The household secondary attack rate of SARS-CoV-2: A rapid review

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40-word summary

Data from 22 published and pre-published studies suggest estimates of the SARS-CoV-2 household secondary attack rate are higher when contacts are tested more frequently. Testing household contacts on multiple occasions may increase the yield for identifying secondary cases.

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Abstract

Background

Although much of the public health effort to combat COVID-19 has focused on disease control strategies in public settings, transmission of SARS-CoV-2 within households remains an important problem. The nature and determinants of household transmission are poorly understood.

Methods

To address this gap, we gathered and analyzed data from 22 published and pre-published studies from 10 countries (20,291 household contacts) that were available through September 2, 2020. Our goal was to combine estimates of the SARS-CoV-2 household secondary attack rate (SAR) and explore variation in estimates of the household SAR.

Results

The overall pooled random-effects estimate of the household SAR was 17.1% (95% CI: 13.7-21.2%). In study-level, random-effects meta-regressions stratified by testing frequency (1 test, 2 tests, >2 tests), SAR estimates were 9.2% (95% CI: 6.7-12.3%), 17.5% (95% CI: 13.9-21.8%), and 21.3% (95% CI: 13.8-31.3%), respectively. Household SAR tended to be higher among older adult contacts and among contacts of symptomatic cases.

Conclusions

These findings suggest that SAR reported using a single follow-up test may be underestimated and that testing household contacts of COVID-19 cases on multiple occasions may increase the yield for identifying secondary cases.

Keywords: SARS-CoV-2, household transmission, secondary attack, testing frequency

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Introduction

Non-pharmaceutical interventions, such as social distancing and mask-wearing, have shown considerable promise in reducing transmission of SARS-CoV-2. However, such measures may be difficult to implement within households, where transmission remains an important challenge for disease control.

Evidence regarding intra-household transmission dynamics is accumulating rapidly. Several primary studies and unpublished reviews have reported household secondary attack rates (SAR) for SARS-CoV-2 that converge in the 15-19% range [1, 2]. Many of the primary studies were conducted in China where household structure (e.g., prevalence of multi-generational households) and roles (e.g., allocation of responsibility for child or elder care) may affect generalizability to other domestic settings. Systematic reviews to date have not examined the sensitivity of SAR estimates to study design features, such as frequency of follow-up testing. Consequently, there are substantial gaps in the understanding of SARS-CoV-2 transmission within households, hampering the development of prevention policies and protocols.

We reviewed and analyzed available studies of the household SAR for SARS-CoV-2. The analysis addressed aspects of measurement and study design that are likely to influence the reported estimates, including details of follow-up and testing, cases and contacts, and geographic settings. Our goal was to muster the best available evidence on infection risk among people living with someone with SARS-CoV-2, both to aid development of optimal disease control policies and improve the accuracy of epidemic forecasts. In addition, we sought to identify key gaps in existing evidence of the household SAR.

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Methods

Search strategy and selection criteria

We searched *PubMed*, *bioRxiv*, and *medRxiv* on September 2, 2020 for published and pre-published studies reporting empirical estimates of household SARs for SARS-CoV-2. The search terms, which are reported in full in Figure 1, paired variants of the disease terminology (e.g., "SARS-CoV*", "COVID*") with terms such as "household", "secondary attack", "family transmission", "family contact", and "indoor transmission". We considered only English-language records posted on or after January 1, 2019.

To identify papers that were clearly out-of-scope, we developed a set of exclusionary and inclusionary keywords to screen out some papers on the basis of their titles alone (Figure 1). The exclusionary keywords were designed to eliminate modeling studies and took precedence over inclusionary keywords. Eligible titles were reviewed at the abstract and full text levels by two authors (H. F. and L. M.) and the bibliographies of studies reviewed in full text were screened for additional papers related to the household SAR.

Studies were included in the final sample if they met the following eligibility criteria: they (i) reported estimates of the household SAR or the data required to compute the household SAR; (ii) comprised data from more than one household; and (iii) tested—at a minimum—all symptomatic household contacts by reverse transcription polymerase chain reaction (RT-PCR). We reviewed the subset of included studies to establish whether there was overlap in the study populations across multiple included studies. We employed more stringent eligibility criteria than existing reviews to mitigate sources of bias in our meta-analyses. For example, we excluded studies that did not test all symptomatic contacts because they were likely to underestimate the

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household SAR. To minimize heterogeneity in case definition, we considered only studies that used RT-PCR testing, rather than antibody testing.

