Report 38: SARS-CoV-2 setting-specific transmission rates: a systematic review and meta-analysis

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Summary

Since the end of 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly across the world. Understanding the drivers of SARS-CoV-2 transmission is crucial for disease control policies but evidence of transmission rates in different settings remains limited. We conducted a systematic review to estimate the secondary attack rate (SAR) and observed reproduction number (Robs) in different settings and to explore differences by age, symptom status, duration of exposure and household size. A total of 97 studies were identified, 45 of which met inclusion criteria for metaanalysis. Households showed the highest transmission rates, with pooled SAR and Robs estimates of 21.1% (95% CI: 17.4%-24.8%) and 0.96 (95% CI: 0.67-1.32), respectively. Household SAR estimates were significantly higher where the duration of household exposure exceeded 5 days compared with exposure of 5 days or less. Attack rates related to familiar and prolonged close contacts, such as social events with family and friends were higher than those related to low-risk casual contacts, such as strangers (SAR of 5.9%, 95% CI: 3.8%-8.1% vs. 1.2%, 95% CI: 0.3%-2.1%). Estimates of SAR for asymptomatic index cases were approximately two thirds of those for symptomatic index (3.5% vs. 12.8%, p<0.001). We find moderate evidence for less transmission both from and to individuals under 20 years of age in the household context, but this difference is less evident when examining all settings. Prolonged contact in households and in settings with familiar close contacts increases the potential for transmission of SARS-CoV-2. Additionally, the differences observed in transmissibility by symptom status of index cases and the potential for age-dependent effects has important implications for outbreak control strategies such as contact tracing, testing and rapid isolation of cases. There was limited data to allow exploration of transmission patterns in workplaces, schools, and care-homes, highlighting the need for further research in such settings.

1. Introduction

The SARS-CoV-2 virus which emerged in China in late 2019 has since spread rapidly around the world, with over 50 million confirmed cases and over 1 million deaths reported globally by November 2020 [1]. The severity of the infection, particularly in the oldest age-groups [2,3], has resulted in many countries implementing socially disruptive interventions to prevent onward spread. Early interventions focused on case isolation alongside identification of close contacts. In countries where these measures were insufficient to contain the virus, other non-pharmaceutical interventions (NPI) were introduced, including "stay at home" recommendations, closing schools, working from home, wearing of face-masks and restrictions on movement. As many countries have lifted the most stringent of these measures, governments are faced with the challenge of balancing the social and economic harms caused by NPI against the resurgence of cases. It is therefore critical to improve understanding of where transmission is taking place so that public health interventions can be better targeted.

To date, there have been relatively few detailed systematic epidemiological studies on transmission of the SARS-CoV-2 virus, with most published studies from the early epidemic in China and reviews focussing on household transmission [4,5]. Such studies provide valuable information on key epidemiological statistics – the secondary attack rate (SAR), defined as the probability of onward infection from an index case among a defined group of close contacts and the observed reproduction number (R_{obs}), defined as the observed average number of secondary cases per index case. Quantifying these parameters can help us understand the relative role that different settings play in sustaining transmission through identifying the location and types of contacts that constitute higher transmission potential.

Here we present a systematic review of published studies and preprints to estimate SAR and R_{obs} of SARS-CoV-2 in households, schools, workplaces, healthcare facilities and other settings. In addition, we examine differences in these parameters by the age of index cases and their contacts, duration of exposure to the index case, household size and symptom status of index cases at the time of exposure.

2. Methods

2.1 Systematic Review

2.1.1 Data Source and Search Strategy

We searched MEDLINE, Embase, MedRxiv, BioRxiv, arXiv and Wellcome Open Research with no language restrictions up to July 6th 2020, using the search strategy: ("COVID-19" OR "Coronavirus" OR "SARS-CoV-2" OR "2019-nCoV") AND ("attack rate*" OR "contact*" OR "cluster*"), adapted for the preprint servers. Boolean operators were removed, and all possible combinations of the search terms were tested to capture all publications on these servers. Studies were screened first according to titles and abstracts, and then by review of full-text articles. Two reviewers (HAT and AM) screened the studies independently, using predetermined inclusion and exclusion criteria. Differences were resolved through consensus and discussion with a third reviewer (AD). Bibliography screening was conducted for all papers in the full-text screening. The study protocol can be accessed through PROSPERO (registration number: CRD42020200177).

2.1.2 Inclusion criteria

Eligible studies for review met the following criteria: 1) provided a definition of the case-contact setting, and 2) reported the number of index cases, the number of secondary cases and the total number of contacts or a SAR and total number of contacts to allow the number of secondary cases to be calculated. Studies were included in the meta-analysis if they met two additional criteria 1) tested all contacts for SARS-CoV-2 infection regardless of symptom status and 2) reported on more than one index case (to minimise publication bias in single case studies towards reporting larger outbreaks).

2.1.3 Data Extraction

We extracted summary data on study design, contact definition, testing method (e.g. RT-PCR or serology), testing strategy (e.g. testing all contacts irrespective of symptoms, testing only contacts with symptoms or a subset of contacts), number of index cases, number of contacts identified, number of contacts tested and the number of secondary cases. Where data were available, we additionally extracted the following elements: age of the index case, age of contacts, household size, duration of household exposure to an index case and symptom status of the index case. Data were obtained directly from the reports, but when not explicitly stated, we obtained additional data from study authors. Studies were assessed for risk of bias by implementing a critical appraisal tool checklist for prevalence studies developed by the Joanna Briggs Institute, adapted to the study objectives [6]. Articles were given a quality score percentage to reflect methodological rigour and clarity and transparency in reporting relevant to this study's outcomes rather than the outcomes of the original study. We did not exclude articles based on quality scoring given the emergency response context within which the studies were conducted; articles that met the inclusion criteria for meta-analysis all had high quality scores and therefore no sensitivity analysis was conducted.

