (36, 450)	220 (117, 415)	25 (12, 50)	56 (36, 88)	44 (9, 215)
0–<60m†					
Studies	2	16	2	2	2
Hospital admission rate (95% UR)	3.4 (1.2, 9.7)	6.2 (3.8, 10.3)	0.6 (0.3, 1.2)	1.5 (1.2, 1.8)	1.1 (0.2, 5.8)
Number of episodes (95% UR)	581 (206, 1643)	1139 (693, 1872)	106 (57, 196)	227 (182, 283)	175 (34, 900)
Lower-middle-income Countries					
Median of stringency index (IQR)*	0	0	57.4 (57.4, 57.4)	45.7 (45.7, 45.7)	52.8 (52.8, 52.8)
Median changes in mobility (IQR)	0	0	-14.4 (-14.4, -14.4)	19.9 (19.9, 19.9)	32.3 (32.3, 32.3)
0–<3m					
Studies	1	11	1	1	0
Hospital admission rate (95% UR)	26.0 (19.5, 34.7)	31.0 (17.0, 56.4)	18.8 (12.5, 28.3)	10.0 (6.1, 16.3)	–
Number of episodes (95% UR)	444 (333, 593)	485 (267, 884)	319 (212, 479)	169 (104, 277)	–
3–<6m					
Studies	1	13	1	1	0
Hospital admission rate (95% UR)	21.6 (15.4, 30.4)	19.2 (11.5, 32.1)	15.5 (9.0, 26.7)	9.3 (5.0, 17.3)	–
Number of episodes (95% UR)	369 (263, 519)	301 (180, 503)	263 (152, 452)	158 (85, 294)	–
0–<6m†					
Studies	1	12	1	1	0
Hospital admission rate (95% UR)	24.0 (19.2, 29.9)	27.9 (16.7, 46.6)	17.5 (12.6, 24.2)	9.7 (6.6, 14.2)	–
Number of episodes (95% UR)	819 (657, 1021)	873 (523, 1460)	593 (428, 822)	328 (223, 481)	–
6–<12m					
Studies	1	13	1	1	0
Hospital admission rate (95% UR)	9.4 (6.3, 13.9)	12.1 (6.5, 22.8)	6.9 (4.2, 11.5)	6.3 (3.8, 10.7)	–
Number of episodes (95% UR)	320 (216, 473)	381 (203, 715)	236 (142, 391)	215 (127, 363)	–
0–<12m†					
Studies	1	20	1	1	0

	2019 (from this study)	2019 (from Li Lancet 2022)[2]	2020	2021‡	Latest (Apr 2021 to Mar 2022)
Hospital admission rate (95% UR)	17.1 (14.1, 20.7)	17.5 (11.5, 26.5)	12.1 (9.2, 15.9)	8.1 (6.0, 11.1)	–
Number of episodes (95% UR)	1168 (964, 1416)	1095 (722, 1661)	820 (623, 1079)	551 (404, 752)	–
12–<60m					
Studies	1	12	1	1	0
Hospital admission rate (95% UR)	0.7 (0.4, 1.2)	1.6 (1.0, 2.7)	0.6 (0.3, 1.2)	1.0 (0.6, 1.6)	–
Number of episodes (95% UR)	195 (118, 323)	396 (235, 667)	171 (92, 317)	262 (158, 435)	–
0–<60m†					
Studies	1	22	1	1	0
Hospital admission rate (95% UR)	4.1 (3.4, 4.9)	6.2 (4.0, 9.4)	2.8 (2.2, 3.6)	2.4 (1.8, 3.1)	–
Number of episodes (95% UR)	1396 (1167, 1671)	1908 (1251, 2909)	942 (733, 1211)	794 (609, 1034)	–

UR=uncertainty range. *The median (IQR) COVID-19 NPI stringency index was calculated based on the last month of corresponding year by income region. † The point estimates and uncertainty range estimates are not necessarily equal to the sum of the estimates by finer age bands; this is because the studies that contributed to different age-group-specific estimates were different. ‡The year of 2021 (that is from Jan 2021 to Dec 2021, overlapping with the latest available period).

Results from the analysis of 12-month moving RSV-associated ALRI hospitalisation rate confirmed the findings above (**Figure 3**). Cross-correlation analysis suggested that the 12-month hospitalisation rate in children aged 0–<60 months was significantly correlated with the population mobility metrics in 10 countries, with 8 countries having correlation coefficients >0.5 (Figure S1 and S2); the optimal time lag ranged from 0 to 2 months in high-income countries, and from 0 to 4 months in upper-middle-income countries for children aged 0–<60 months (Table S7).

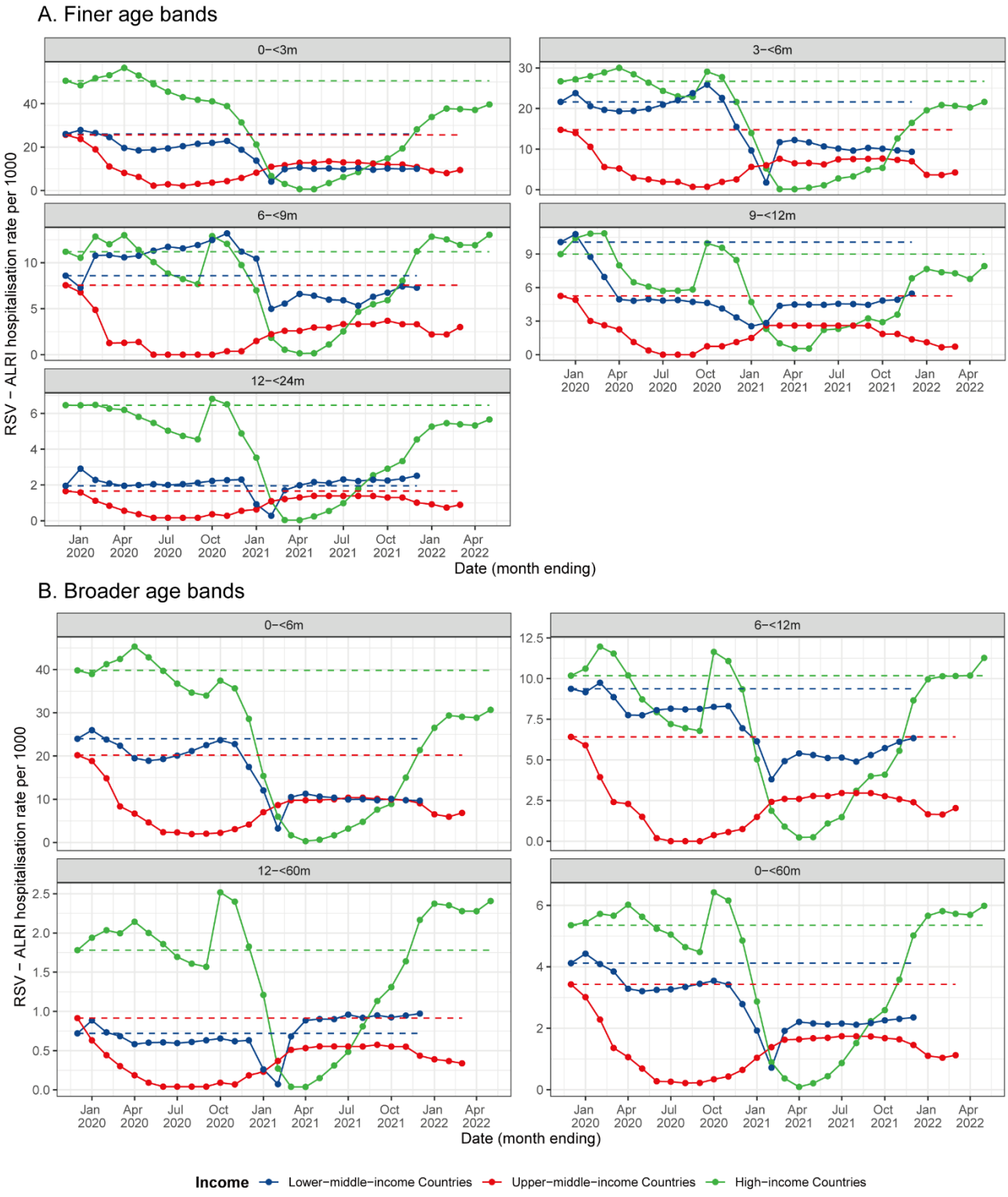

Figure 3. Change in the 12-month retrospective hospitalisation rates of RSV-associated ALRI by age group and World Bank income region. (A) 12-month moving average hospitalisation rate for finer age bands. (B) 12-month moving average hospitalisation rate for broader age bands.

3.2. Age distribution

When using age group of 0–<3 months as the reference, there was a significantly increased proportion of RSV-associated ALRI case in children aged 12–<24 months during all time periods of the pandemic (i.e., the year of 2020, 2021 and the latest available period) compared with the pre-pandemic year for high-income countries; the corresponding ORs ranged from 1.42 (95% CI: 1.08-1.85) in 2020 to 1.74 (95% CI: 1.43-2.12) in 2021 **(Figure 4, panel A)**. Results from subgroup analysis showed that both children aged 12–<18 months and 18–<24 months accounted for significantly higher proportion of RSV-associated ALRI (Figure S3). In addition, the age group of 9–<12 months accounted for significantly higher proportion in 2020 and 2021 in high-income countries but not in latest available period. In upper-middle-income countries, a significantly increased proportion of RSV-associated ALRI case was found only in children aged 12–<24 months from the latest available period **(Figure 4, panel A)**.

Similar patterns were observed, albeit with wider URs, when restricting to RSV-associated ALRI hospitalisation that required supplemental oxygen (Figure S4) and when restricting to RSV-associated ALRI hospitalisation that required mechanical ventilation or ICU admission **(Figure 4, panel B)**.

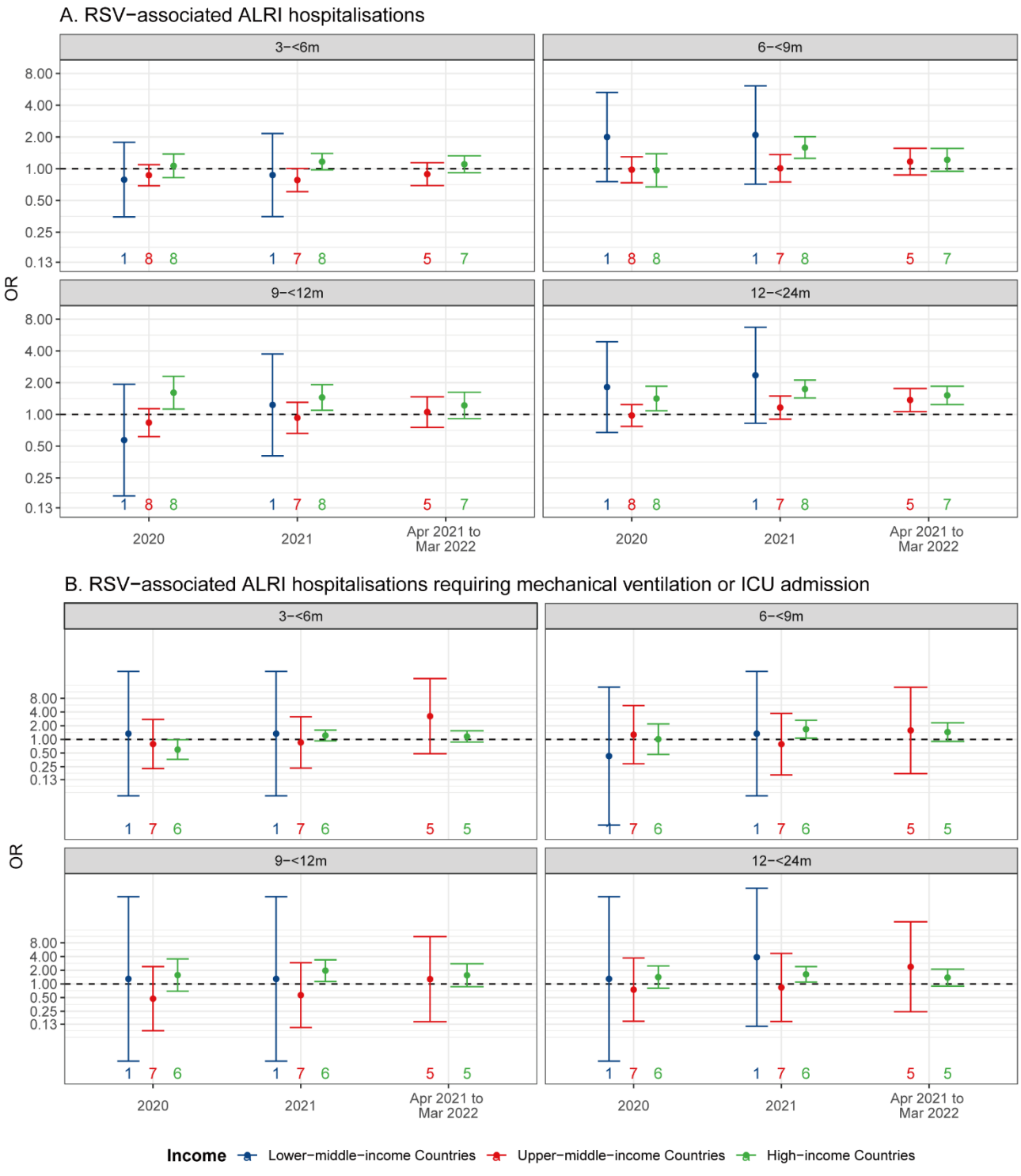

Figure 4. Odds ratio for observing RSV-associated ALRI hospitalisation in older age groups (compared with 0–<3 months) during the COVID-19 pandemic period. A) RSV-associated ALRI hospitalisation; B) RSV-associated ALRI hospitalisation requiring mechanical ventilation or ICU admission (a subset of ALRI). Number at the bottom of each panel indicates the number of data-points contributing to each group. OR=odds ratio. ICU=intensive care unit.

