BMC Infectious Diseases

SYSTEMATIC REVIEW

Open Access

# Impact of disease severity, age, sex, comorbidity, and vaccination on secondary attack rates of SARS-CoV-2: a global systematic review and meta-analysis

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## Abstract

**Background** Understanding the key drivers of SARS-CoV-2 transmission is essential for shaping effective public health strategies. However, transmission risk is subject to substantial heterogeneity related to disease severity, age, sex, comorbidities, and vaccination status in different population settings and regions. We aimed to quantify the impact of these factors on secondary attack rates (SARs) of SARS-CoV-2 across diverse population settings and regions, and identify key determinants of transmission to inform targeted interventions for improving global pandemic response.

**Methods** To retrieve relevant literature covering the duration of the COVID-19 pandemic, we searched Ovid MEDLINE, Ovid Embase, Web of Science, and the Cochrane COVID-19 Study Register between January 1, 2020 and January 18, 2024 to identify studies estimating SARs of SARS-CoV-2, defined as the proportion of close contacts infected. We pooled SAR estimates using a random-effects model with the Freeman-Tukey double arcsine transformation and derived Clopper-Pearson 95% confidence intervals (CIs). Risk of bias was assessed using a modified Newcastle–Ottawa scale. This study was registered with PROSPERO, CRD42024503782.

**Results** A total of 159 eligible studies, involving over 19 million close contacts and 6.8 million cases from 41 countries across five continents, were included in the analysis. SARs increased with disease severity in index cases, ranging from 0.10 (95% CI: 0.06–0.14; $I^2 = 99.65\%$) in asymptomatic infection to 0.15 (95% CI: 0.09–0.21; $I^2 = 92.49\%$) in those with severe or critical conditions. SARs by age were lowest at 0.20 (95% CI: 0.16–0.23; $I^2 = 99.44\%$) for close contacts under 18 years and highest at 0.29 (95% CI: 0.24–0.34; $I^2 = 99.65\%$) for index cases aged 65 years or older. Among both index cases and close contacts, pooled SAR estimates were highest for Omicron and lowest for Delta, and declined with increasing vaccine doses. Regionally, North America had the highest SAR at 0.27 (95% CI: 0.24–0.30; $I^2 = 99.31\%$), significantly surpassing SARs in Europe (0.19; 95% CI: 0.15–0.25; $I^2 = 99.99\%$), Southeast Asia (0.18; 95% CI: 0.13–0.24; $I^2 = 99.24\%$), and the Western Pacific (0.11; 95% CI: 0.08–0.15; $I^2 = 99.95\%$). Among close contacts with comorbidities, chronic lung disease and hypertension were associated with the highest SARs. No significant association was found between SARs and the sex of either index cases or close contacts.

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**Conclusions** Secondary attack rates varied substantially by demographic and regional characteristics of the studied populations. Our findings demonstrate the role of booster vaccinations in curbing transmission, underscoring the importance of maintaining population immunity as variants of SARS-CoV-2 continue to emerge. Effective pandemic responses should prioritise tailored interventions that consider population demographics and social dynamics across different regions.

**Keywords** SARS-CoV-2, Secondary attack rate, Disease severity, Vaccination, Systematic review, Meta-analysis

## Background

The emergence of SARS-CoV-2 in 2019, causing the COVID-19 pandemic, exacted a devastating toll on global health with over 770 million cases and 7 million deaths reported worldwide as of October 2024 [1]. Public health has continually faced the challenge of emerging highly transmissible, immune-evading variants with waves of infections throughout the pandemic [2, 3]. Understanding how population-level and disease-specific factors—including age, community settings, comorbidities, disease severity and heterogeneity across these factors—influence SARS-CoV-2 transmission is crucial for mitigating its impact [4–9].

Secondary attack rates (SARs) of SARS-CoV-2, ranging from 5 to 85% in published studies, show significant variability, influenced by temporal dynamics, settings, and geographical contexts. Existing systematic reviews have predominantly evaluated asymptomatic transmission rates [10–14], but the transmission dynamics of SARS-CoV-2 across the full spectrum of disease severity, from asymptomatic to presymptomatic, mild, moderate, severe, and critical conditions, are largely unexplored. Reviews conducted in the early stages of the pandemic primarily focused on household transmission, limiting our understanding of broader transmission patterns [13, 15–19]. Moreover, the inclusion of diverse study designs in previous systematic reviews—such as case series, case reports, cross-sectional analyses, and mathematical modelling studies—undermines cohesive synthesis, raising questions about the reliability of their findings. Furthermore, the lack of stratification of SARS-CoV-2 transmission data by geographical regions or countries' income levels limits the applicability of results in different populations. While substantial evidence indicates that vaccines reduce infection rates and disease severity [20], their impact on viral shedding and transmission of SARS-CoV-2 remains debated.

To address the limitations of previous studies and existing knowledge gaps, we conducted a comprehensive systematic review and meta-analysis to quantify the impact of disease severity, age, sex, vaccination status, and comorbidities on SARS-CoV-2 transmission. We categorised study participants by these factors for both index cases and close contacts, recognising that the characteristics of both groups influence transmission dynamics. Our analysis spans the entire duration of the COVID-19 pandemic and includes data from regions of North America, Europe, Western Pacific, and Southeast Asia.

## Methods

This study adhered to the updated Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [21]. The protocol was registered in the PROSPERO (CRD42024503782).

### Search strategy and selection criteria

We initially searched MEDLINE (Ovid), Embase (Ovid), Web of Science, and the Cochrane COVID-19 Study Register from January 1, 2020 to January 18, 2024, with no language or study design restrictions to identify studies reporting the SARs of SARS-CoV-2, defined as the proportion of close contacts infected. Close contacts in our study refer to individuals who shared living spaces or had social interactions with index cases from 2 days before, to 14 days after the onset of symptoms. The interaction is defined as being within 1 m of index cases for at least 15 min. The search included combinations of terms related to COVID-19, disease transmission, and transmission sources (Additional file 1 pp. 4–9). We tested the search strategy through an iterative process before finalising the combinations of terms and reviewed it using the Peer-Review for Electronic Search Strategies (PRESS) guidelines [22], incorporating feedback into the final strategy. We also examined reference lists from articles that met our inclusion criteria (Additional file 1 p. 10), as well as previously published systematic reviews on similar topics, to identify additional relevant studies.

We used EndNote 20 to organise, manage, and deduplicate references. The remaining unique articles were then uploaded to Covidence. Titles, abstracts, and full texts were independently screened by three reviewers (DMS, YY, and ZW), with discrepancies resolved by consensus or referred to a fourth reviewer (SMM). We included articles with original data reporting at least two of the following factors: the number of close contacts infected, total number of close contacts, and SARs among close contacts, which were published in English. Studies that

were inaccessible, mathematical modelling or simulation studies, case series, editorials, reviews, and conference abstracts were excluded (Additional file 1 p. 10).