Two reviewers (H. F. and L. M.) independently assessed the quality of each study using a modified 9-point Newcastle-Ottawa scale for observational studies [3]. Specifically, each study was evaluated on the basis of three criteria: selection of participants (4 points), comparability of studies (1 point), and ascertainment of the outcome of interest (3 points; Supplementary Table 1). Studies that scored 7 points or higher were classified as 'high quality', those that scored 4 to 6 points as 'moderate quality', and those with 3 or fewer points as 'low quality'. The two reviewers discussed discrepancies in their scores and jointly re-evaluated the relevant studies to reach consensus.

Study definitions

We defined 'household contacts' as people living in the same residence as the index case, and the 'household SAR' as the percentage of all household contacts who were reported to have tested positive for SARS-CoV-2 by RT-PCR. Definitions of an 'index case' came from the studies themselves, and were defined as either the first case to be confirmed in a household or the confirmed case with the earliest date of symptom onset. Such definitions run the risk of misclassifying asymptomatic index cases as secondary cases.

Data analysis

All analyses were performed in R version 3.6.1 (R Foundation for Statistical Computing). We computed exact binomial confidence intervals for SAR estimates reported without uncertainty through the 'Hmisc' package. We used random- and mixed-effects binomial-normal models ('metafor' package) to generate pooled estimates of the household SAR and quantified the

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residual heterogeneity between studies using the I^2 statistic. A *p*-value of <0.05 was considered statistically significant. We did not account for household clustering as the studies rarely reported the data needed for these calculations.

Results

We found 826 papers from our multi-database search and two additional papers from the bibliographies of studies reviewed in full text, yielding 828 papers in total. Five hundred and eighty-five were excluded at the title review stage and 186 were excluded after abstract review (Figure 1). After conducting full text reviews of the remaining 57 papers, we identified a final set of 22 papers that met our eligibility criteria. Twenty of the papers were published and two were unpublished. Six of the papers reported results of prospective studies and 16 reported retrospective studies.

The number of household contacts evaluated per study ranged from 11 to 10,592 (Table 1 and Figure 2). Four of the studies were classified as high quality; 14 were classified as moderate quality; and four classified as low quality (Supplementary Table 1). Eleven studies analyzed households in China [4–14]; the rest analyzed households in South Korea [15, 16], Taiwan [17], Singapore [18], Brunei [19], Israel [20], Germany [21], the Netherlands [22], the United States [23, 24], and Australia [25]. Testing criteria were largely congruent across studies: 19 of the 22 studies tested all household contacts regardless of symptoms.

Six of the China-based studies examined households in Guangdong province [7–9, 11, 12, 14]; the cohorts used in these studies did not overlap (personal communication, Guangdong CDC). The households followed in the two studies from South Korea [15, 16] were not discrete: Park SY *et al.* used a subcohort of the cohort used in Park YJ *et al.* Nevertheless, we chose to

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include the smaller study in our sample because it reported information that the larger one did not (namely, household SAR by index case symptoms), but we excluded it from analyses of the overall household SAR. The two studies from Wuhan, China [4, 5] recruited index cases from different hospitals and were considered distinct populations. The study from Singapore [18] focused on pediatric household contacts (≤16 years) and was included in our analysis only for purposes of examining how the household SAR varied by age of contact.

In total, the 22 studies considered 20,291 household contacts, 3,151 (15.5%) of whom tested positive for SARS-CoV-2. Household SAR estimates ranged from 3.9% in the Northern Territory, Australia [25] to 36.4% in Shandong, China [6] (Figure 2). The overall pooled random-effects estimate of SAR was 17.1% (95% CI: 13.7-21.2%), with significant heterogeneity (p<0.0001; Supplementary Table 2).

Excluding the two unpublished studies had little effect on the pooled SAR estimate (16.8% [95% CI: 13.4-20.8%]; Supplementary Table 2). Similarly, study timing, operationalized as the enrollment start date, was not significantly related to SAR estimates (Supplementary Table 2).

Next, we computed SAR estimates by region to explore geographic differences. The SAR estimates were 18.1% (95% CI: 14.2-22.8%), 13.5% (95% CI: 7.2-23.9%), and 17.4% (95% CI: 9.7-29.4) for China, Asian countries outside of China, and countries outside of Asia, respectively (Supplementary Table 2). The pooled estimate tended to be higher among studies that defined the index case by symptom onset date (21.0% [95% CI: 14.9-28.8%]) than among studies that defined the index case as the first confirmed case (15.6% [95% CI: 11.7-20.3%]; Supplementary Table 2).