3.3. Proportion of severe outcomes and in-hospital CFR

We did not observe consistent patterns regarding the changes in the proportion of severe outcomes (i.e., proportion of RSV-associated ALRI hospitalisation that required supplemental oxygen and proportion of RSV-associated ALRI hospitalisation that required mechanical ventilation or ICU admission) although statistically significant findings were noted for certain combinations of age groups and time periods (**Figure 5**). Based on 32 studies (25 from Spain), an additional analysis suggested that the pandemic period was associated with increased risk of hospitalisation requiring mechanical ventilation or ICU admission for children aged 0–<24 months in 2020 (Figure S5).

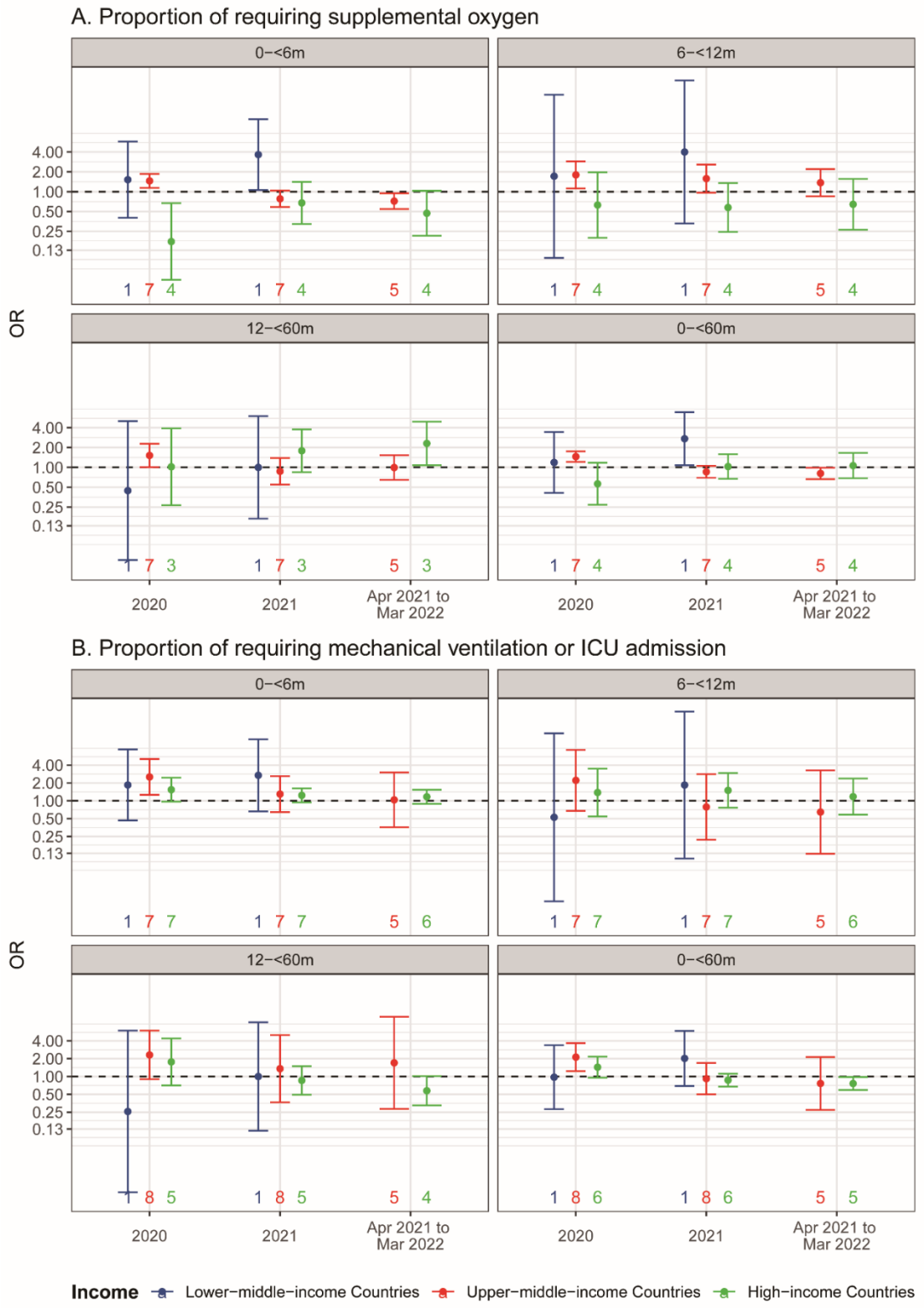

Figure 5. Comparison of proportion of RSV-associated ALRI that needed supplemental oxygen and ALRI requiring mechanical ventilation or ICU admission (both are subsets of RSV-ALRI) between pre-pandemic and pandemic period, by World Bank Income Region and age group. Number at the bottom of each panel indicates the number of data-points contributing to each group. OR=odds ratio. ICU=intensive care unit.

As shown in **Table 2**, the in-hospital CFR of RSV-associated ALRI appeared to be lower among infants during the pandemic period across high-income and upper-middle-income regions albeit with wide URs due to sparse data on in-hospital RSV deaths; for lower-middle-income region (i.e., Kenya), increased in-hospital CFR was observed in infants.

Table 2. Estimates of RSV-associated ALRI in-hospital CFR in children younger than 5 years by World Bank income region in different time periods

	2019 (from this study)	2019 (from Li Lancet 2022) [2]	2020 to latest (May 2022)
High-income Countries			
0–<12m			
Studies	10	29	13
In-hospital CFR (%) (95% UR)	0.2 (<0.05, 0.6)	0.1 (0.1, 0.3)	<0.05 (<0.05, 0.3)
12–<60m			
Studies	9	17	10
In-hospital CFR (%) (95% UR)	0.3 (<0.05, 2.2)	0.2 (0.1, 0.4)	0.3 (0.1, 1.2)
0–<60m			
Studies	10	26	13
In-hospital CFR (%) (95% UR)	0.2 (0.1, 0.6)	0.1 (0.1, 0.2)	0.1 (<0.05, 0.3)
Upper-middle income Countries			
0–<12m			
Studies	8	27	8
In-hospital CFR (%) (95% UR)	0.4 (0.1, 1.0)	0.8 (0.5,1.3)	0.1 (0.0, 0.4)
0–<60m			
Studies	9	30	9
In-hospital CFR (%) (95% UR)	0.2 (0.1, 0.7)	0.6 (0.3, 1.0)	0.1 (0.0, 0.3)
Low-middle-income Countries			
0–<12m			
Studies	1	22	1
In-hospital CFR (%) (95% UR)	1.9 (0.5, 7.4)	1.5 (0.7, 3.2)	2.2 (0.6, 8.4)
0–<60m			
Studies	1	26	1
In-hospital CFR (%) (95% UR)	1.7 (0.4, 6.5)	0.8 (0.4, 1.5)	1.7 (0.4, 6.6)

UR=uncertainty range. CFR=case fatality ratio.

4. Discussion

In the present study, we found that RSV-associated ALRI hospitalisation rates decreased consistently across different regions following the onset of the COVID-19 pandemic in 2020, along with the decrease in the population mobility; in 2021, however, hospitalisation rates of RSV started to increase in high-income countries and returned to the pre-pandemic level as of March 2022 whereas hospitalisation rates of RSV in middle-income regions remained lower than the pre-pandemic level. Consistent with the pre-pandemic period, RSV-associated ALRI hospitalisation rate peaked at the age of 0–<3 months and declined substantially with increase in age during the pandemic period, although there was a significantly increased proportion of RSV-associated ALRI hospitalisation in those aged 12–<24 months in both high-income and upper-middle-income regions. No substantial changes in disease severity were observed.

We used the year of 2019 as the reference for assessing the changes in RSV epidemiology during the pandemic period, assuming that RSV epidemiology would have remained stable had there been no COVID-19 pandemic. This assumption was supported by our previous analysis of RSV-associated hospitalisations across 58 countries, in which we showed that the hospitalisation rate of RSV-associated ALRI in children aged younger than 5 years fluctuated from 0.8 to 1.2 times the country's median yearly rate for most of the years and that there was not a consistent trend over time [21]. The assumption was also supported by the broadly consistent estimates for the year 2019 from this analysis and those from our previous global estimates that pooled all data in 2019 and before [2].

The consistently low hospitalisation rates of RSV in young children in 2020 is well expected along with the substantial decrease in the population mobility. This was reflected in the cross-correlation results between population mobility and hospitalisation rate. However, the relatively low hospitalisation rates of RSV starting from 2021 in middle-income countries could not be well explained by population mobility alone given that the population mobility in middle-income countries including in this study had returned to (if not already exceeded) the pre-pandemic level. By contrast, the hospitalisation rates of RSV had returned to the pre-pandemic level by March 2022 in high-income countries despite the lower population mobility compared to the pre-pandemic period. One explanation for the discrepancy is that the health-care system in middle-income countries had been over-burdened by COVID-19 patients and was less resilient than the high-income countries included in this study [22,23]; in addition, access to health-care services might also have been impacted in these middle-income countries [24]. We previously highlighted the striking gap between the RSV morbidity and mortality in the community and in hospitals in low- and middle-income countries [2]; taken together with the findings from this study, this gap could be even more substantial than the pre-pandemic period although active community-based studies are warranted to confirm this speculation. The findings above reinforce the need of RSV immunisation programme for the low- and middle-income countries.

Consistent with the pre-pandemic period, RSV-associated ALRI hospitalisation rate peaked at the age of 0–<3 months and declined with increase in age across all regions. Those aged 0–<6 months (primarily 0–<3 months) continued to have the highest hospitalisation burden of RSV and therefore RSV passive immunisation programmes targeting at the first six months of life should remain impactful. Despite the overall consistency in age patterns of RSV-associated ALRI hospitalisation rate between pre-pandemic and pandemic periods, we did observe significantly higher proportions of RSV related hospitalisation in older children aged 12–<24 months (which also held for 12–<18 and 18–<24 months, separately) during the pandemic period, which was consistent with existing local reports [6,8,9,25]. This age shift was likely a result of the "immunity debt" that was caused by the reduced exposure to RSV in those born during the early phase of the pandemic when large-scale non-pharmaceutical interventions were implemented [6,8,9,25]; this cohort of infants remained susceptible

later when RSV activity resurged. A recently published mathematical modelling study supported the speculation of “immunity debt” by replicating a similar age shift in those hospitalised for RSV [26], although it remains unknown whether and for how long this age shift will hold in the upcoming years.