#### Data extraction and quality assessment

Three independent reviewers (DMS, YY, and ZW) conducted a training exercise with 10 articles to finalise the data extraction form and determine the specific information to be extracted. We recorded relevant information, including the first author's name, year of publication, study design, country, setting, funding, and population characteristics into Microsoft Excel 365. To analyse SARs of SARS-CoV-2, we extracted data on the number of index cases, number of contacts, and number of secondary cases. We further stratified the articles based on the World Health Organization (WHO) regions and country income levels according to World Bank classifications (low, lower-middle, upper-middle, and high) [23]. Study participants were categorised by age, sex, disease severity, vaccination status, and comorbidity. Vaccination status was classified as unvaccinated, partially vaccinated, fully vaccinated, and booster-vaccinated for approved vaccines in the study population. For studies reporting SARs for multiple settings, we extracted data from all reported settings. Given the variability in age stratification across studies, we reclassified the age groups into < 18, 18–49, 50–64, and ≥ 65 years old. We redistributed counts from the original age ranges assuming a uniform distribution and adjusted these counts using country-specific life expectancy data from the WHO [24].

To understand the association between the strictness of non-pharmaceutical interventions (NPIs) and SARs within the timeframe of included studies, we applied the Oxford COVID-19 Stringency Index (SI) [25]. The daily strictness of NPIs was categorised according to the COVIDSurg Collaborative framework, with SI < 20 for light restrictions, SI between 20 and 60 for moderate lockdowns, and SI > 60 for full lockdowns [26]. For each study, we calculated the weighted mean of SI (WM-SI) by averaging the index over the duration of each category and summing their weighted values as the proportion of days in each index category over the study period (Additional file 1 p. 10). This weighted mean reflects the influence of each strictness level proportionally. We also evaluated timelines for the implementation of NPIs and their strictness level relative to the identification date of the first case of SARS-CoV-2 in each country [1, 25]. Additionally, data on healthcare expenditure as a percentage of gross domestic product (GDP) for 2020 were obtained from the World Bank to explore any potential relationship between healthcare expenditure and SARs [27].

After reconciling discrepancies in screening studies, the three reviewers (DMS, YY, and ZW) independently extracted and discussed the data, accounting for disease severity, vaccination status, and community settings used in our study (Additional file 1 pp. 11–13). The reviewers also rated each study's quality using a modified 9-point Newcastle–Ottawa scale [17], based on three criteria: participant selection (4 points), comparability of studies (1 point), and ascertainment of the outcome of interest (4 points). Studies were classified as having high (≤ 3 points), moderate (4–6 points), or low (≥ 7 points) risk of bias. Discrepancies in scores among reviewers were resolved through collaborative re-evaluation to reach consensus.

#### Data analyses

Statistical analyses were conducted using the *Metaprop* package [28] in Stata/SE software (version 16.1). SARs were calculated from raw data in each study, dividing the number of infected close contacts of index cases by the total number of close contacts. A pooled analysis of SARs was performed using a random-effects model to account for the expected heterogeneity among the included studies. The Freeman-Tukey double-arcsine variance-stabilising transformation was employed to combine data, offering advantages over log and logit transformations when zero event counts are present [29]. Confidence intervals (CIs) for individual studies were calculated using the Clopper-Pearson method [30]. SARs were presented as proportions along with 95% CIs in forest plots to illustrate their variability and precision across studies. Statistical heterogeneity of effect size estimates across studies was assessed using the $I^2$ test, with values of 0–40% indicating low heterogeneity, 41–75% indicating moderate heterogeneity, and values greater than 75% indicating high heterogeneity, as defined by the Cochrane Statistical Methods Group. Subgroup analyses were performed when more than 3 studies were available to determine the pooled SAR and to explore potential sources of heterogeneity, based on the WHO regions, World Bank income classification, country, strictness level of NPIs as computed by the weighted mean SI, study characteristics, and community setting. The Kruskal–Wallis test was used to compare SARs across groups. Meta-regression analyses were conducted with at least 10 studies available to assess the association between SARs and the time interval from the first reported case to the implementation of NPIs, the varying SI, study duration, and healthcare expenditure. Publication bias was assessed by visually inspecting the symmetry of funnel plots and using Egger's regression test, with a $P$-value < 0.05 indicating the presence of publication bias when at least ten studies were included. If publication bias was detected, the trim-and-fill method was used to estimate the adjusted effect size. Sensitivity analyses were conducted to assess the robustness of

our findings by excluding studies with exceptionally high SARs (>60%), which could introduce statistical heterogeneity.

### Role of the funding source

The funders had no role in the study design, data collection, analysis, interpretation of results, writing of the paper, or decision to publish.

## Results

### Identification and selection of studies

A PRISMA flowchart summarising the literature search and article selection process is presented in Fig. 1. Initially, 36,348 records were identified from the database search. After removing duplicates ($n=15,297$), 21,051 titles and abstracts were screened, and 20,531 records were excluded. Consequently, 517 full-text articles were reviewed. An additional 28 studies were identified by manually searching the reference lists of included papers and previous systematic reviews on similar topics, bringing the total number of eligible articles to 545. After excluding 386 articles in the full-text review (Additional file 1 pp. 61–91), 159 studies were included in the systematic review and meta-analysis.

### Characteristics of the studies

Included studies were conducted across 41 countries within the Western Pacific ($n=54$), European ($n=50$),