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The amount of residual heterogeneity, as measured by the I^2 statistic, decreased from 96.7% to 91.2% after accounting for follow-up duration and testing frequency, suggesting these study features were important determinants of the household SAR estimates (Supplementary Table 2 and Table 1). Between-study variation could not be explained by differences in study quality (I^2 was 96.5% when study quality was included as a moderator variable; Supplementary Table 2).

Estimates of the household SAR were lower, on average, in studies with less frequent testing of contacts. Random-effects regressions stratified by frequency of follow-up testing revealed that studies with >2 follow-up tests of contacts reported an average household SAR of 21.3% (95% CI: 13.8-31.3%), whereas those with 2 follow-up tests averaged 17.5% (95% CI: 13.9-21.8%), and those with a single follow-up test averaged 9.2% (95% CI: 6.7-12.3%; Supplementary Table 2).

The household SAR was higher among adults and older adults than among children, and higher among female contacts and contacts of symptomatic cases (Table 2 and Supplementary Figure). SARs were also elevated among spouses or significant others of index cases relative to non-spouse household members (Supplementary Table 5).

Two studies reported the household SAR by age of the index case (Table 2). In the study from Qingdao, China [13], the household SAR was higher when index cases were 55 years or older than when cases were younger than 55 years (Table 2). In South Korea [16], the household SAR was highest for index cases aged 10-19 years (18.6%; 95% CI: 14.0-24.0%) and lowest for those younger than 9 (5.3%; 95% CI: 1.3-13.7%); by comparison, the SAR estimates for adult age groups ranged from 7.0 to 18.0% (Supplementary Table 3).

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There are a number of additional factors that could have influenced household SAR estimates, including mask use and index case severity. A small subset of the studies considered these factors, and their findings are summarized in Supplementary Table 5.

Discussion

While much of the public health effort in controlling SARS-CoV-2 has appropriately focused on preventing community transmission, people who reside with infected individuals are an important group; they are at substantial risk of infection due to prolonged, close contact. Available estimates of the SAR within households vary widely, and the determinants of transmission risk, including age of index cases and contacts, are only beginning to be understood. In this review of studies to date, we calculated a household SAR of 17.1% (95% CI: 13.7-21.2%). Importantly, we observed considerable heterogeneity in household SAR estimates, and there appeared to be systematic variation according to identifiable aspects of study design.

In particular, studies that tested contacts more frequently tended to generate larger SARs. This suggests that studies with less intensive testing may have missed cases and underestimated the household SAR. Other aspects of study design and setting are likely to contribute to variation in the observed estimates; they include approaches to case selection, how quickly symptomatic index and secondary cases were detected, the timing of testing, and the phase of the epidemic.

Although only a minority of studies reported household SARs by contact age, the available evidence suggests that the estimates are sensitive to this variable. Most of these studies found higher SARs among adults than children. Whether this is due to differential susceptibility to

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infection or differential exposure to the index case is not yet clear for SARS-CoV-2, but the higher SAR in children for other respiratory viruses (such as 2009 H1N1 pandemic influenza [26, 27]) suggests that differential exposure is unlikely to fully explain these discrepancies. Other hypotheses for lower household SARs among children (and asymptomatic contacts) include lower viral loads leading to low sensitivity of RT-PCR tests or a lower probability of testing.

Our review identified only a few studies that examined the relationships between household SAR and the age and symptomatic status of the index case. While results suggest that index cases who are young children (between 0 and 9 years) and index cases who are asymptomatic may have lower household SAR, further studies are critically needed to clarify the effects of age and symptoms of cases on household transmission risk.

Other characteristics of households and household members—including some that were not observed or reported in existing studies—are likely to affect the household SAR, and explain some of the substantial heterogeneity in reported estimates. The number of cohabitants and the density of living conditions (e.g., number of household members per room) are almost certainly influential, as are, relatedly, isolation and prevention practices within the household—both what is feasible and the extent to which feasible options are pursued. For example, the study based in Bnei Brak, Israel [20], followed a cohort of households with relatively large numbers of cohabitants living in a close-knit community; these factors plausibly contributed to the study's reported household SAR of 32.1% (95% CI: 30.4-33.9%), which was at the high-end of all estimates in our sample. Furthermore, mask use within households is likely to be protective, but only one study [8] stratified the household SAR by index case mask use. Additional studies are required to elucidate the effect of masks on household transmission. Lastly, index case severity

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and the timing of testing are likely determinants of transmission potential. Few studies, however, considered these factors in the context of household SAR.