We observed large variations in the proportion of severe outcomes among those hospitalised for RSV across the world (based on local reports); as a result, the pooled global estimate remained inconclusive. Several factors could help explain the observed large variations. First, health-care seeking behaviour could have altered during the pandemic period; parents might only choose to seek health-care when their children were severely ill; meanwhile, eligibility for hospitalisation might have changed as a response to the pandemic. Second, data showed that coverage of pneumococcal conjugate vaccine (PCV) declined during the pandemic [27]; this could have resulted in an increased number of severe ALRI hospitalisations where pneumococcal infection was involved. Third, the prevalence of common risk factors for severe outcomes, such as prematurity and comorbidities [28], could have changed. Fourth, the overall increase in the susceptibility due to the reduced exposure to RSV in the early phase of the pandemic might be associated with increased RSV disease severity; a recently published cohort study in Denmark found that older children without known risk factors for severe RSV disease had atypical complications that led to intubation [8].

Our study has limitations. First, as a global-level systematic analysis, we acknowledged common sources of heterogeneities such as study setting, case definition, health-care seeking behaviour, RSV testing criteria and diagnostic assay, and criteria for admission. In addition, we also acknowledged new sources of heterogeneities specific to our analysis. Study sites across the globe had different trajectories of COVID-19 epidemics and response; such asynchrony could complicate interpretation of the meta-estimates. We tried to reconcile these heterogeneities by focusing only on the annualised hospitalisation burden of RSV (rather than a month-by-month estimate) that could help filter out the atypical timing of RSV epidemics. Second, testing practices would have varied substantially during the pandemic period and the impact of the COVID-19 pandemic on RSV testing practices varied in different income countries, although under-testing for RSV was adjusted as before [2]; due to the same reason, we did not consider routine health-care data in this analysis as testing practices were not known. Third, we used the Google community mobility and the COVID-19 NPI stringency index data to help interpret the observed changes in hospitalisation rates of RSV during different time periods; however, both data had shortcomings — the mobility metrics were based on Google services users who enabled their location history, so might not represent the mobility patterns of infant and children population; the COVID-19 NPI stringency index was one single composite metric that might not capture well the substantial variations in the contents of different NPIs across different countries.

During the COVID-19 pandemic, resources were reallocated to the prevention and treatment for COVID-19, and especially for adult population; as a result, data on RSV disease burden in young children were relatively sparse and most of these data were from high-income countries (mainly in European region) when compared with our previously published RSV disease burden estimate for the year of 2019 [2]. This was reflected in the relatively wide URs reported in this study, particularly for the CFR estimates. Non-significant estimates should not be interpreted as absence of significance. Low- and lower-middle-income countries that were believed to have most substantial RSV disease burden were largely underrepresented. In this study, only one country (i.e., Kenya) was from lower-middle-income region and no countries were included from low-income region. More studies / high quality surveillance data from low- and lower-middle-income countries are warranted to understand how the RSV disease burden might have changed after the onset of the COVID-19 pandemic. This underscores the need to maintain robust surveillance for common respiratory pathogens during future pandemics. Moreover, the ongoing COVID-19 pandemic has also disrupted community-based studies that are essential for understanding the underlying disease burden of RSV that could not receive quality health care in low- and middle-income countries.

5. Conclusion and next steps

In summary, our study provides a comprehensive global overview of the changes of hospitalisation burden of RSV in young children during the COVID-19 pandemic. Despite the observed age-shift to older children in the hospitalisation burden, RSV passive immunisation strategy is expected to remain impactful in targeting protection during the first 6 months of life. While the hospitalisation rates of RSV have returned to the pre-pandemic level in high-income region, the consistently lower hospitalisation rates in middle-income regions than the pre-pandemic period might be a result of the negative impact of COVID-19 pandemic on health-care system and health-care accessibility. RSV surveillance needs to be established (or re-established) to monitor the changes in RSV epidemiology, especially in low- and lower-middle-income countries.

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Supplemental Material

Understanding the disease burden of respiratory syncytial virus in young children after the start of the COVID-19 pandemic

CONTENTS

Text S1. Search Strategy

Medline

1. exp Respiratory Syncytial Viruses/ or exp Respiratory Syncytial Virus, Human/ or exp Respiratory Syncytial Virus Infections/ or RSV.mp.
2. respiratory syncytial virus*.mp.
3. pneumonia.mp. or exp Pneumonia/ or exp Pneumonia, Viral/
4. bronchiolitis.mp. or exp Bronchiolitis/ or exp Bronchiolitis, Viral/
5. exp Respiratory Tract Infections/ or respiratory infection*.mp.
6. exp Respiratory Tract Diseases/ or respiratory disease*.mp.
7. incidence.mp. or exp Incidence/
8. prevalence.mp. or exp Prevalence/
9. exp Child Mortality/ or exp Infant Mortality/ or mortality.mp. or exp Hospital Mortality/ or exp Mortality/
10. death*.mp. or exp Death/ or exp "Cause of Death"/
11. morbidity.mp. or exp Morbidity/
12. burden.mp.
13. epidemiology.mp. or exp Epidemiology/
14. 1 or 2
15. 3 or 4 or 5 or 6
16. 7 or 8 or 9 or 10 or 11 or 12 or 13
17. 15 or 16
18. 14 and 17
19. limit 18 to (yr="Jan 2020–Jun 2022" and ("all infant (birth to 23 months)" or "newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)") and (female or humans or male))

EMBASE

1. RSV.mp. or exp Respiratory syncytial pneumovirus/ or exp respiratory syncytial virus infection/
2. respiratory syncytial virus*.mp.

3. exp community acquired pneumonia/ or exp pneumonia/ or exp virus pneumonia/ or exp infectious pneumonia/ or pneumonia.mp.

4. bronchiolitis.mp. or exp bronchiolitis/ or exp viral bronchiolitis/

5. exp respiratory tract infection/ or exp lower respiratory tract infection/ or respiratory infection*.mp.

6. exp respiratory tract disease/ or respiratory disease*.mp.

7. exp incidence/ or incidence.mp.

8. prevalence.mp. or exp prevalence/

9. exp newborn mortality/ or exp mortality/ or exp childhood mortality/ or mortality.mp. or exp infant mortality/

10. exp death/ or death*.mp. or exp "cause of death"/ or exp child death/

11. morbidity.mp. or exp morbidity/ or exp newborn morbidity/

12. burden.mp.

13. exp epidemiology/ or epidemiology.mp.

14. 1 or 2

15. 3 or 4 or 5 or 6

16. 7 or 8 or 9 or 10 or 11 or 12 or 13

17. 15 or 16

18. 14 and 17

19. limit 18 to (yr=" Jan 2020 –Jun 2022" and (infant or preschool child <1 to 6 years>))

Global Health

1. RSV.mp.

2. exp human respiratory syncytial virus/

3. respiratory syncytial virus*.mp.

4. exp community acquired pneumonia/ or pneumonia*.mp. or exp pneumonia/

5. bronchiolitis.mp. or exp bronchiolitis/

6. respiratory infection*.mp.

7. exp respiratory diseases/

8. respiratory disease*.mp.

9. incidence.mp. or exp disease incidence/ or exp incidence/

10. prevalence*.mp. or exp disease prevalence/

11. mortality.mp. or exp infant mortality/ or exp neonatal mortality/ or exp mortality/

12. death*.mp. or exp death/ or exp "causes of death"/

13. morbidity.mp. or exp morbidity/

14. exp epidemiology/ or epidemiology.mp.

15. burden.mp.

16. 1 or 2 or 3

17. 4 or 5 or 6 or 7 or 8

18. 9 or 10 or 11 or 12 or 13 or 14 or 15

19. 17 or 18

20. 16 and 19

21. limit 20 to yr="Jan 2020 –Jun 2022"

CINAHL

S1= (MH “respiratory syncytial virus infections”) OR (MH “respiratory syncytial viruses”) OR “respiratory syncytial virus”

S2= “RSV”

S3= (MH “pneumonia+”) OR “pneumonia” OR (MH “pneumonia, viral”) OR (MH “community-acquired pneumonia”)

S4= (MH “bronchiolitis+”) OR “bronchiolitis”

S5= (MH “respiratory tract infections+”) OR “respiratory infection”

S6= (MH “respiratory tract diseases+”) OR “respiratory disease”

S7= (MH “incidence”) OR “incidence”

S8= (MH “prevalence”) OR “prevalence”

S9= (MH “mortality+”) OR “mortality” OR (MH “infant mortality”) OR (MH “child mortality”) OR (MH “hospital mortality”)

S10= (MH “death+”) OR “death” OR (MH “cause of death”) OR (MH “infant death+”)

S11= (MH “morbidity+”) OR “morbidity”

S12= “burden”

S13= (MH “epidemiology+”) OR “epidemiology”

S14= S1 OR S2

S15= S3 OR S4 OR S5 OR S6

S16= S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13

S17= S15 OR S16

S18= S14 AND S17

Limiters: Published year: Jan 2020 – Jun 2022; Age groups: infant, newborn: birth–1 month, infant: 1–23 months, child, preschool: 2–5 years

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Web of Science

Topic= (respiratory syncytial virus) AND Topic= (epidemiology) AND Topic= (children)

From Jan 2020 to Jun 2022

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the WHO COVID-19 Global literature on coronavirus disease database

(RSV OR respiratory syncytial virus) AND (respiratory infection* or pneumonia or bronchiolitis) AND (child* or infant*)

LILACS (AMRO/PAHO)

Respiratory syncytial virus in All Indexes

OpenGrey (former: SIGLE)

Respiratory syncytial virus

CNKI

Topic: respiratory infection or pneumonia or bronchiolitis

And Topic: respiratory syncytial virus

And Topic: children

Publication time: Jan 2020 – Jun 2022

Wanfang Data

All (vague): respiratory infection or

All (vague): pneumonia or

All (vague): bronchiolitis and

All (vague): respiratory syncytial virus and

All (vague): children

Time: Jan 2020 – Jun 2022

Subject field: Medicine and health

CQVIP

Title/key word: respiratory tract infection

Or Title/key word: pneumonia

Or Title/key word: bronchiolitis

And Title/key word: respiratory syncytial virus

And Title/key word: children

Time: Jan 2020 – Jun 2022

Subject field: Medicine and health

Table S1. Summary of unpublished data from Respiratory Virus Global Epidemiology Network (i.e., previously RSV GEN) investigators

SID	Reference	Location	Study period	Published reference
U301	Josko Markic and colleagues	Croatia, Split	2019/1-2022/5	Mrcela et al. 2022 [1]
U302_01	Quique Bassat and colleagues	Spain, de Albacete	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_02	Quique Bassat and colleagues	Spain, de Navarra	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_03	Quique Bassat and colleagues	Spain, Madrid	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_04	Quique Bassat and colleagues	Spain, Madrid	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_05	Quique Bassat and colleagues	Spain, Madrid	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_06	Quique Bassat and colleagues	Spain, de Alicante	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_07	Quique Bassat and colleagues	Spain, de Castellon	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_08	Quique Bassat and colleagues	Spain, Madrid	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_10	Quique Bassat and colleagues	Spain, Madrid	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_13	Quique Bassat and colleagues	Spain, de Zaragoza	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_14	Quique Bassat and colleagues	Spain, Tarragona	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_16	Quique Bassat and colleagues	Spain, Madrid	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_17	Quique Bassat and colleagues	Spain, Catalonia	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_18	Quique Bassat and colleagues	Spain, Granada	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_19	Quique Bassat and colleagues	Spain, Madrid	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_20	Quique Bassat and colleagues	Spain, de Valladolid	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]