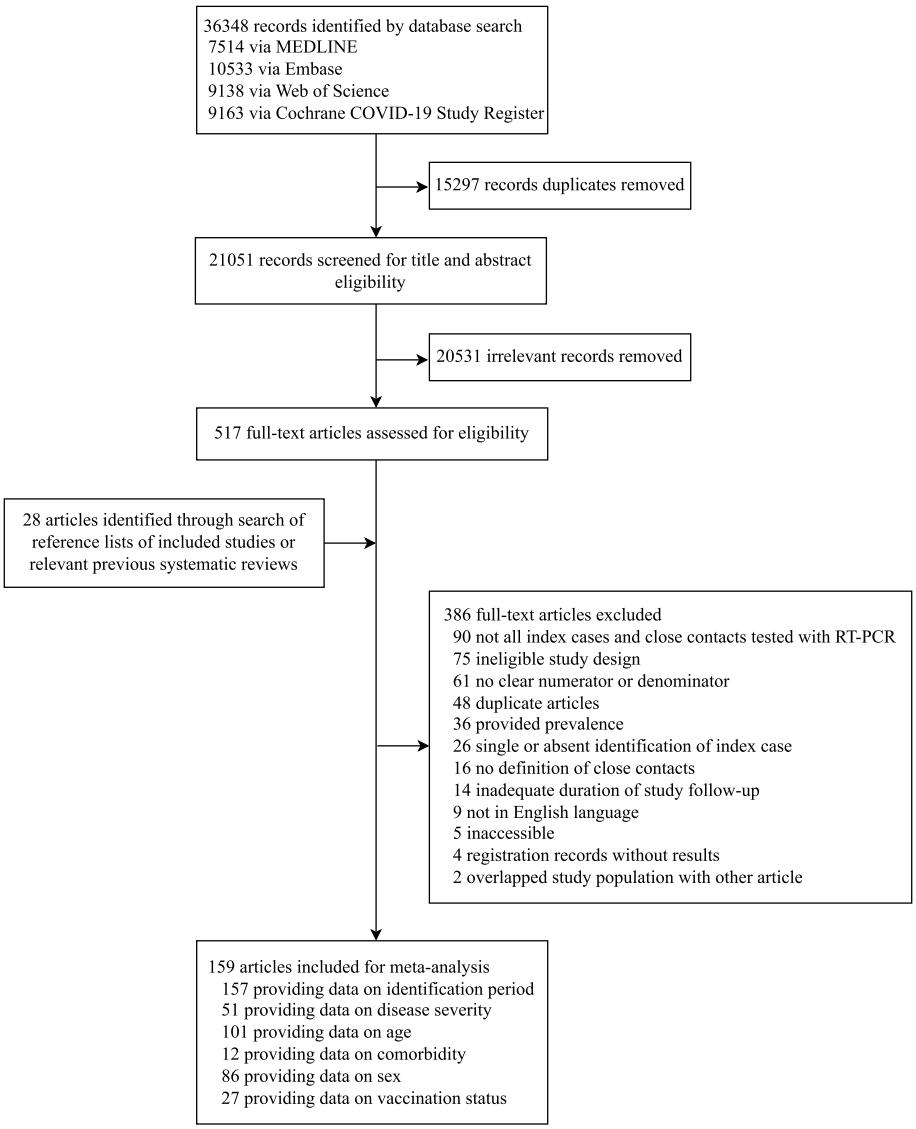


**Fig. 1** PRISMA flowchart of the systematic search and selection process

North American ($n=25$), Southeast Asia ($n=19$), African ($n=6$), and other WHO regions ($n=5$) [31–189]. The included studies involved over 19 million subjects across five continents. The sex distribution was balanced, with males representing 48.6% and females 51.4%. Stratifying by World Bank income classifications, 98 studies were carried out in high-income countries (HICs), 35 in upper-middle-income countries (UMICs), 21 in lower-middle-income countries (LMICs), and 5 in low-income countries (LICs) (Additional file 1 pp. 92–100). Follow-up periods for close contacts were ≥ 14 days in 128 studies, 7 to 13 days in 23 studies, and unspecified in 8 studies. For the identification period of index cases from January 2020 to August 2022 (Table 1), 126 studies were carried out in households, 26 in social settings, 25 in healthcare settings, 15 in workplaces, 13 in non-household environments, 11 in educational settings, 11 in transportation, and 9 in institutional settings. Of the 159 included studies, 118 (74.21%) were rated as low risk of bias, 39 (24.53%) as moderate risk, and 2 (1.26%) as high risk of bias (Additional file 1 pp. 101–107).

**Table 1** Secondary attack rates by subgroup

| Identification period | N[a] | SAR (95% CI) | $I^2$ | Egger's *P*-value |
|---|---|---|---|---|
| 2020 | 162 | 0.13 (0.12, 0.15) | 99.81% | 0.3058 |
| 2021 | 64 | 0.26 (0.17, 0.36) | 99.99% | 0.0067 |
| 2022 | 14 | 0.15 (0.07, 0.24) | 99.96% | 0.2194 |
| **Stringency index** | | | | |
| Light restrictions | 6 | 0.18 (0.10, 0.27) | 95.68% | NA** |
| Moderate lockdowns | 106 | 0.14 (0.09, 0.19) | 99.99% | 0.9214 |
| Full lockdowns | 128 | 0.19 (0.16, 0.21) | 99.86% | 0.2129 |
| **World Bank income classification** | | | | |
| Low income | 10 | 0.12 (0.05, 0.19) | 98.16% | 0.1108 |
| Lower middle income | 35 | 0.17 (0.12, 0.23) | 99.24% | 0.5806 |
| Upper middle income | 64 | 0.11 (0.08, 0.14) | 99.84% | 0.4486 |
| High income | 131 | 0.20 (0.15, 0.25) | 99.99% | 0.1402 |
| **Population setting** | | | | |
| Household | 126 | 0.26 (0.23, 0.29) | 99.98% | 0.0338 |
| Social | 26 | 0.11 (0.06, 0.16) | 99.72% | 0.8227 |
| Transportation | 11 | 0.06 (0.02, 0.11) | 97.67% | 0.2942 |
| Non-household | 13 | 0.08 (0.03, 0.15) | 99.69% | 0.8397 |
| Healthcare | 25 | 0.06 (0.03, 0.10) | 98.38% | 0.7359 |
| Workplace | 15 | 0.07 (0.04, 0.11) | 98.39% | 0.8142 |
| Educational | 11 | 0.05 (0.02, 0.08) | 99.80% | 0.7554 |
| Institutional | 9 | 0.15 (0.09, 0.22) | 98.58% | NA |
| **Country** | | | | |
| China | 53 | 0.08 (0.05, 0.12) | 99.86% | 0.6042 |
| USA | 26 | 0.28 (0.23, 0.33) | 99.24% | 0.6939 |
| India | 21 | 0.19 (0.13, 0.27) | 99.44% | 0.7675 |
| Spain | 15 | 0.24 (0.18, 0.30) | 99.82% | 0.959 |
| South Korea | 13 | 0.24 (0.14, 0.34) | 99.86% | 0.8886 |
| Japan | 12 | 0.15 (0.10, 0.20) | 97.44% | 0.3077 |
| Italy | 10 | 0.07 (0.05, 0.09) | 95.97% | 0.0635 |
| UK | 8 | 0.19 (0.14, 0.26) | 99.70% | NA |
| Bangladesh | 7 | 0.09 (0.05, 0.14) | 60.31% | NA |
| Germany | 7 | 0.20 (0.10, 0.32) | 98.57% | NA |
| Norway | 6 | 0.23 (0.07, 0.45) | 99.99% | NA |
| Thailand | 6 | 0.20 (0.07, 0.38) | 97.97% | NA |
| Rwanda | 5 | 0.02 (0.02, 0.04) | 78.48% | NA |
| Brunei | 4 | 0.06 (0.01, 0.15) | 95.28% | NA |
| Canada | 4 | 0.21 (0.15, 0.28) | 99.68% | NA |
| Greece | 4 | 0.20 (0.13, 0.27) | 94.32% | NA |