The main limitations of our analysis spring from limitations in available data and studies, though much has been accomplished in understanding a pandemic that has raged for less than a year. In particular, caution must be taken in generalizing summary statistics, like household SARs, across countries and regions. Household size and composition, contact patterns, and testing and isolation practices all vary substantially geographically. None of the included studies come from South Asia, Latin America or Africa—places that account for a substantial proportion of the global caseload [28]. This review suggests there is a critical need for studies in these regions to investigate whether there are setting-specific differences that influence the household SAR.

The COVID-19 pandemic has been devastating, and many countries are working actively to formulate effective strategies for containment. While preventing spread in congregate public settings is a critical first step, a full-fledged strategy for reducing transmission must also involve interventions to prevent transmission within households [29, 30]. Such interventions have begun to take place in some settings and may include early case detection, isolation of cases, systematic investigation and quarantine of exposed household contacts, and the development and use of effective post-exposure chemoprophylaxis among exposed household members [31]. Design and implementation of these strategies—including prioritization of cases and contacts who pose and face the greatest risk—should be informed by a better understanding of the extent, nature, and determinants of transmission in households.

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Notes

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Potential Conflicts of interest

We declare that we have no potential conflicts of interest.

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Table 1. Household secondary attack rates stratified by study design.

Study	Enrollment dates	No. index cases	No. contacts	% contacts tested	No. tests per contact	Household secondary attack rate, % (95% confidence interval)		
						By observation period (days)		
						<14	14	>14
Contacts tested regardless of symptoms								
Dattner *et al.* (Bnei Brak, Israel)	~2020-03-17 / 2020-05-02	637	2,716	100	>2	32.1 (30.4-33.9)		
Luo *et al.* (Guangzhou, China)	2020-01-13 / 2020-03-06	391	1,015	Not provided	>2		10.3 (8.5-12.2)	
Burke *et al.* (USA)	2020-01-19 / 2020-01-30	9	15	100	>2		13.3 (3.7-37.9)	
Li *et al.* (Wuhan, China)	2020-01-01 / 2020-02-13	105	392	100	>2		16.3 (12.8-20.4)	
Jiang *et al.*[a] (Shandong, China)	2020-01-21 / 2020-01-29	4	11	100	>2		36.4 (10.9-69.2)	
Wu *et al.* (Zhuhai, China)	2020-01-17 / 2020-02-29	35	148	100	>2			32.4 (22.4-44.4)
Liu *et al.* (Guangdong, China)	2020-01-10 / 2020-03-15	1,158	2,441	100	2	13.5 (12.2-14.9)		
Bi *et al.* (Shenzhen, China)	2020-01-14 / 2020-02-12	391	686	100	2		11.2 (9.1-13.8)	
Zhang *et al.*[b] (Guangzhou,	2020-01-28 / 2020-03-	38	62	100	2		16.1 (9.0-	

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China)	15					27.2)	
Jing *et al.* (Guangzhou, China)	2020-01-07 / 2020-02-18	215	542	100	2	17.2 (14.1-20.6)	
Xin *et al.* (Qingdao, China)	2020-01-20 / 2020-03-27	31	106	100	2	17.9 (11.2-26.6)	
Böhmer *et al.* (Bavaria, Germany)	2020-01-27 / 2020-02-11	Not provided	24	100	2	20.8 (7.1-42.1)	
Yousaf *et al.* (Milwaukee & Salt Lake City, USA)	2020-03-22 / 2020-04-22	Not provided	198	100	2	23.7 (18.0-30.3)	
van der Hoek *et al.*[c] (Netherlands)	2020-03-23 / 2020-04-16	54	174	100	2		28.2 (21.6-35.5)
Cheng *et al.* (Taiwan)	2020-01-15 / 2020-03-18	100	151	100	1	6.6 (3.2-11.8)	
Chaw *et al.* (Brunei)	2020-03-09 / ~2020-04-03	19	264	100	1	10.6 (7.3-15.1)	
Park YJ *et al.* (South Korea)	2020-01-20 / 2020-03-27	5,706	10,592	100	Not provided	11.8 (11.2-12.4)	
Only symptomatic contacts tested							
Draper *et al.* (Northern Territory, Australia)	2020-03-01 / 2020-04-30	28	51	18	1	3.9 (0.5-13.5)	
Wang Z *et al.* (Wuhan, China)	2020-02-13 / 2020-02-14	85	155	67	1	30.3 (23.2-38.2)	