SID	Reference	Location	Study period	Published reference
U302_21	Quique Bassat and colleagues	Spain, Madrid	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_23	Quique Bassat and colleagues	Spain, Madrid	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_24	Quique Bassat and colleagues	Spain, de Leon	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_25	Quique Bassat and colleagues	Spain, Extremadura	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_27	Quique Bassat and colleagues	Spain, Andalucia	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_29	Quique Bassat and colleagues	Spain, Madrid	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_31	Quique Bassat and colleagues	Spain, de Gran Canaria	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_32	Quique Bassat and colleagues	Spain, Madrid	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U302_33	Quique Bassat and colleagues	Spain, Catalonia	2019/1-2020/12	Torres-Fernandez et al. 2021 [2]
U303	Ainara Mira and colleagues	Spain, Valencia Region	2019/1-2022/5	Mira-Iglesias et al. 2022 [3]
U304	Heather Zar and colleagues	South Africa, Edendale	2019/1-2022/3	Update of the previous RSV GEN data (original data id: U113*) [4]
U305	Heather Zar and colleagues	South Africa, Klerksdorp	2019/1-2022/3	Update of the previous RSV GEN data (original data id: U114*) [4]
U306	Euri Seo and colleagues	Republic of Korea, Goyang-si, Gyeonggi-do	2019/1-2022/5	Update of the previous RSV GEN data (original data id: U129*) [4]
U307	Marie-Noelle and colleagues	Netherlands, Netherlands	2019/1-2022/5	None

SID	Reference	Location	Study period	Published reference
U308	Rosalyn Singleton and colleagues	United States of America, Yukon Kuskokwim, Alaska	2019/1-2022/5	None
U309	Rosalyn Singleton and colleagues	United States of America, Southwest United States	2019/1-2022/5	None
U310	Rosalyn Singleton and colleagues	United States of America, Yukon Kuskokwim, Alaska	2019/1-2022/5	Update of the previous RSV GEN data (original data id: U116*) [4]
U311	Giorgi Chakhunashvili and colleagues	Georgia, Tbilisi, Kutaisi	2019/1-2022/5	Update of the previous RSV GEN data (original data id: U122*) [4]
U312	Terho Heikkinen and colleagues	Finland, Turku	2019/1-2022/5	Update of the previous RSV GEN data (original data id: U102*) [4]
U313	Teresa Bandeira and colleagues	Portugal, Lisbon	2019/1-2022/5	None
U314	Heather Zar and colleagues	South Africa, Agincourt and Tintswalo	2019/1-2022/5	None
U315	Heather Zar and colleagues	South Africa, Helen Joseph and Rahima Moosa	2019/1-2022/5	None

SID	Reference	Location	Study period	Published reference
U316	Heather Zar and colleagues	South Africa, Cape Town	2019/1-2022/5	None
U317	James Nokes and colleagues	Kenya, Kilifi	2019/1-2021/12	Update of the previous RSV GEN data (original data id: U110*) [4]
U318	Yung Chee Fu and colleagues	Singapore, Singapore city (KK hospital)	2019/1-2022/5	None
U319	Daria Baibus and colleagues	Russian Federation, St. Petersburg	2019/1-2022/4	None
U320	Daria Baibus and colleagues	Russian Federation, St. Petersburg	2019/1-2022/5	None
U321	Daria Baibus and colleagues	Russian Federation, St. Petersburg	2019/1-2022/5	None
U322	Jean-sebastien Casalegno and colleagues	France, Lyon	2019/1-2022/5	Casalegno et al. 2021 [5]
U323_p	Sue Huang and colleagues	New Zealand, Auckland	2019/5-2022/5	Huang et al. 2022 [6]
U323_r	Sue Huang and colleagues	New Zealand, Auckland	2019/5-2022/5	Huang et al. 2022 [6]

*See pp 9–11 in the appendix of Li et al. Lancet 2022 [4].

Table S2. Summary of studies that contributed to RSV-associated ALRI hospital admission rate estimates.

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Chiu et al. 2022 [7]	China, Hong Kong	Hong Kong	2017/01–2021/01	65	0-<6m, 6-<12m, 12–<24m, 24–<60m	acute febrile illness or respiratory signs/ symptoms	respiratory samples	PCR	0.67
Reyes-Dominguez et al. 2021 [8]	Spain	Gran Canaria	2016/01–2021/06	87	0–<24m	RSV acute bronchiolitis	NPW, nasal swabs or aspirate specimens	immunochromatography, PCR	0.60
Foley et al. 2022 [9]	Australia	Cologne	2019/01–2021/03	328	0–<12m, 12–<24m, 24–<48m	symptomatic children	respiratory samples	PCR	0.67
Markic et al. Unpub	Croatia	Split	2019/01–2022/05	203	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	Physician diagnosed	NPA	Rapid antigen tests	0.50
Mira et al. Unpub	Spain	Valencia Region	2019/01–2022/05	286	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	ILI (WHO)	NPS and/or pharyngeal/ nasal swabs	PCR	0.84

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Zar et al. Unpub	South Africa	Edendale	2019/01–2022/03	256	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	Physician diagnosed LRTI	NPS	PCR	0.84
Zar et al. Unpub	South Africa	Klerksdorp	2019/01–2022/03	116	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	Physician diagnosed LRTI	NPS	PCR	0.84
Singleton et al. Unpub	United States of America	Yukon Kuskokwim, Alaska	2019/01–2022/05	125	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	ARI	MT swab	PCR	0.84
Singleton et al. Unpub	United States of America	Southwest United States	2019/01–2022/05	93	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<36m	ARI	MT swab	PCR	0.84
Singleton et al. Unpub	United States of America	Yukon Kuskokwim, Alaska	2019/01–2022/05	200	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	ARI hospitalization	NPS	PCR, rapid antigen	0.67

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Heikkinen et al. Unpub	Finland	Turku	2019/01–2022/05	296	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	hospitalised Bronchiolitis and/or pneumonia	NPS	Antigen test	0.50
Nokes et al. Unpub	Kenya	Kilifi	2019/01–2021/012	235	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	WHO syndromic pneumonia	NP/OP	Multiplex PCR testing	0.84
Yung et al. Unpub	Singapore	Singapore city (KK hospital)	2019/01–2022/05	3873	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	Physician diagnosed	NPS	PCR	0.84
Casalegno et al. Unpub	France	Lyon	2019/01–2022/05	1538	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	WHO definition LRTI	NPS, NPA, BAL	PCR	0.84
Huang et al. Unpub	New Zealand	Auckland	2019/05–2022/05	466	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	SARI (WHO)	NPS, NPA	PCR	1.00

ŧNumber of RSV associated ALRI hospital admissions; m = months; RSV = respiratory syncytial virus; ALRI = acute lower respiratory infection; LRTI = lower respiratory tract infection; NPA = nasopharyngeal aspirate; NPS = nasopharyngeal swab; NPW = nasopharyngeal wash; OPS = oropharyngeal swab; BAL = bronchoalveolar lavage; PCR = polymerase chain reaction; SARI = Severe acute respiratory infection; ILI = influenza-like illness; WHO = World Health Organization; QA = quality assessment; Unpub = unpublished data.

Table S3. Summary of studies that contributed to RSV in-hospital case fatality ratio or proportion of requiring supplemental oxygen or ICU admission estimates.

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Markic et al. Unpub	Croatia	Split	2019/01-2022/05	203	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	Physician diagnosed	NPA	Rapid antigen tests	0.50
Bassat et al. Unpub *	Spain	de Albacete	2019/01-2020/12	153	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	de Navarra	2019/01-2020/12	126	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Madrid	2019/01-2020/12	88	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Madrid	2019/01-2020/12	179	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Madrid	2019/01-2020/12	69	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Bassat et al. Unpub*	Spain	De Alicante	2019/01-2020/12	231	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	de Castellon	2019/01-2020/12	118	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Madrid	2019/01-2020/12	109	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Madrid	2019/01-2020/12	88	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	de Zaragoza	2019/01-2020/12	226	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Tarragona	2019/01-2020/12	39	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Madrid	2019/01-2020/12	16	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Catalonia	2019/01-2020/12	603	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Bassat et al. Unpub*	Spain	Granada	2019/01-2020/12	244	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Madrid	2019/01-2020/12	63	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	de Valladolid	2019/01-2020/12	72	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Madrid	2019/01-2020/12	82	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Madrid	2019/01-2020/12	105	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	de Leon	2019/01-2020/12	138	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Extremadura	2019/01-2020/12	50	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Andalucia	2019/01-2020/12	79	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Bassat et al. Unpub*	Spain	Madrid	2019/01-2020/12	59	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	de Gran Canaria	2019/01-2020/12	279	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Madrid	2019/01-2020/12	94	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Bassat et al. Unpub*	Spain	Catalonia	2019/01-2020/12	309	0–<24m	acute bronchiolitis	NPS and/or pharyngeal/nasal swabs	PCR	0.40
Mira et al. Unpub	Spain	Valencia Region	2019/01-2022/05	286	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	ILI (WHO)	NPS and/or pharyngeal/nasal swabs	PCR	0.83
Zar et al. Unpub	South Africa	Edendale	2019/01-2022/03	256	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	Physician diagnosed LRTI	NPS	PCR	0.83
Zar et al. Unpub	South Africa	Klerksdorp	2019/01-2022/03	116	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	Physician diagnosed LRTI	NPS	PCR	0.83

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Seo et al. Unpub	Republic of Korea	Goyang-si, Gyeonggi-do	2019/01-2022/05	167	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	fever, respiratory infection	NPS	PCR	0.80
Marie-Noelle et al. Unpub*	Netherlands	Netherlands	2019/01-2022/05	740	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	Systematic testing during COVID-19 pandemic up to the end of 2021. In 2022, only bronchiolitis cases are tested (RSV bronchiolitis, other LRTI, and rhinitis, otitis, tonsillitis)	NPS	Rapid antigen test during the pandemic; Mix of PCR and antigen tests in pre-pandemic years (with a majority of PCR)	0.40
Singleton et al. Unpub	United States of America	Yukon Kuskokwim, Alaska	2019/01-2022/05	125	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m and 18–<24m	ARI	MT swab	PCR	0.83

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Singleton et al. Unpub	United States of America	Southwest United States	2019/01-2022/05	93	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	ARI	MT swab	PCR	0.83
Chakhunashvili et al. Unpub	Georgia	Tbilisi, Kutaisi	2019/01-2022/05	451	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	SARI	NPS	PCR	0.60
Heikkinen et al. Unpub	Finland	Turku	2019/01-2022/05	296	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	hospitalised Bronchiolitis and/or pneumonia	NPS	Antigen test	0.60
Bandeira et al. Unpub	Portugal	Lisbon	2019/01-2022/05	193	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	Physician diagnosed	NPS	PCR	0.60
Zar et al. Unpub	South Africa	Agincourt and Tintswalo	2019/01-2022/05	103	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	Physician diagnosed LRTI	NPS	PCR	0.80

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Zar et al. Unpub	South Africa	Helen Joseph and Rahima Moosa	2019/01-2022/05	418	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	Physician diagnosed LRTI	NPS	PCR	0.80
Zar et al. Unpub	South Africa	Cape Town	2019/01-2022/05	2725	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	Physician diagnosed LRTI	NPS	PCR	0.80
Nokes et al. Unpub	Kenya	Kilifi	2019/01-2021/12	235	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	WHO syndromic pneumonia	NP/OP	Multiplex PCR	0.83
Baibus et al. Unpub	Russian Federation	St. Petersburg	2019/01-2022/04	205	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	ILI (Euro)	NPS	PCR	0.80
Baibus et al. Unpub	Russian Federation	St. Petersburg	2019/01-2022/05	390	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	ILI (Euro)	NPS	PCR	0.80

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Baibus et al. Unpub	Russian Federation	St. Petersburg	2019/01-2022/05	69	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	SARI (WHO 2011)	NPS	PCR	0.80
Casalegno et al. Unpub	France	Lyon	2019/01-2022/05	1538	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	WHO definition LRTI	NPS, NPA, BAL	PCR	0.83
Huang et al. Unpub	New Zealand	Auckland	2019/05-2022/05	283	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	non-SARI inpatients	NPS, NPA	PCR	0.67
Huang et al. Unpub	New Zealand	Auckland	2019/05-2022/05	466	0–<3m, 3–<6m, 6–<9m, 9–<12m, 12–<18m, 18–<24m and 24–<60m	SARI (WHO)	NPS, NPA	PCR	1.00
Lee et al. 2021* [10]	China, Taiwan Province of China	Zhanghua	2019/10-2021/02	80	0–<48m	hospitalized for wheezing (LRTI)	NPS	PCR	1.00