[a] N: number of observations

** Not applicable: less than 10 studies in the analysis lacked sufficient statistical power for the Egger's test

### SARs by disease severity of index cases

Of 159 studies analysed, 51 provided data on SARs associated with the disease severity in index cases. SARs increased from 0.10 (95% CI: 0.06–0.14) for asymptomatic index cases to 0.15 (95% CI: 0.09–0.21) for those with severe/critical conditions (Fig. 2). The subgroup analysis of asymptomatic cases across WHO regions revealed higher SARs in Southeast Asia than in Europe, North America, and the Western Pacific regions (Additional file 1 p. 14). Further analysis based on World Bank income classifications showed that LMICs had the highest SARs for asymptomatic cases, followed by UMICs and HICs. HICs exhibited the highest SARs for both mild/moderate and severe/critical cases, whereas LMICs demonstrated the lowest SARs for mild/moderate cases (Additional file 1 pp. 15–17). However, the differences among groups were not statistically significant.

### SARs by age of index cases and close contacts

Among index cases, the SARs were 0.22 (95% CI 0.15–0.29) for those under 18 years of age, 0.27 (95% CI 0.22–0.33) for those aged 18–49 years, 0.28 (95% CI 0.23–0.34) for those aged 50–64 years, 0.29 (95% CI 0.24–0.34) for those aged 65 years or older, although these differences were not statistically significant (*P*-value = 0.096). A similar increasing pattern of SARs by age was also observed among close contacts (Table 2, Additional file 1 pp. 18–21). Regionally, North America had the highest SARs among index cases and close contacts for all age groups, in contrast to the lowest SARs in Southeast Asia for index cases and in the Western Pacific for close contacts (Additional file 1 p. 108). Furthermore, age-dependent SARs varied across World Bank income classifications for both index cases and close contacts, particularly for age groups under18 and 65 years or older (Additional file 1 p. 108).