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Wang Y *et al.*[a] (Beijing, China)	2020-02-28 / 2020-03-27	41	335	Not provided	23.0 (18.6-27.9)

Exact binomial confidence intervals were computed for estimates reported without uncertainty.

[a]Some households had more than one index case.

[b]Secondary attack rate among household contacts of presymptomatic cases.

[c]Included only households with children.

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Table 2. Household secondary attack rates by index case and contact characteristics.

Study	Sample size	Household secondary attack rate, % (95% confidence interval)		
		By index case symptoms		
		Symptomatic	Presymptomatic	Asymptomatic
Chaw *et al.* (Brunei)	264	14.4 (8.8-19.9)	6.1 (0.3-11.8)	4.4 (0.0-10.5)
Park SY *et al.* (Seoul, South Korea)	225	16.2 (11.6-22.0)	0.0 (0.0-28.5)	0.0 (0.0-60.2)
Zhang *et al.* (Guangzhou, China)	62	—	16.1 (9.0-27.2)	—
		By index case age group		
		Children	Adults	Older adults
Park YJ *et al.* (South Korea)	10,592	16.0 (11.9-20.7)[a]	10.5 (9.9-11.2)	16.8 (15.1-18.6)[b]
Xin *et al.* (Qingdao, China)	106		12.5 (5.9-22.4)	29.4 (15.1-47.5)[c]
		Rising trend with age? Y/N	**By household contact age group**	
			Children	Adults	Older adults
Dattner *et al.* (Bnei Brak, Israel)	2,716	Y	25.4 (23.3-27.5)[a]	43.9 (40.4-47.4)	45.7 (38.0-53.6)[b]
Bi *et al.* (Shenzhen, China)	628	Y	9.6 (5.6-15.2)[a]	11.4 (8.2-15.4)	17.7 (11.6-25.4)[b]
Jing *et al.* (Guangzhou, China)	537	Y	6.4 (2.8-12.2)[a]	18.5 (14.4-23.2)	28.0 (19.1-38.2)[b]
Li *et al.* (Wuhan,	392	N	4.0	22.4	12.7

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China)			(1.1-9.9)[d]	(17.2-28.2)	(5.3-24.5)[e]
Yung *et al.* (Singapore)	213	—	6.1 (3.3-10.2)[f]	—	—
Yousaf *et al.* (Milwaukee & Salt Lake City, USA)	198	Y	20.3 (11.6-31.7)[d]	25.4 (17.9-34.3)	37.5 (8.5-75.5)[g]
van der Hoek *et al.* (Netherlands)	174	Y	24.3 (16.5-33.5)[d]	27.8 (14.2-45.2)	41.9 (24.6-60.9)[h]
Wu *et al.* (Zhuhai, China)	143	Y	16.1 (5.5-33.7)[i]	37.0 (24.2-52)	41.9 (23.5-62.9)[e]
Xin *et al.* (Qingdao, China)	106	N	20.5 (12.4-30.8)		8.7 (1.1-28.0)[c]

Age group definitions:

[a]0-19 years [b]≥60 years [c]≥55 years [d]0-17 years [e]>60 years

[f]0-16 years [g]≥65 years [h]>45 years [i]0-18 years

Exact binomial confidence intervals were computed for estimates reported without uncertainty.

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Table 2. Household secondary attack rates by index case and contact characteristics.

Study	Sample size	Household secondary attack rate, % (95% confidence interval)	
		By household contact sex	
		Female	Male
Jing *et al.* (Guangzhou, China)	538	18.9 (14.5-24.0)	15.5 (11.3-20.5)
Li *et al.* (Wuhan, China)	392	17.1 (11.9-23.4)	15.6 (11.0-21.3)
Yung *et al.* (Singapore)	212	5.0 (1.6-11.2)[f]	7.1 (3.1-13.6)[f]
Yousaf *et al.* (Milwaukee & Salt Lake City, USA)	198	29.3 (20.6-39.3)	18.8 (11.5-28.0)
Wu *et al.* (Zhuhai, China)	143	36.3 (24.6-49.7)	30.2 (18.5-45.1)
Xin *et al.* (Qingdao, China)	106	21.6 (11.3-35.3)	14.5 (6.5-26.7)

Age group definitions:

[a]0-19 years [b]≥60 years [c]≥55 years [d]0-17 years [e]>60 years

[f]0-16 years [g]≥65 years [h]>45 years [i]0-18 years

Exact binomial confidence intervals were computed for estimates reported without uncertainty.