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Reyes-Dominguez et al. 2021 [8]	Spain	Gran Canaria	2016/01-2021/06	87	0–<24m	RSV acute bronchiolitis	nasal swabs, NPW, NPA	immunochromatography and PCR	0.60
Guitart et al. 2022 [11]	Spain	Barcelona	2010/09-2021/06	49	0–<12m	severe bronchiolitis admitted to the Paediatric Intensive Care Unit	NPA or a tracheal aspirate/BAL (in intubated patients)	PCR	0.50
Meyer et al. 2022 [12]	Germany	Cologne	2020/03-2021/11	169	0–<60m	symptomatic children	NPS, OPS	PCR	0.60
Pappa et al. 2022 [13]	Greece	Thessaloniki and Giannitsa	2021/09-2021/11	41	0–<24m	acute bronchiolitis	NPS	PCR/antigen detection	0.60
Hernández-Rivas et al. 2021 [14]	Spain	Madrid	2018/09-2021/07	179	0–<60m	hospitalized for RSV	NA	rapid test and/or PCR	0.80
Fourgeaud et al. 2021 [15]	France	Paris	2018/08-2021/04	212	0–<6m, 6–<12m, 12–<24m	RSV-associated ALRI	nose/throat swabs/BAL	PCR	1.00

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Lin et al. 2022 [16]	China, Taiwan	Xinbei and Gaoxiong	2018/02-2021/01	99	0–<60m	hospitalized with respiratory symptoms	throat swabs or NPA	culture	0.40
Saravanos et al. 2022* [17]	Australia	Sydney	2014/01-2020/12	713	0–<6m, 6–<12m, 12–<24m, 24–<60m	all RSV-coded hospitalizations and all unspecified bronchiolitis–coded hospitalizations based on principal and additional diagnosis fields	NA	PCR	0.60
Camporesi et al. 2022 [18]	Italy	Milano, Bologna, Rome and Catania	2021/07-2022/01	87	0–<24m	clinical diagnosis of bronchiolitis or a first episode of acute viral wheeze	NPS	PCR	0.80
Bermúdez Barrezueta et al. 2022* [19]	Spain	Valladolid	2014/10-2021.09	17	0–<24m	acute bronchiolitis	respiratory samples	molecular diagnostic tests	0.80

Study	Country	Location	Study period	Number of subjects†	Age groups reported	Case definitions	Specimen	Diagnostic test	QA score
Loconsole et al. 2022 [20]	Italy	Bari	2017/01-2021/12	128	0–<24m	hospitalized with a positive PCR test for RSV	NPS and/or aspirates	PCR	0.40

†Number of RSV-ALRI hospital admissions. *****Studies only reporting proportion of requiring intensive care unit admission among RSV-ALRI in children aged 0–<24 months (retrospective multicentric national study using data obtained from the Pediatric Spanish Society) [2]. m = months; RSV = respiratory syncytial virus; ALRI = acute lower respiratory infection; LRTI = lower respiratory tract infection; NPA = nasopharyngeal aspirate; NPS = nasopharyngeal swab; NPW = nasopharyngeal wash; OPS = oropharyngeal swab; BAL = bronchoalveolar lavage; PCR = polymerase chain reaction; SARI = Severe acute respiratory infection; ILI = influenza-like illness; WHO = World Health Organization; NA = not available; QA = quality assessment; Unpub = unpublished data.

Table S4. Estimates of RSV-associated ALRI hospitalisation burden (hospitalisation rate per 1000 and number in thousands) in children aged 12–<24 months and 24-<60 months by World Bank income region in different time periods

	2019 (from this study)	2019 (from Li Lancet 2022)[4]	2020	2021†	Latest (Apr 2021 to Mar 2022)
High-income Countries					
Median of stringency index (IQR)*	0	0	63.5	43.1	36.0
			(50.7, 71.2)	(40.4, 46.2)	(26.4, 39.5)
Median changes in mobility (IQR)	0	0	-16.1	-9.4	-7.8
			(-23.2, -14.4)	(-14.7, -5.8)	(-10.4, -4.8)
12–<24m					
Studies	7	28	11	9	8
Hospital admission rate (95% UR)	6.1	4.4	2.2	3.7	5.4
	(2.8,13.5)	(3.1, 6.1)	(0.6, 7.4)	(2.2, 6.3)	(3.5, 8.2)
Number of episodes (95% UR)	79	58	27	46	66
	(36, 173)	(41, 81)	(8, 93)	(27, 77)	(44, 101)
24–<60m					
Studies	6	–	9	8	7
Hospital admission rate (95% UR)	0.9	–	0.5	1.0	1.4
	(0.5, 1.9)		(0.1, 1.6)	(0.5, 2.0)	(0.9, 2.3)
Number of episodes (95% UR)	37	–	19	39	55
	(19, 74)		(6, 64)	(20, 77)	(34, 90)
Upper-middle-income Countries					
Median of stringency index (IQR)*	0	0	46.0	56.6	38.6
			(46.0, 46.0)	(56.6, 56.6)	(38.6, 38.6)
Median changes in mobility (IQR)	0	0	-23.6	-4.6	3.4
			(-23.6, -19.0)	(-4.6, 7.6)	(3.4, 3.4)
12–<24m					
Studies	2	14	2	2	2
Hospital admission rate (95% UR)	1.7	5.1	0.6	1.0	0.9
	(0.7, 4.0)	(2.8, 9.3)	(0.2, 1.3)	(0.6, 1.8)	(0.2, 4.2)
Number of episodes (95% UR)	55	207	17	30	26
	(23, 132)	(113,376)	(7, 40)	(16, 54)	(6, 123)
24–<60m					
Studies	2	–	2	2	2
Hospital admission rate (95% UR)	0.6	–	0.1	0.2	0.2
	(0.1, 3.3)		(<0.05, 0.2)	(0.1, 0.5)	(<0.05, 0.9)
Number of episodes (95% UR)	66	–	6	24	17
	(13, 343)		(2, 25)	(12, 49)	(3, 90)
Lower-middle-income Countries					
Median of stringency index (IQR)*	0	0	57.4	45.7	52.8
			(57.4, 57.4)	(45.7, 45.7)	(52.8, 52.8)
Median changes in mobility (IQR)	0	0	-14.4	19.9	–
			(-14.4, -14.4)	(19.9, 19.9)	
12–<24m					
Studies	1	14	1	1	0

	2019 (from this study)	2019 (from Li Lancet 2022)[4]	2020	2021†	Latest (Apr 2021 to Mar 2022)
Hospital admission rate (95% UR)	2.0 (1.1, 3.5)	7.6 (4.2,13.8)	2.3 (1.2, 4.3)	2.5 (1.3, 4.8)	–
Number of episodes (95% UR)	132 (73, 239)	466 (256,846)	156 (84, 289)	169 (88, 325)	–
24–<60m					
Studies	1	–	1	1	0
Hospital admission rate (95% UR)	0.3 (0.1, 0.8)	–	–	0.5 (0.2, 1.1)	–
Number of episodes (95% UR)	59 (22, 158)	–	–	103 (46, 230)	–

UR=uncertainty range. *The median (IQR) COVID-19 NPI stringency index was calculated based on the last month of corresponding year by income region. †The year of 2021 (that is from Jan 2021 to Dec 2021, overlapping with the latest available period).

Table S5. Estimates of RSV-associated ALRI hospitalisation burden (hospitalisation rate per 1000 and number in thousands) in children younger than 5 years by Country Development Status in different time periods

	2019 (from this study)	2019 (from Li Lancet 2022) [4]	2020	2021‡
Industrised countries				
Median of stringency index (IQR)*	0	0	63.5 (53.1, 71.1)	43.3 (39.3, 47.5)
Median changes in mobility (IQR)	0	0	-16.1 (-16.1, -14.4)	-9.4 (-9.7, -5.8)
0–<3m				
Studies	6	16	8	8
Hospital admission rate (95% UR)	42.1 (22.4,79.1)	36.9 (20.9,65.0)	18.3 (5.4,62.3)	24.0 (13.4,43.1)
Number of episodes (95% UR)	137 (73, 257)	122 (69, 215)	58 (17, 197)	74 (41, 133)
3–<6m				
Studies	6	18	8	8
Hospital admission rate (95% UR)	23.6 (11.4,48.8)	20.6 (12.4,34.1)	11.7 (3.0,46.0)	12.5 (7.6,20.5)
Number of episodes (95% UR)	77 (37, 158)	68 (41, 113)	37 (9, 145)	38 (23, 63)
0–<6m†				
Studies	6	24	8	8
Hospital admission rate (95% UR)	34.1 (17.7,65.5)	29.3 (20.0,42.8)	14.6 (3.5,60.6)	17.7 (10.3,30.6)
Number of episodes (95% UR)	221 (115, 425)	194 (133, 283)	92 (22, 383)	109 (63, 188)
6–<12m				
Studies	6	24	8	8
Hospital admission rate (95% UR)	9.3 (3.8,23.1)	11.1 (7.1,17.4)	4.4 (0.8,22.9)	6.5 (3.7,11.5)
Number of episodes (95% UR)	61 (25, 150)	74 (47, 116)	28 (5, 144)	40 (23, 71)
0–<12m†				
Studies	6	38	9	8
Hospital admission rate (95% UR)	23.0 (11.8,44.9)	22.5 (17.1,29.5)	9.6 (2.4,37.8)	12.6 (7.4,21.4)
Number of episodes (95% UR)	299 (153, 583)	298 (227, 391)	121 (31, 477)	155 (92, 264)
12–<60m				
Studies	5	15	7	7
Hospital admission rate (95% UR)	1.3 (1.0, 1.7)	1.7 (1.3, 2.3)	0.6 (0.1, 3.2)	1.4 (0.9, 2.3)
Number of episodes (95% UR)	70 (53, 94)	95 (72, 125)	32 (6, 171)	72 (44, 118)
0–<60m†				
Studies	5	48	7	7

	2019 (from this study)	2019 (from Li Lancet 2022) [4]	2020	2021‡
Hospital admission rate (95% UR)	4.4 (3.7, 5.3)	6.1 (4.7, 7.9)	1.7 (0.3,10.3)	3.6 (2.3, 5.7)
Number of episodes (95% UR)	296 (247, 355)	413 (318, 537)	113 (19, 674)	229 (144, 366)
Developing countries				
Median of stringency index (IQR)*	0	0	52.8 (47.7, 60.8)	45.7 (44.2, 51.1)
Median changes in mobility (IQR)	0	0	-23.4 (-24.1, -21.3)	-4.6 (-8.4, 1.5)
0–<3m				
Studies	4	36	4	4
Hospital admission rate (95% UR)	29.8 (16.9,52.5)	23.5 (15.2,36.3)	8.4 (4.8,14.6)	13.2 (9.2,18.9)
Number of episodes (95% UR)	921 (522,1625)	721 (466,1115)	256 (148, 445)	396 (276, 568)
3–<6m				
Studies	4	38	4	4
Hospital admission rate (95% UR)	20.2 (11.5,35.4)	16.7 (11.2,24.9)	5.8 (2.4,13.6)	10.1 (6.3,16.2)
Number of episodes (95% UR)	625 (357,1096)	513 (345, 765)	175 (74, 415)	304 (190, 487)
0–<6m†				
Studies	4	41	5	4
Hospital admission rate (95% UR)	24.9 (14.1,44.0)	19.3 (13.1,28.6)	6.1 (3.3,11.3)	11.5 (8.0,16.5)
Number of episodes (95% UR)	1540 (871,2724)	1188 (802,1759)	373 (203, 687)	691 (482, 990)
6–<12m				
Studies	4	41	5	4
Hospital admission rate (95% UR)	9.6 (5.4,17.1)	10.0 (6.9,14.4)	2.1 (0.9, 5.0)	4.8 (2.2,10.5)
Number of episodes (95% UR)	593 (332,1059)	612 (422, 886)	129 (55, 302)	289 (133, 630)
0–<12m†				
Studies	4	51	5	4
Hospital admission rate (95% UR)	17.4 (9.9,30.6)	15.3 (11.3,20.8)	4.1 (2.2, 7.8)	8.2 (5.3,12.9)
Number of episodes (95% UR)	2153 (1225,3784)	1881 (1386,2552)	503 (265, 954)	990 (633,1548)
12–<60m				
Studies	4	31	5	4
Hospital admission rate (95% UR)	1.4 (0.5, 4.2)	1.5 (1.0, 2.3)	0.6 (0.2, 1.4)	1.1 (0.3, 3.2)
Number of episodes (95% UR)	700 (235,2087)	735 (491,1101)	294 (121, 713)	517 (170,1570)
0–<60m†				
Studies	4	57	5	4