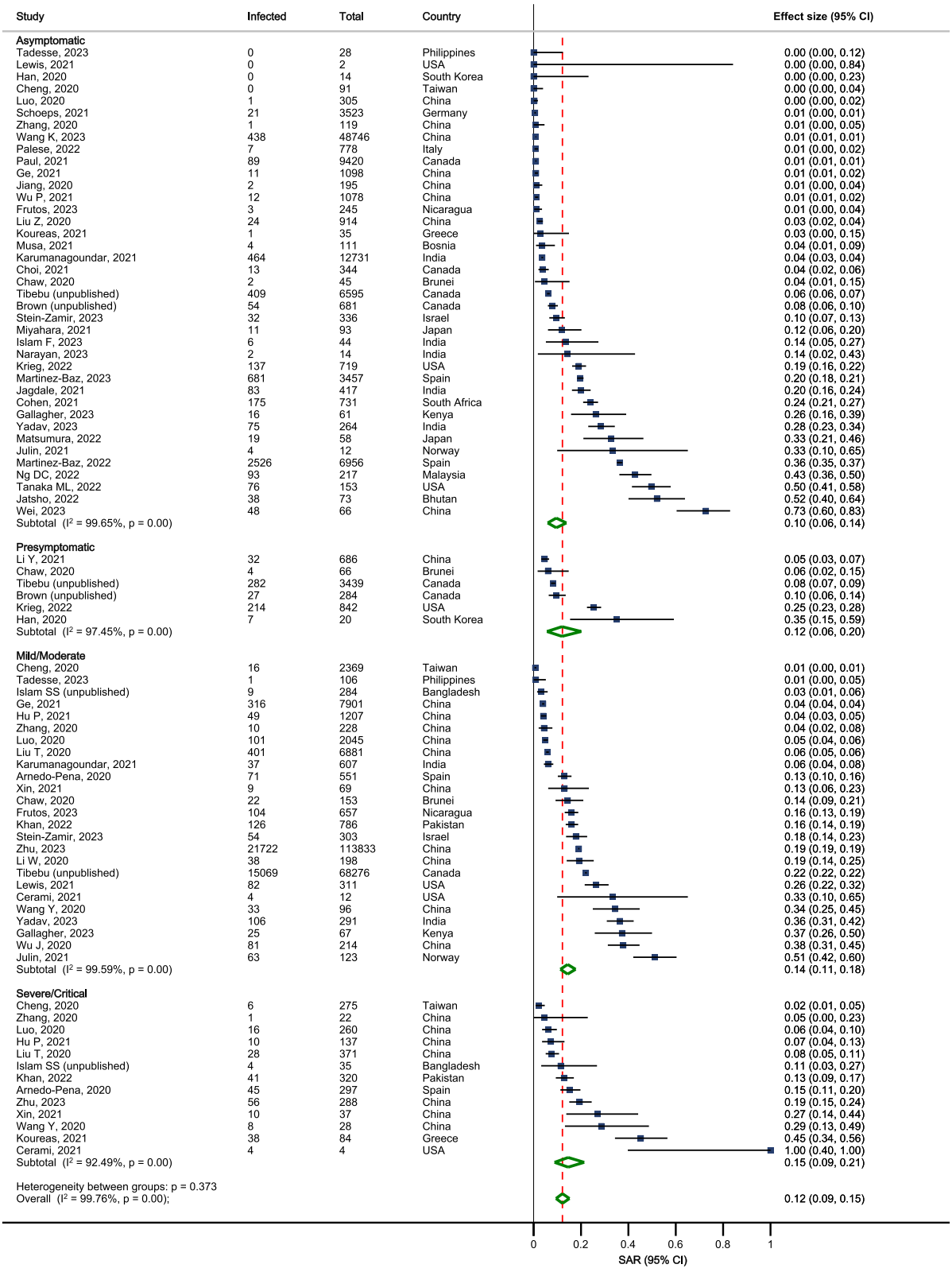


**Fig. 2** Secondary attack rates (SARs) by disease severity of index cases

**Table 2** SARs and adjusted SARs by age and sex of index cases and close contacts

| Subgroup | Age (years) | N[a] | SAR (95% CI) | $I^2$ | Egger's *P*-value | Adjusted SAR |
|---|---|---|---|---|---|---|
| Index cases | < 18 | 56 | 0.22 (0.15, 0.29) | 99.93% | 0.6555 | NA |
| | 18–49 | 53 | 0.27 (0.22, 0.33) | 99.98% | 0.0050 | 0.25 (0.20, 0.29) |
| | 50–64 | 53 | 0.28 (0.23, 0.34) | 99.92% | 0.0171 | 0.24 (0.20, 0.29) |
| | ≥ 65 | 52 | 0.29 (0.24, 0.34) | 99.65% | 0.0622 | NA |
| Close contacts | < 18 | 70 | 0.20 (0.16, 0.23) | 99.44% | 0.0649 | NA[b] |
| | 18–49 | 71 | 0.22 (0.19, 0.25) | 99.75% | 0.0008 | 0.21 (0.14, 0.27) |
| | 50–64 | 65 | 0.23 (0.20, 0.26) | 99.20% | 0.0006 | 0.20 (0.14, 0.27) |
| | ≥ 65 | 63 | 0.24 (0.21, 0.27) | 99.01% | 0.0134 | 0.22 (0.16, 0.29) |
| | **Sex** | | | | | |
| Index cases | Male | 44 | 0.25 (0.16, 0.36) | 99.99% | 0.0001 | 0.27 (0.21, 0.33) |
| | Female | 44 | 0.25 (0.15, 0.35) | 99.99%, | 0.0001 | 0.26 (0.20, 0.31) |
| Close contacts | Male | 67 | 0.20 (0.17, 0.22) | 99.72% | 0.0069 | 0.23 (0.19, 0.27) |
| | Female | 68 | 0.22 (0.20, 0.25) | 99.71% | 0.0037 | 0.26 (0.21, 0.30) |

[a] N: number of observations

[b] Not applicable: less than 10 studies in the analysis lacked sufficient statistical power for the Egger's test

#### SARs by SARS-CoV-2 variants and vaccination status

For index cases, SARs were highest for Omicron at 0.32 (95% CI: 0.28–0.36), followed by Alpha at 0.31 (95% CI: 0.21–0.42), and Delta at 0.19 (95% CI: 0.15–0.23), irrespective of the vaccination status (Fig. 3). Similar results were observed for close contacts regardless of their vaccination status (Additional file 1 p. 22).

When considering the vaccination status of index cases and close contacts, SARs decreased with an increase in the number of vaccine doses, with reductions observed for the Omicron, Delta, and Alpha variants. For the Omicron variant (Additional file 1 p. 23), SARs reduced from 0.41 (95% CI: 0.24–0.59) for unvaccinated individuals to 0.32 (95% CI: 0.17–0.49) for partially vaccinated, 0.31 (95% CI: 0.21–0.42) for fully vaccinated, and 0.26 (95% CI: 0.14–0.41) for booster recipients among index cases, with comparable declines noted for the Delta and Alpha variants (Additional file 1 p. 24–25). For close contacts, we obtained similar results for variant-specific SARs to those derived from the index case analysis (Additional file 1 pp. 26–28).

#### SARs by comorbidity of close contacts

In our analysis of seven comorbidities, chronic lung disease had the highest SAR at 0.38 (95% CI: 0.26–0.50), followed by hypertension at 0.32 (95% CI: 0.21–0.45) and asthma at 0.30 (95% CI: 0.15–0.47) (Additional file 1 p. 29). Diabetes and cerebrovascular disease had similar SARs at 0.29 (95% CI: 0.20–0.39) and 0.29 (95% CI: 0.16–0.43), respectively. The lowest SARs were associated with chronic obstructive pulmonary disease and cardiovascular disease, estimated at 0.27 (95% CI: 0.18–0.36) and 0.26 (95% CI: 0.18–0.36), respectively.

#### SARs by sex of index cases and close contacts

Among index cases, both males and females showed similar SARs of 0.25 (95% CI: 0.16–0.36) and 0.25 (95% CI: 0.15–0.35), respectively (Table 2, Additional file 1 p. 30). Likewise, for close contacts, there was no significant difference ($P$-value = 0.435) in SARs observed between males and females (Additional file 1 p. 31). Analysis by the WHO regions revealed notably higher SARs for both males and females in North America compared to other regions, which were observed across both index cases and close contacts (Additional file 1 p. 109). In the subgroup analysis by World Bank income classifications, SARs were higher in HICs for both males and females compared to LMICs and UMICs (Additional file 1 p. 109).

#### SARs by identification period, setting, region and income status

During the identification period from January 2020 to August 2022, the highest SAR was 0.26 (95% CI: 0.17–0.36) in 2021 (Table 1). Despite the continual emergence of highly transmissible variants, SARs in 2022 significantly decreased compared to 2021 ($P$-value = 0.008). We observed a significant difference in SARs across population settings ($P$-value < 0.001), with households exhibiting the highest SAR at 0.26 (95% CI: 0.23–0.29), followed by institutional settings at 0.15 (95% CI: 0.09–0.22) and social settings at 0.11 (95% CI: 0.06–0.16). Regionally, North America had the highest SAR (0.27, 95% CI: 0.24–0.30), significantly surpassing SARs in Europe (0.19, 95% CI: 0.15–0.25), Southeast Asia (0.18, 95% CI: 0.13–0.24), and the Western Pacific (0.11, 95% CI: 0.08–0.15) ($P$-value < 0.001). Analysing the World Bank