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Figure legends

Figure 1. Study selection.

Excluded records may have had more than one reason for exclusion, but only one reason was listed for each record. Records from *bioRxiv* and *medRxiv* that fell outside the 50 best matches were largely irrelevant (e.g., not related to SARS-CoV-2 or examined the economic impact of the pandemic).

Figure 2. Estimates of the household secondary attack rate stratified by country and study design.

Exact binomial confidence intervals were computed for estimates reported without uncertainty.

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Figure 1

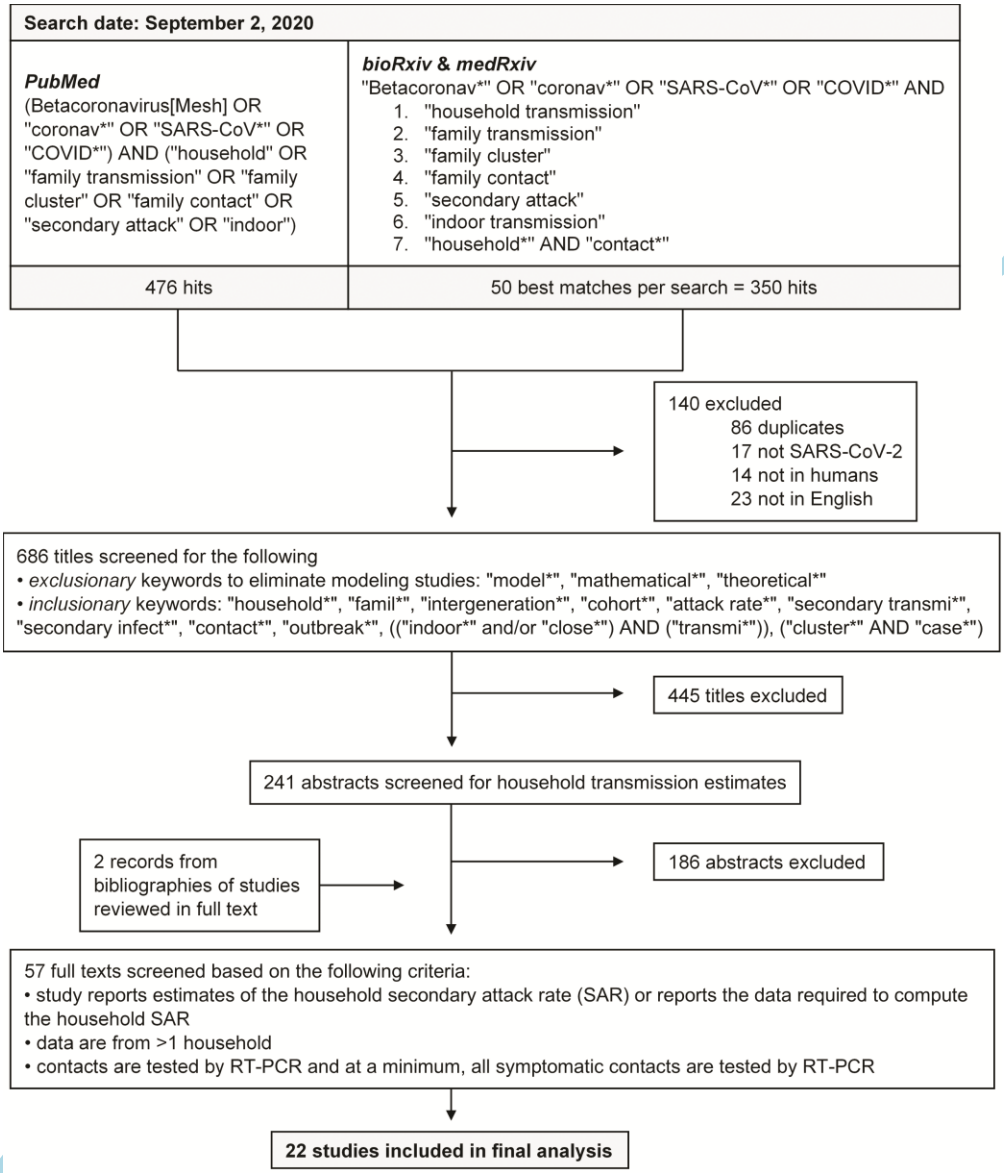

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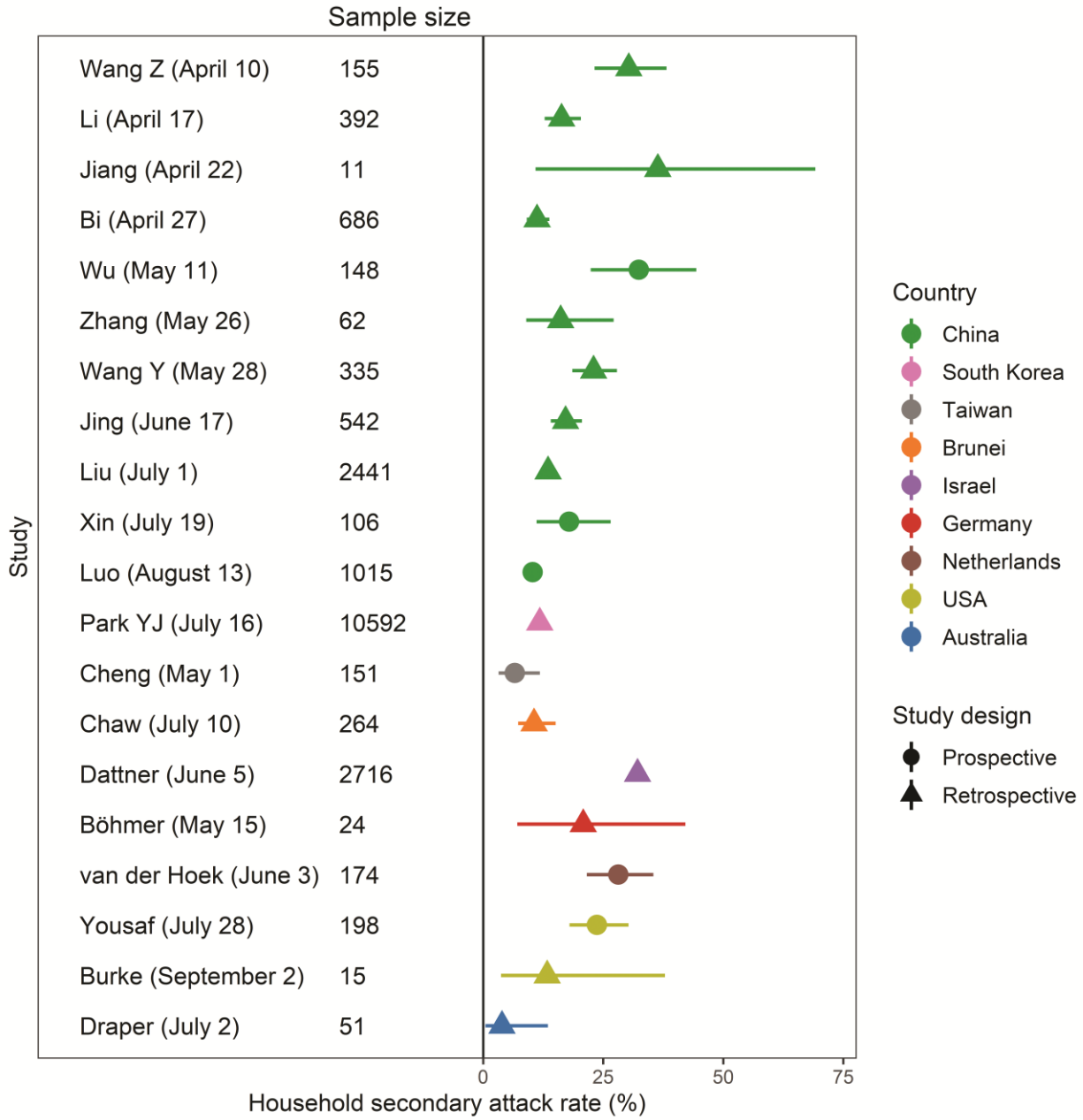
Figure 2



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