	2019 (from this study)	2019 (from Li Lancet 2022) [4]	2020	2021‡
Hospital admission rate (95% UR)	4.8 (2.4, 9.7)	5.2 (3.9, 6.9)	1.4 (0.8, 2.6)	2.6 (1.3, 5.2)
Number of episodes (95% UR)	2983 (1479,6017)	3163 (2395,4179)	863 (462,1612)	1567 (773,3177)
Global§				
Median of stringency index (IQR)*	0	0	57.8 (49.0, 70.5)	43.5 (42.8, 48.8)
Median changes in mobility (IQR)	0	0	-16.1 (-23.6, -14.8)	-9.4 (-9.7, -3.4)
0–<3m				
Studies	10	52	12	12
Hospital admission rate (95% UR)	30.9 (19.8,52.7)	24.7 (17.5,37.1)	9.6 (5.8,16.2)	14.2 (10.6,19.8)
Number of episodes (95% UR)	1055 (675,1799)	841 (597,1261)	324 (195, 545)	470 (351, 654)
3–<6m				
Studies	10	56	12	12
Hospital admission rate (95% UR)	20.5 (13.0,35.1)	17.0 (12.4,24.9)	6.5 (3.2,14.2)	10.3 (7.1,16.1)
Number of episodes (95% UR)	701 (446,1198)	579 (422, 846)	220 (107, 479)	341 (234, 534)
0–<6m†				
Studies	10	65	13	12
Hospital admission rate (95% UR)	25.7 (16.4,44.0)	20.2 (14.9,29.1)	7.3 (4.0,13.3)	12.1 (9.0,16.9)
Number of episodes (95% UR)	1758 (1120,3009)	1376 (1017,1982)	488 (272, 897)	798 (598,1119)
6–<12m				
Studies	10	65	13	12
Hospital admission rate (95% UR)	9.6 (5.9,16.8)	10.0 (7.4,14.3)	2.5 (1.2, 5.5)	5.0 (2.7,10.3)
Number of episodes (95% UR)	653 (405,1145)	683 (507, 973)	166 (78, 372)	328 (180, 680)
0–<12m†				
Studies	10	89	14	12
Hospital admission rate (95% UR)	17.9 (11.4,30.5)	15.9 (12.6,21.2)	4.8 (2.7, 8.9)	8.6 (6.1,13.1)
Number of episodes (95% UR)	2447 (1564,4170)	2170 (1713,2882)	652 (360,1204)	1142 (803,1736)
12–<60m				
Studies	9	46	12	11
Hospital admission rate (95% UR)	1.4 (0.6, 4.0)	1.5 (1.1, 2.2)	0.6 (0.3, 1.5)	1.1 (0.5, 3.1)
Number of episodes (95% UR)	762 (324,2175)	827 (600,1207)	337 (158, 792)	585 (256,1681)
0–<60m†				
Studies	9	105	12	11

	2019 (from this study)	2019 (from Li Lancet 2022) [4]	2020	2021‡
Hospital admission rate (95% UR)	4.7 (2.7, 9.3)	5.3 (4.2, 6.8)	1.5 (0.8, 2.9)	2.7 (1.5, 5.1)
Number of episodes (95% UR)	3255 (1840,6350)	3567 (2856,4634)	1022 (572,1952)	1790 (1041,3454)

UR=uncertainty range. *The median (IQR) COVID-19 NPI stringency index was calculated based on the last month of corresponding year by income region. † The point estimates and uncertainty range estimates are not necessarily equal to the sum of the estimates by finer age bands; this is because the studies that contributed to different age-group-specific estimates were different. ‡The year of 2021 (that is from Jan 2021 to Dec 2021, overlapping with the latest available period). §Global estimates were obtained by summing the numbers of developing and industrialised countries for each of the 1000 samples in the Monte Carlo simulation.

Table S6. Estimates of RSV-associated ALRI hospitalisation burden that requiring mechanical ventilation and ICU admission (hospitalisation rate per 1000 and number in thousands) in children younger than 5 years by World Bank income region in different time periods

	2019 (from this study)	2019 (from Li Lancet 2022)[4]	2020	2021‡	Latest (Apr 2021 to Mar 2022)
High-income Countries					
Median of stringency index (IQR)*	0	0	63.5	43.3	31.7
			(53.1, 71.1)	(39.3, 47.5)	(25.8, 36.1)
Median changes in mobility (IQR)	0	0	-16.1	-9.4	-7.8
			(-23.2, -14.4)	(-14.7, -5.8)	(-10.4, -4.8)
0–<3m					
Studies	5	7	7	7	6
Hospital admission rate (95% UR)	3.6 (0.7,19.2)	4.3 (2.5, 7.1)	0.4 (<0.05, 5.3)	2.2 (0.3,14.9)	4.5 (1.1,18.3)
Number of episodes (95% UR)	11 (2, 60)	14 (8, 24)	1 (0, 16)	7 (1, 45)	14 (3, 56)
3–<6m					
Studies	5	8	7	7	6
Hospital admission rate (95% UR)	1.0 (0.1, 6.9)	0.9 (0.5, 1.5)	<0.05 (<0.05,60.0)	0.1 (<0.05, 8.5)	0.3 (<0.05,10.5)
Number of episodes (95% UR)	3 (0, 22)	3 (2, 5)	0 (0,184)	0 (0, 26)	1 (0, 32)
0–<6m†					
Studies	5	8	7	7	6
Hospital admission rate (95% UR)	2.4 (0.5,12.1)	2.7 (1.8, 4.3)	0.2 (0.0, 2.8)	1.2 (0.2, 8.7)	2.4 (0.5,10.8)
Number of episodes (95% UR)	15 (3, 76)	18 (12, 29)	1 (0, 17)	7 (1, 53)	14 (3, 65)
6–<12m					
Studies	5	8	7	7	6
Hospital admission rate (95% UR)	0.3 (0.1, 1.8)	0.3 (0.2, 0.6)	<0.05 (<0.05,17.4)	0.1 (0.0, 2.8)	0.1 (<0.05, 3.2)
Number of episodes (95% UR)	2 (0, 11)	2 (1, 4)	0 (0,107)	0 (0, 17)	1 (0, 19)
0–<12m†					
Studies	5	11	7	7	6
Hospital admission rate (95% UR)	1.3 (0.3, 6.6)	1.2 (0.7, 2.1)	0.1 (<0.05, 1.4)	0.6 (0.1, 4.6)	1.2 (0.3, 5.7)
Number of episodes (95% UR)	17 (3, 83)	16 (10, 28)	1 (0, 18)	7 (1, 56)	15 (3, 70)
12–<60m					
Studies	5	10	7	7	6
Hospital admission rate (95% UR)	0.1 (0.0, 0.4)	0.1 (<0.05, 0.1)	<0.05 (<0.05, 0.4)	0.1 (<0.05, 0.4)	0.3 (0.1, 0.5)
Number of episodes (95% UR)	5 (1, 20)	4 (2, 7)	1 (0, 19)	5 (1, 22)	13 (7, 26)
0–<60m†					

	2019 (from this study)	2019 (from Li Lancet 2022)[4]	2020	2021‡	Latest (Apr 2021 to Mar 2022)
Studies	5	10	7	7	6
Hospital admission rate (95% UR)	0.3 (0.1, 1.6)	0.3 (0.2, 0.5)	<0.05 (<0.05, 0.4)	0.1 (<0.05, 1.2)	0.3 (0.1– 1.5)
Number of episodes (95% UR)	21 (4,103)	19 (11, 32)	1 (0, 25)	9 (1, 76)	22 (5, 97)
Upper-middle-income Countries					
Median of stringency index (IQR)*	0	0	46.0 (46.0, 46.0)	56.6 (56.6, 56.6)	38.6 (38.6, 38.6)
Median changes in mobility (IQR)	0	0	-23.6 (-23.6, -19.0)	-4.6 (-4.6, 7.6)	3.4 (3.4, 3.4)
0–<3m					
Studies	2	4	2	2	2
Hospital admission rate (95% UR)	1.3 (0.1,15.6)	3.3 (0.3,34.5)	0.7 (0.2, 2.9)	1.1 (0.4, 3.4)	<0.05 (<0.05, Inf)
Number of episodes (95% UR)	10 (1,122)	30 (3, 308)	5 (1, 21)	7 (2, 23)	<0.05 (<0.05, Inf)
3–<6m					
Studies	2	4	2	2	2
Hospital admission rate (95% UR)	1.4 (0.2,11.2)	2.1 (0.2,18.3)	<0.05 (<0.05, Inf)	1.2 (0.4, 3.8)	0.8 (0.2, 3.2)
Number of episodes (95% UR)	11 (1, 87)	19 (2, 164)	0 (0,Inf)	8 (3, 26)	5 (1, 22)
0–<6m†					
Studies	2	4	2	2	2
Hospital admission rate (95% UR)	0.6 (0.0,22.8)	2.7 (0.3,26.1)	0.4 (0.1, 1.5)	1.2 (0.5, 2.6)	0.4 (0.1, 1.5)
Number of episodes (95% UR)	10 (0,357)	48 (5, 466)	5 (1, 22)	16 (7, 35)	5 (1, 21)
6–<12m					
Studies	2	4	2	2	2
Hospital admission rate (95% UR)	0.7 (0.1, 7.9)	0.8 (<0.05,15.1)	<0.05 (<0.05, Inf)	0.2 (<0.05, 1.3)	<0.05 (<0.05, Inf)
Number of episodes (95% UR)	10 (1,124)	13 (1, 269)	0 (0,Inf)	3 (0, 18)	0 (0,Inf)
0–<12m†					
Studies	2	4	2	2	2
Hospital admission rate (95% UR)	0.3 (<0.05,23.1)	1.7 (0.2,19.2)	0.2 (<0.05, 0.7)	0.7 (0.3, 1.4)	0.2 (<0.05, 0.7)
Number of episodes (95% UR)	10 (0,722)	61 (5, 685)	5 (1, 22)	18 (9, 38)	5 (1, 20)
12–<60m					
Studies	2	2	2	2	2
Hospital admission rate (95% UR)	<0.05 (<0.05, Inf)	<0.05 (<0.05, 0.1)	<0.05 (<0.05, Inf)	<0.05 (<0.05, Inf)	<0.05 (<0.05, Inf)
Number of episodes (95% UR)	0 (0,Inf)	5 (1, 22)	0 (0,Inf)	0 (0,Inf)	0 (0,Inf)
0–<60m†					