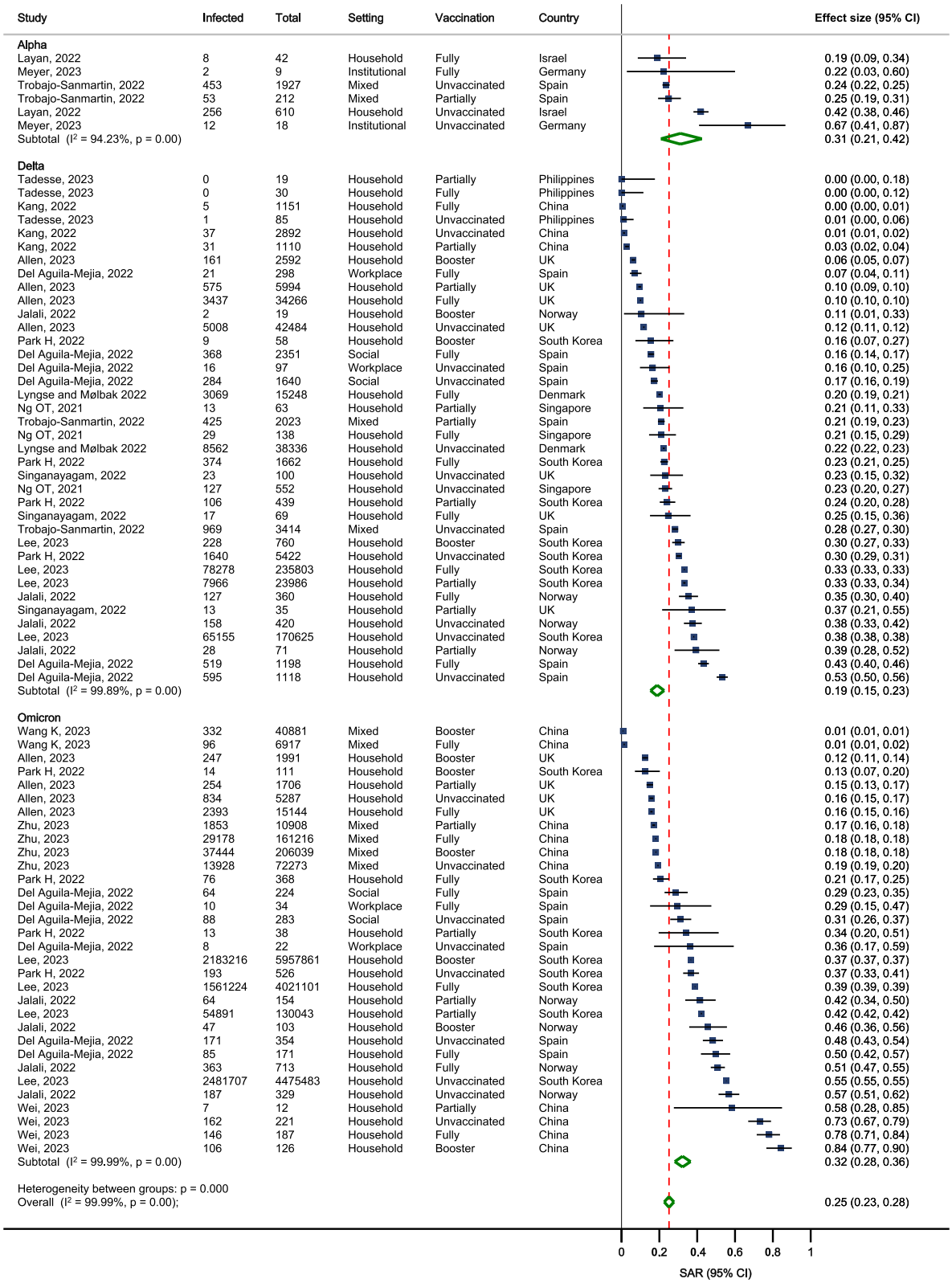


**Fig. 3** Secondary attack rates (SARs) by SARS-CoV-2 variants

income classification, we found a significant difference (*P*-value = 0.001), with HICs showing the highest SAR at 0.20 (95% CI: 0.15–0.25), contrasting with the lowest SAR of 0.11 (95% CI 0.08–0.14) in UMICs (Table 1). Across countries, the United States had the highest SAR while China and Italy reported the lowest SARs (Additional file 1 pp. 32–39).

#### SARs by stringency index and study characteristics

We classified studies based on the WM-SI for the strictness of NPIs during the study period as light restriction (WM-SI < 20), moderate lockdown (20 ≤ WM-SI ≤ 60), and full lockdown (WM-SI > 60). SARs were 0.18 (95% CI: 0.10–0.27) for light restriction, 0.14 (95% CI: 0.09–0.19) for moderate lockdown, and 0.19 (0.16–0.21) for full lockdown (Table 1). The subgroup analyses indicated higher SARs under full lockdowns for all levels of disease severities in index cases compared to moderate lockdowns (Additional file 1 pp. 40–42). Additionally, the SARs for the Omicron variant among index cases and close contacts were similar in moderate and full lockdowns (Additional file 1 pp. 43–44). Studies with a sample size of ≤ 300 reported a significantly higher (*P*-value = 0.012) SARs compared to those with a sample size > 300 (Additional file 1 pp. 45–46).

#### Meta-regression analyses

Meta-regression analyses were conducted to examine the relationship between the strictness of NPIs, represented by the WM-SI, and SARs (Fig. 4). We found a significant positive association between the delay in implementing NPIs relative to the identification of the first SARS-CoV-2 case and SARs for light restrictions (*P*-value = 0.019, coefficient = 0.00123), moderate lockdowns (*P*-value < 0.001, coefficient = 0.00216), and full lockdowns (*P*-value = 0.002, coefficient = 0.00152).

To assess the association between WM-SI and SARs, we classified included studies by their timeframes based on the median of 75 days for the durations of all studies. Although there was an increasing trend for SARs with higher WM-SI (Fig. 4E-F), we found no significant association between the WM-SI and SARs for studies lasting 75 days or less (*P*-value = 0.081) or those exceeding 75 days (*P*-value = 0.513). Similarly, no significant association was observed between WM-SI and SARs when considering all studies irrespective of their duration (*P*-value = 0.071, Fig. 4G). However, for studies with a duration exceeding 75 days in the first year of the pandemic between January 5, 2020 and December 31, 2020 there was a negative association between full lockdown and SARs (*P*-value = 0.0243; coefficient = −0.00972, Additional file 1 p. 47). Furthermore, a positive association was found between healthcare expenditure and SARs (*P*-value < 0.0001, coefficient = 0.00853) in our meta-regression analyses (Additional file 1 p. 48).

#### Publication bias

SARs across identification periods for different subgroups showed mostly symmetric funnel plots. However, publication bias was detected using Egger's test for identification periods in 2021, household settings, and the European region (Table 1), affecting SAR estimates (Additional file 1 pp. 49–52). No publication bias was detected for the stringency index of the NPIs, but bias was identified in studies with a sample size of 300 or fewer observations and in studies of high or moderate quality (Additional file 1 p. 53). Studies that were classified as low risk showed significantly higher SARs compared to those classified as having moderate risk of bias (*P*-value = 0.036) (Additional file 1 p. 54–55). For disease severity, no bias was found for asymptomatic cases, but bias was present for mild/moderate and severe/critical cases (Additional file 1 p. 56). For age, bias was found in close contacts aged 18–49 and 50–64 years, and index cases aged 18–49, 50–54, and 65 + years (Additional file 1 p. 57), with adjusted SARs provided in Table 2. For the variants of SARS-CoV-2 in index cases and close contacts (Additional file 1 p. 58), no bias was found for Delta; however, bias was present for Omicron among index cases and close contacts. Publication bias was identified for both sexes among index cases and close contacts (Additional file 1 p. 59) with similar estimates for the adjusted SARs (Table 2).

#### Sensitivity analyses

The post-hoc sensitivity analyses, excluding studies with SARs above 60%, showed robustness in the findings, with consistent effect estimates across factors examined in our study (Additional file 1 pp. 60, 110–111).

## Discussion

This study presents the largest systematic review and meta-analysis of SARs of SARS-CoV-2 for the entire duration of the COVID-19 pandemic, synthesising data from 41 countries across WHO regions. Analysis of population settings (Additional file 1 pp. 32–33) revealed that households accounted for the highest SARs, markedly exceeding those observed in other settings. Geographic and income-based stratification showed significant variations across regions, with North America and HICs experiencing the highest SARs, while the Western Pacific and UMICs had the lowest SARs.

For the first time, we report on the impact of the full spectrum of disease severity on SARs. The highest SAR in asymptomatic index cases was observed in LMICs, while mild/moderate and severe/critical conditions exhibited highest SARs in HICs and UMICs, respectively. Our findings indicate that SARs for the Omicron variant were significantly higher than those for Delta

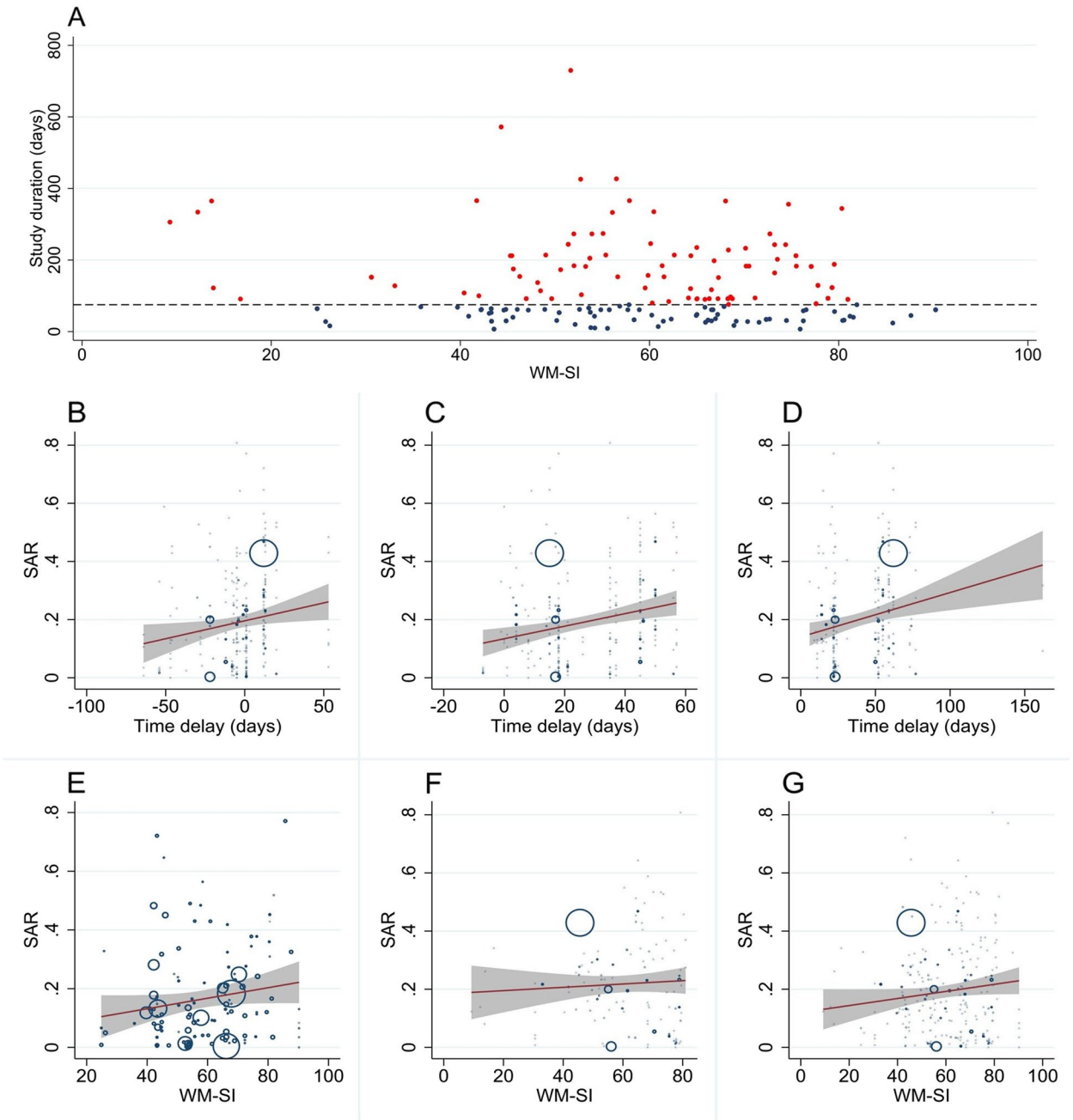


**Fig. 4** Distribution of WM-SI across study durations and meta-regression analysis illustrating the association between WM-SI and secondary attack rates (SARs). **A** Distribution of WM-SI for studies with durations of 75 or fewer days (blue circles) and those with longer than 75 days (red circles). The dashed line represents the median of 75 days duration across all studies. Panels **B**-**D** display the meta-regression analysis for the association between SAR and the delay in implementation of NPIs relative to the timing of the first identified SARS-CoV-2 case, categorised by light restrictions (**B**), moderate lockdowns (**C**), and full lockdowns (**D**). Panels **E**–**G** show the meta-regression analysis for the association between SAR and WM-SI for studies with durations shorter than 75 days (**E**), longer than 75 days (**F**), and for all studies regardless of duration (**G**)

regardless of vaccination status, reflecting the higher transmissibility of Omicron. Furthermore, we observed a declining trend in SARs with an increasing number of vaccine doses, highlighting the importance of vaccination in mitigating transmission risks, particularly in the context of emerging variants [190]. SARs were most elevated among individuals aged 65 years or older and lowest among those under 18 years of age. Our analysis of seven

comorbidities revealed that close contacts with chronic lung diseases and hypertension had the highest SARs. Additionally, we found no significant differences in SARs of SARS-CoV-2 between males and females. Lastly, we found that delays in implementing NPIs relative to the identification of the first SARS-CoV-2 case were positively associated with higher SARs.

Compared with previous studies predominantly conducted during the early stages of the pandemic [16, 17], our pooled estimates show a higher SAR in household settings. This finding aligns with the results of earlier work focusing on household SARs after the emergence of the Omicron variant [191]. When considering SARS-CoV-2 variants, our results showed similar patterns of SARs, with Omicron exhibiting the highest, followed by Alpha and Delta, irrespective of the vaccination status of index cases or close contacts. However, our estimates for the overall, and the Omicron and Delta variants SARs are lower than those reported in a previous meta-analysis conducted for studies published before March 2022 [191]. The longer timeframe of our study, from the beginning of the COVID-19 pandemic through January 2024, includes studies with evolving subvariants post-Omicron emergence and the introduction of booster vaccinations. These factors, influenced by changes in population immunity, likely affected SARs.