	2019 (from this study)	2019 (from Li Lancet 2022)[4]	2020	2021‡	Latest (Apr 2021 to Mar 2022)
Studies	2	2	2	2	2
Hospital admission rate (95% UR)	0.1 (<0.05, 4.7)	0.1 (<0.05, 0.8)	<0.05 (<0.05, 0.1)	0.1 (0.1, 0.3)	<0.05 (<0.05, 0.1)
Number of episodes (95% UR)	11 (0,793)	14 (1, 144)	6 (2, 24)	20 (10, 42)	6 (1, 23)
Lower-middle-income Countries					
Median of stringency index (IQR)*	0	0	57.4 (57.4, 57.4)	45.7 (45.7, 45.7)	52.8 (52.8, 52.8)
Median changes in mobility (IQR)	0	0	-14.4 (-14.4, -14.4)	19.9 (19.9, 19.9)	–
0–<3m					
Studies	1	6	1	1	0
Hospital admission rate (95% UR)	2.0 (0.8, 5.4)	19.9 (10.3,38.5)	1.6 (0.5, 4.8)	1.5 (0.5, 4.6)	–
Number of episodes (95% UR)	34 (13, 92)	312 (161, 603)	26 (8, 82)	25 (8, 78)	–
3–<6m					
Studies	1	8	1	1	0
Hospital admission rate (95% UR)	0.8 (0.1, 5.4)	7.5 (4.2,13.2)	0.8 (0.1, 5.8)	0.7 (0.1, 5.2)	–
Number of episodes (95% UR)	13 (2, 92)	117 (66, 207)	14 (2, 99)	12 (2, 88)	–
0–<6m†					
Studies	1	6	1	1	0
Hospital admission rate (95% UR)	1.5 (0.6, 3.6)	14.8 (8.0,27.5)	1.3 (0.5, 3.5)	1.2 (0.4, 3.1)	–
Number of episodes (95% UR)	51 (21,124)	464 (250, 862)	44 (17,118)	40 (15,106)	–
6–<12m					
Studies	1	8	1	1	0
Hospital admission rate (95% UR)	0.3 (<0.05, 2.4)	4.7 (2.2,10.0)	<0.05 (<0.05, Inf)	0.4 (<0.05, 2.5)	–
Number of episodes (95% UR)	12 (2, 82)	147 (69, 313)	0 (0,Inf)	12 (2, 84)	–
0–<12m†					
Studies	1	8	1	1	0
Hospital admission rate (95% UR)	0.9 (0.4, 2.1)	7.2 (3.5,14.9)	0.8 (0.3, 2.2)	0.8 (0.3, 1.9)	–
Number of episodes (95% UR)	65 (29,144)	453 (220, 936)	56 (21,150)	54 (22,129)	–
12–<60m					
Studies	1	6	1	1	0
Hospital admission rate (95% UR)	0.1 (<0.05, 0.2)	0.4 (0.2, 0.9)	<0.05 (<0.05, Inf)	0.1 (<0.05, 0.3)	–
Number of episodes (95% UR)	17 (4, 66)	98 (45, 214)	0 (0,Inf)	20 (5, 78)	–
0–<60m†					

	2019 (from this study)	2019 (from Li Lancet 2022)[4]	2020	2021‡	Latest (Apr 2021 to Mar 2022)
Studies	1	6	1	1	0
Hospital admission rate (95% UR)	0.2 (0.1, 0.5)	1.4 (0.7, 2.8)	0.2 (0.1, 0.4)	0.2 (0.1, 0.4)	–
Number of episodes (95% UR)	79 (39,157)	423 (205, 874)	55 (20,145)	69 (33,146)	–

UR=uncertainty range. *The median (IQR) COVID-19 NPI stringency index was calculated based on the last month of corresponding year by income region. † The point estimates and uncertainty range estimates are not necessarily equal to the sum of the estimates by finer age bands; this is because the studies that contributed to different age-group-specific estimates were different. ‡The year of 2021 (that is from Jan 2021 to Dec 2021, overlapping with the latest available period).

Table S7. Median, IQR and range of lag time between 12-month moving average RSV-associated ALRI hospitalisation rates and Retail & recreation index by World Bank income region.

	High-income Countries		**Upper-middle-income Countries**		**Lower-middle-income Countries**	
Age groups	Lag time (IQR)	Lag time (Range)	Lag time (IQR)	Lag time (Range)	Lag time (IQR)	Lag time (Range)
0-<3m	0.0(0.0-0.0)	0.0(0.0-2.0)	2.0(1.0-3.0)	2.0(0.0-4.0)	—	—
3-<6m	0.0(0.0-1.0)	0.0(0.0-2.0)	3.0(3.0-3.0)	3.0(3.0-3.0)	—	—
6-<9m	0.0(0.0-0.0)	0.0(0.0-2.0)	2.5(2.2-2.8)	2.5(2.0-3.0)	—	—
9-<12m	0.0(0.0-1.5)	0.0(0.0-3.0)	3.0(3.0-3.0)	3.0(3.0-3.0)	—	—
12-<24m	0.0(0.0-0.5)	0.0(0.0-2.0)	4.0(4.0-4.0)	4.0(4.0-4.0)	—	—
0-<6m	0.0(0.0-0.0)	0.0(0.0-2.0)	2.0(1.0-3.0)	2.0(0.0-4.0)	—	—
6-<12m	0.0(0.0-1.0)	0.0(0.0-3.0)	1.5(0.8-2.2)	1.5(0.0-3.0)	—	—
12-<60m	0.0(0.0-1.5)	0.0(0.0-2.0)	3.5(3.2-3.8)	3.5(3.0-4.0)	1.0(1.0-1.0)	1.0(1.0-1.0)
0-<60m	0.0(0.0-0.8)	0.0(0.0-2.0)	2.0(1.0-3.0)	2.0(0.0-4.0)	—	—

m = months; lag time unit: months.

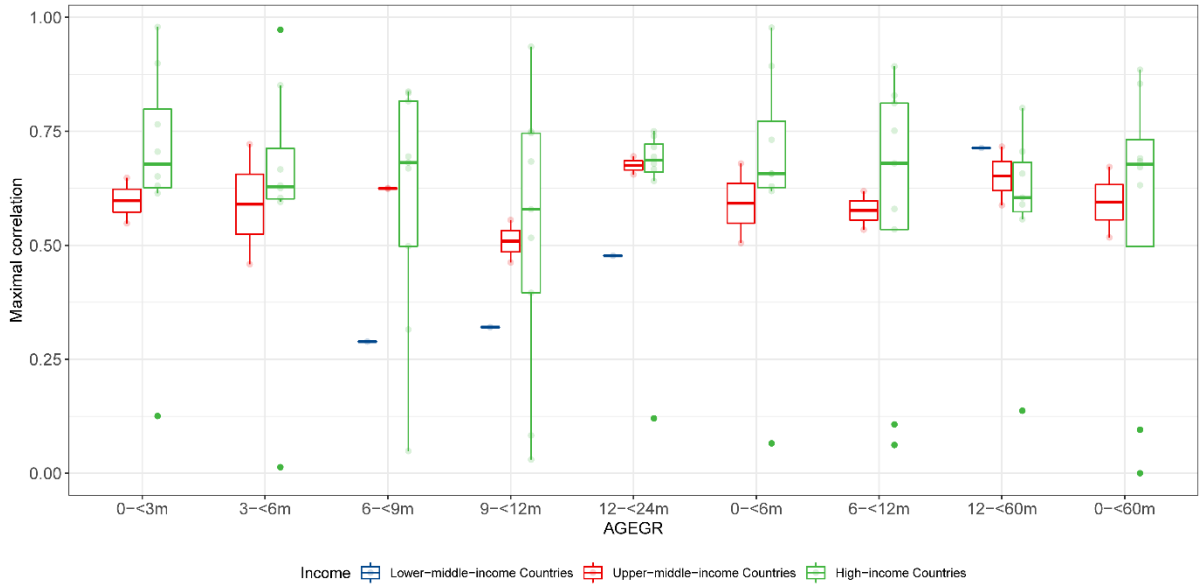

Figure S1. Maximal correlation coefficient of 12-month moving average RSV-associated ALRI hospitalisation rates and Retail & recreation index by ager group and World Bank income region

Retail & recreation index (an index of Google COVID-19 Community Mobility Trends), its change was relative to baseline days before the pandemic outbreak (the median value over the five‑week period from January 3rd to February 6th 2020).

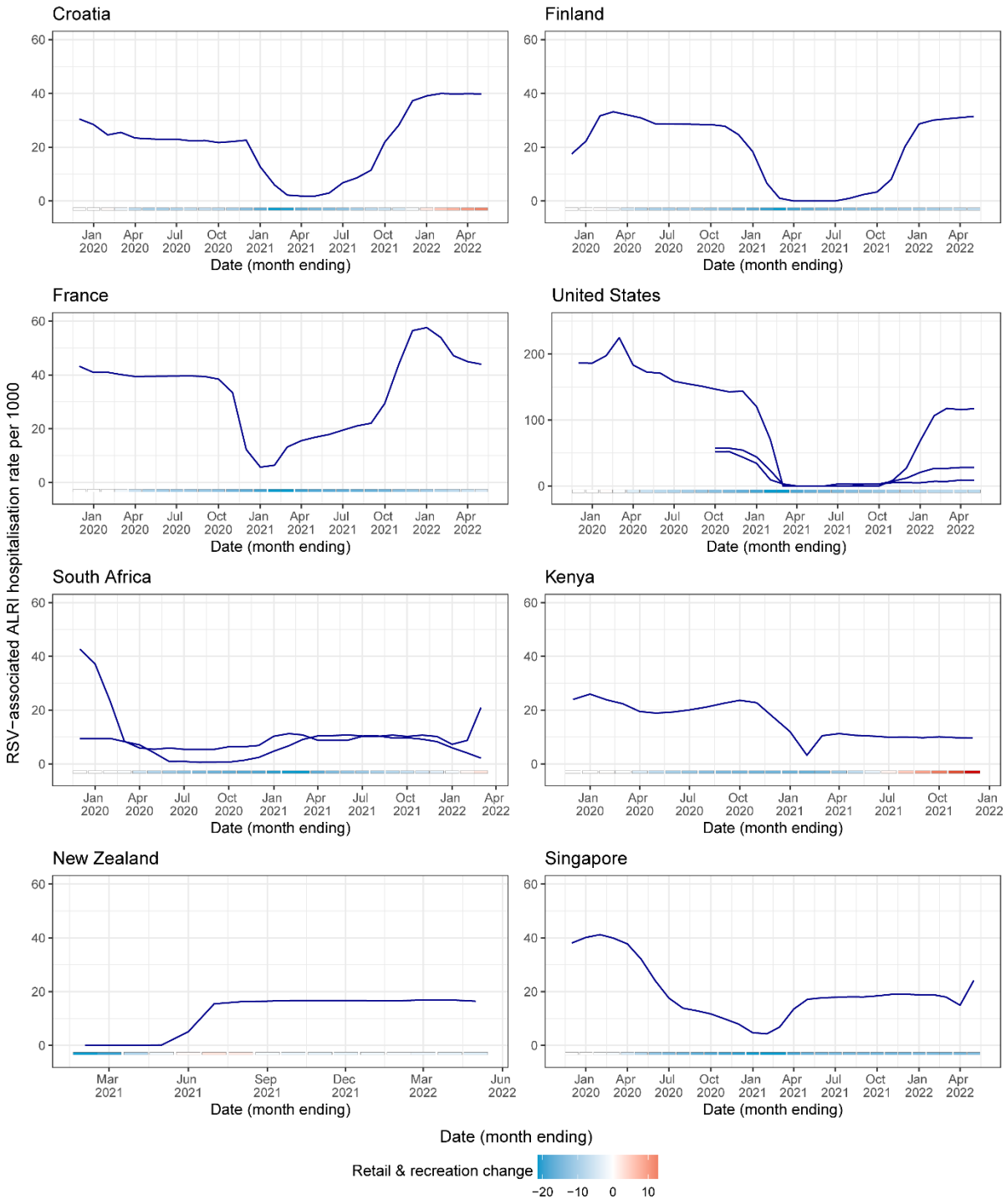

Figure S2. Changes over time of 12-month moving average RSV-associated ALRI hospitalisation rate and Retail & recreation index by country

Retail & recreation index (an index of Google COVID-19 Community Mobility Trends), its change was relative to baseline days before the pandemic outbreak (the median value over the five‑week period from January 3rd to February 6th 2020).

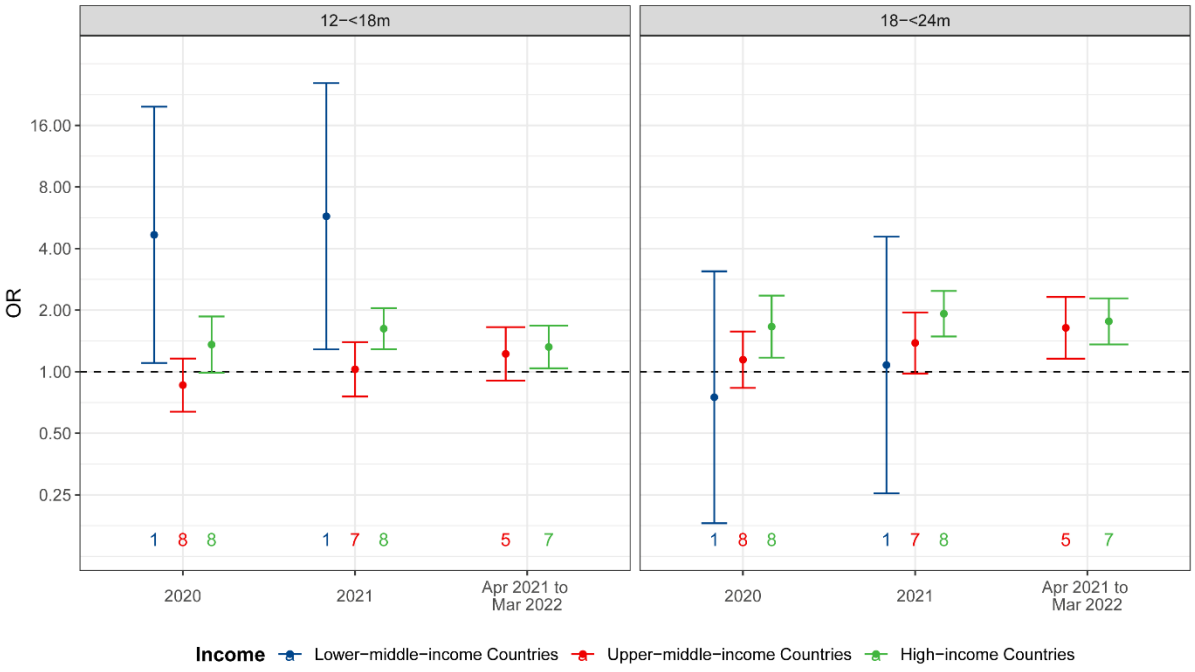

Figure S3. Odds ratio for observing RSV-associated ALRI hospitalisation requiring supplemental oxygen in children aged 12–<18 months and 18–<24 months (compared with 0–<3 months) during the COVID-19 pandemic period.

Number at the bottom of each panel indicates the number of data-points contributing to each group. OR=odds ratio.

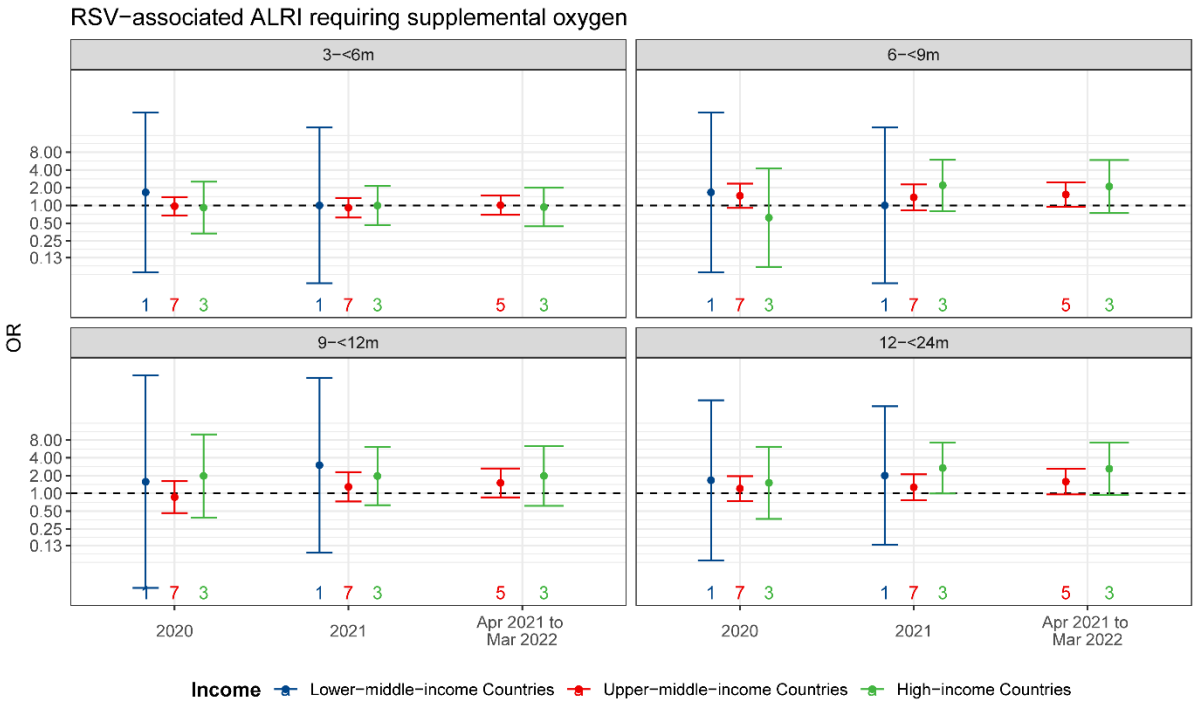

Figure S4. Odds ratio for observing RSV-associated ALRI hospitalisation requiring supplemental oxygen in older age groups (compared with 0–<3 months) during the COVID-19 pandemic period.

Number at the bottom of each panel indicates the number of data-points contributing to each group. OR=odds ratio.

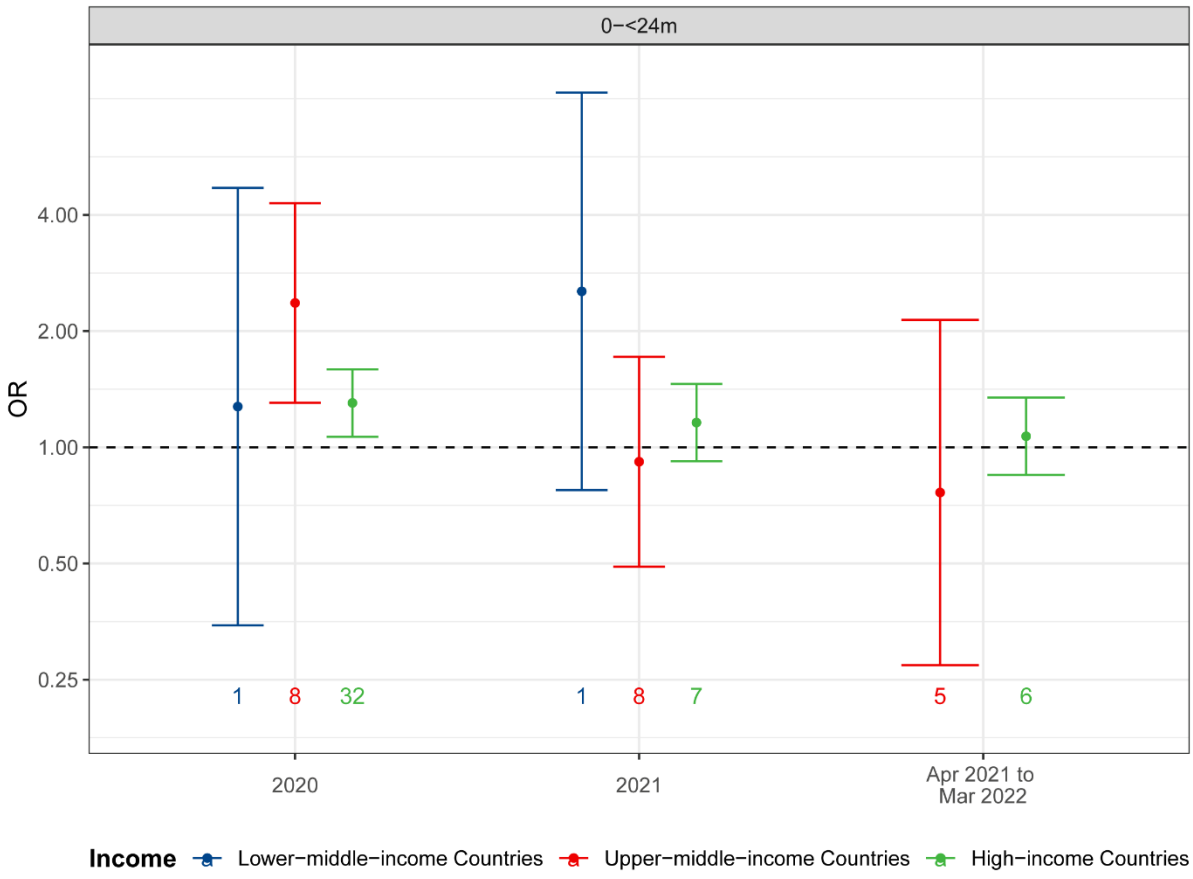

Figure S5. Comparison of proportion of RSV-associated ALRI requiring mechanical ventilation or ICU admission in children aged 0–<24 months between pre-pandemic and pandemic period, by World Bank Income Region.

Number at the bottom of each panel indicates the number of data-points contributing to each group. OR=odds ratio. ICU=intensive care unit.

GATHER checklist

Checklist of information that should be included in new reports of global health estimates

Item #	Checklist item	Reported on page #
Objectives and funding		
1	Define the indicator(s), populations (including age, sex, and geographic entities), and time period(s) for which estimates were made.	7-8
2	List the funding sources for the work.	-
Data Inputs		
For all data inputs from multiple sources that are synthesized as part of the study:		
3	Describe how the data were identified and how the data were accessed.	8-9
4	Specify the inclusion and exclusion criteria. Identify all ad-hoc exclusions.	8
5	Provide information on all included data sources and their main characteristics. For each data source used, report reference information or contact name/institution, population represented, data collection method, year(s) of data collection, sex and age range, diagnostic criteria or measurement method, and sample size, as relevant.	8-9
6	Identify and describe any categories of input data that have potentially important biases (e.g., based on characteristics listed in item 5).	8-9
For data inputs that contribute to the analysis but were not synthesized as part of the study:		
7	Describe and give sources for any other data inputs.	NA
For all data inputs:		
8	Provide all data inputs in a file format from which data can be efficiently extracted (e.g., a spreadsheet rather than a PDF), including all relevant meta-data listed in item 5. For any data inputs that cannot be shared because of ethical or legal reasons, such as third-party ownership, provide a contact name or the name of the institution that retains the right to the data.	NA
Data analysis		
9	Provide a conceptual overview of the data analysis method. A diagram may be helpful.	9-10
10	Provide a detailed description of all steps of the analysis, including mathematical formulae. This description should cover, as relevant, data cleaning, data pre-processing, data adjustments and weighting of data sources, and mathematical or statistical model(s).	9-10
11	Describe how candidate models were evaluated and how the final model(s) were selected.	NA
12	Provide the results of an evaluation of model performance, if done, as well as the results of any relevant sensitivity analysis.	9-10
13	Describe methods for calculating uncertainty of the estimates. State which sources of uncertainty were, and were not, accounted for in the uncertainty analysis.	10
14	State how analytic or statistical source code used to generate estimates can be accessed.	9-10
Results and Discussion		

15	Provide published estimates in a file format from which data can be efficiently extracted.	11-25
16	Report a quantitative measure of the uncertainty of the estimates (e.g., uncertainty intervals).	11-25
17	Interpret results in light of existing evidence. If updating a previous set of estimates, describe the reasons for changes in estimates.	26-27
18	Discuss limitations of the estimates. Include a discussion of any modelling assumptions or data limitations that affect interpretation of the estimates.	27

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	6
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	7
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	7
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	8
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	8
Search strategy	7	present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix pp 3-6
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	8
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	8
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	8-9
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	NA
Study risk of bias	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many	8-9

Section and Topic	Item #	Checklist item	Location where item is reported
assessment		reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	9-10
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	9-10
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	9-10
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	9-10
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	9-10
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	9-10
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	9-10
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	9-10
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	9-10
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	12
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	12
Study characteristics	17	Cite each included study and present its characteristics.	Appendix pp 8-26
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Appendix pp 12-26
Results of individual	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect	NA

Section and Topic	Item #	Checklist item	Location where item is reported
studies		estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	NA
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Table 1,2; appendix pp 27-36
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	26, Appendix pp 12-26
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	-
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Table 1,2; appendix pp 12-26
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	26
	23b	Discuss any limitations of the evidence included in the review.	27
	23c	Discuss any limitations of the review processes used.	27
	23d	Discuss implications of the results for practice, policy, and future research.	27-28
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	10
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	10
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	-
Competing interests	26	Declare any competing interests of review authors.	-
Availability of data, code and other	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	-

Section and Topic	Item #	Checklist item	Location where item is reported
materials			

REFERENCES

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