Previous meta-analyses have noted significant unexplained heterogeneity in SARs, likely due to the diversity of regions in the included studies. Our study addressed this heterogeneity by systematically examining SARS-CoV-2 transmission across WHO regions. We found the lowest and highest SARs in Western Pacific and North America, respectively. Several factors may have contributed to lower SARs in the Western Pacific, including border closures, COVID-zero policies, prolonged lockdowns, and stronger compliance with public health measures [192]. Furthermore, the timing of NPI implementation—measured relative to the timing of the first detected COVID-19 case—may correlate with SARS-CoV-2 transmission dynamics and help explain these variations. Our meta-regression analyses further support this, demonstrating that delays in enacting NPIs were positively associated with increased SARs, underscoring the importance of timely interventions in mitigating SARS-CoV-2 spread across regions. While the duration and strictness of NPIs could influence disease transmission, their effectiveness varied based on individual-level adherence throughout the pandemic [193]. Assessing adherence levels and their impact on SARs is challenging to quantify, and beyond the scope of this study. Consequently, we analysed associations between the stringency index of NPIs and SARs across study periods, finding no significant association. Notably, subgroup analyses revealed that full lockdowns were often implemented during periods of relatively high SARs (Additional file 1 pp. 29–30), suggesting a reactive rather than proactive approach to mitigating disease spread.

Our study revealed higher SARs from asymptomatic and presymptomatic index cases compared to those reported in previous meta-analyses [15–17]. Specifically, Southeast Asia and LMICs showed the highest SARs, potentially influenced by factors such as high population density and cultural and social practices. There was no prior meta-analysis quantifying SARs for index cases with mild/moderate or severe/critical conditions, and thus no comparison with our results could be made. For the stratification of SARs by age, our findings align with published estimates [17], indicating age-dependent increase in SARs among index cases and close contacts. Although existing evidence suggests that males had a higher SAR [7, 194], we found no significant differences between SARs among males and females. Our study identified chronic lung diseases and hypertension as the two comorbidities with the highest SARs, expanding previous systematic reviews that evaluated the association between the presence of comorbidities and the risk of infection [17, 195, 196].

#### Study limitations

Our study has several limitations. First, we were unable to account for the type of vaccine, time elapsed since the last dose of vaccination, or the Omicron subvariants in our analyses due to data constraints; however, the waning of immunity over time or exposure to more transmissible subvariants may have resulted in higher SARs. Second, residual confounding factors such as healthcare access disparities and population density may not have been fully addressed in the included studies, potentially influencing SARs through factors such as timely diagnosis, treatment, isolation, and increase in the risk of exposure in densely populated areas. Third, despite efforts to include a wide range of studies, our focus on English-language publications and indexed databases may have excluded relevant non-English studies or unpublished data. Furthermore, given significant heterogeneity among the included studies, coupled with a limited number of studies in each subgroup, a conservative interpretation of the results is warranted. Fourth, while the weighted mean stringency index provides a standardised measure for assessing the association between NPI strictness and SARs across studies with varying durations and contexts, it is based on the proportion of days in each strictness category and does not fully capture variations in the actual interventions, their intensity, or local adherence. Over the study period, many countries transitioned from strict lockdowns to more moderate measures, which

likely influenced SARs by altering transmission dynamics through increased mobility, changing behaviours, and varying adherence to public health guidance. Additionally, differences in the type and intensity of interventions, such as mask mandates, social distancing, and testing policies, could have further influenced SARs, with stricter measures potentially leading to lower SARs. These variations in policies and enforcement may have introduced additional heterogeneity into SAR estimates. The lack of information on these factors in the included studies did not allow us to quantify the direct effect of NPIs on SARs of SARS-CoV-2. Finally, limited data from Central and South America, Eastern Mediterranean, and Africa restricted the scope of our regional analysis.

## Conclusions

Our findings have important implications for controlling the spread of SARS-CoV-2 and preparing for future pandemics. The observed heterogeneity and regional variations in SARs highlight the need for tailored measures that fit the demographic, geographic, and social characteristics of different populations. Furthermore, our results indicate that a substantial portion of transmission occurs in settings outside households. The evolving nature of SARS-CoV-2 requires adaptable strategies in vaccination and public health measures. Future research should evaluate the effectiveness of vaccination programs, including booster doses, assess the impact of vaccine formulations and timing, and develop public health policies to address emerging variants and changing transmission patterns. Further investigation is also needed to quantify SARs in Africa, Central and South America, and the Eastern Mediterranean regions. For long-term pandemic preparedness, especially in resource-constrained settings, research priorities should examine the resilience of healthcare systems, the effectiveness of sustained interventions, and the potential emergence of viral variants to enhance a more robust global response framework.

### Abbreviations

| | |
|---|---|
| SARs | Secondary attack rates |
| WHO | World Health Organization |
| SI | Stringency Index |
| WM-SI | Weighted mean stringency index |
| PRISMA | Preferred Reporting Items for Systematic reviews and Meta-Analyses |
| LICs | Low-income countries |
| HICs | High-income countries |
| UMICs | Upper-middle-income countries |
| LMICs | Lower-middle-income countries |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-025-10610-5.

Additional file 1. Details of the search, study characteristics, and results of sensitivity analyses.

### Authors' contributions

DMS, SMM conceptualised and designed the study; DMS and YY performed systematic searches; DMS, YY and ZW conducted screening search results, data collection, and risk-of-bias assessments; SMM, AP, and APG assisted with conflicts; DMS and SMM performed statistical analyses; DMS, AP, JML, APG and SMM wrote the manuscript and interpreted the results; SMM supervised the study; SMM and APG Obtained funding. All authors have reviewed and approved the manuscript.

### Funding

This study was supported by the Canadian Immunization Research Network (CIRN). Seyed M. Moghadas acknowledges support from the Natural Sciences and Engineering Research Council of Canada (Discovery and Alliance grants). Alison P. Galvani acknowledges support from the The Notsew Orm Sands Foundation.

### Data availability

All study data are included in the main text and Additional file 1.

## Declarations

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Competing interests

JM Langley's institution, Dalhousie University, has received funds for clinical trials conducted by the Canadian Center for Vaccinology from GSK, Janssen, Sanofi, Immunovaccine, Inventprise, Merck, Pfizer, VIDO, VBI and Entos. SM Moghadas and AP Galvani have received consultation fees from Sanofi for evaluating their vaccine products unrelated to this study. SM Moghadas had advisory roles for Janssen Canada and Sanofi and received personal fees outside the work presented here. AP Galvani has received personal fees from Sanofi outside the work presented here. Other authors declare that they have no competing interests.

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Received: 22 November 2024 Accepted: 6 February 2025
Published online: 13 February 2025

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