2.2 Statistical Analysis

Articles eligible for meta-analysis were stratified into the following settings: households, schools, workplaces, healthcare, group-living, and social contacts. Given that onward transmission of the virus is likely to be determined by the extent of exposure to the index case, within household contacts we undertook a subgroup analysis stratifying by the duration between symptom onset/confirmation and isolation of the index case (<5 days vs. >5 days or never isolated). And to explore whether household size influences transmission, we stratified the available data into three household sizes (1, 2 or 3+ contacts). We explored age dependent differences in infectivity and susceptibility across all contact locations and household only contacts. Finally, we examined differences in transmissibility by symptom status of index cases (asymptomatic, pre-symptomatic and symptomatic) across all exposure locations due to limited studies stratifying by symptom status and exposure location. Stratifications were chosen to maximise the available data across studies.

Due to potential within-study correlation (e.g. individuals in the same locations experiencing the same public health interventions and country-specific home, travel and work practices) and between-study heterogeneity due to study and population differences, we employed a Beta-Binomial model to pool SARs and a Poisson-Gamma mixture model to pool R_{obs} across studies (see details in Supplementary Methods)[7–9]. All analysis was conducted using R version 3.6.3.

3. Results

We identified 1,872 published studies, 78 of which were included after full-text screening (Figure 1). A further 22 eligible studies were identified through pre-print servers and bibliography screening. Of these 97 studies, summarised in Tables S1-S7, 67 tested all contacts regardless of symptom status. Among those, 45 reported data from >1 index case and were included in the meta-analysis.



Figure 1. PRISMA flow diagram of study selection

3.1 Household

We identified 29 eligible studies reporting household contacts [10–38], with more than half carried out in China (Table S1). Household definitions were broadly consistent across studies, requiring contacts to be living in the same residence as the index case. One study additionally included non-resident contacts who spent \leq 24 hours in the same residence as the index case [22](Table S1).

Study estimates of household SARs ranged from 6.1% [25] to 51.2% [38] with a pooled estimate of 21.1% (95% CI: 17.4%-24.8%) (Figure 2A). The relationship between the number of secondary cases and the number of index cases is shown in Figure S1. R_{obs} varied across studies from 0.05 [25] to 5.5 [38], with a pooled household R_{obs} of 0.96 (95% CI: 0.67-1.32) (Table S8). The SAR increased with longer duration of exposure (14.8%, 95% CI: 6.5%-23.0% with \leq 5 days of exposure to a household index case versus 28.3%, 95% CI: 18.3%-38.4% with >5 days of exposure) although this was of border-line significance (p = 0.05; Figure 2B). Longer durations of exposure were similarly associated with an increase in the pooled estimate of R_{obs} (0.40, 95% CI: 0.21-0.72 with \leq 5 days to 1.52, 95% CI: 0.78-2.69 with >5 days, p = 0.03) (Table S9, Figure S1). This \leq 5 days estimate was sensitive to the inclusion of a familial outbreak from a large dwelling in India (4 index cases) [38]. Exclusion of this study resulted in an R_{obs} of 0.91 (95% CI: 0.46-1.57)(Figure S1, Table S9).

There was a trend in differences in transmission by household size: 45.0% (95% CI: 31.2%-58.8%) with 1 contact, 32.6% (95% CI: 0.6%-64.5%) with 2 contacts and 28.8% (95% CI: 15.6-42.0%) in households with 3 or more contacts but this was not statistically significant (p = 0.29). We note that the study-level estimates for the small subset of studies reporting household sizes were highly variable (Figure S2).

3.2 Workplaces

We identified seven studies reporting workplace contacts (Table S3)[13,27,28,31,39–41]. Three of these studies were cluster investigations from a single index case, including a boardroom meeting in Germany (SAR: 91.7% [95% CI: 61.5%-99.8%, 11/12])[41], employees in a supermarket in China (SAR: 9.2% [95% CI: 4.7%-15.8%, 10/120])[28] and colleagues in a call centre in South Korea (SAR: 43.5% [95% CI: 36.8%-50.4%, 94/216])[40]. With these three studies excluded, the pooled SAR reduced from 12.3% (95% CI: 1.3%-12.5%) (Figure S3) to 1.9% (95% CI: 0.0%-3.9%) (Figure 3A). Workplace contacts likely represented a variety of sectors across studies, and only one study provided a detailed definition [40].

A		_	Index	Secondary	/ Total		
	Study	Country	cases	cases	contacts		Secondary Attack rate
	Mahapure et al	India	4	22	43	•	0.51 (95% CI: 0.35-0.67)
	Burke et al	USA	9	2	15	⊢−−−−	0.13 (95% CI: 0.02-0.40)
	Zhang et al	China	13	12	93		0.13 (95% CI: 0.07-0.21)
	Bohmer et al	Germany	16	5	24	⊢−−−− +	0.21 (95% CI: 0.07-0.42)
	Chaw et al	Brunei	19	16	123		0.13 (95% CI: 0.08-0.20)
	Wang et al	China	25	10	43	• • • • • • • • • • • • • • • • • • •	0.23 (95% CI: 0.12-0.39)
	Dawson et al	USA	26	16	64	· ─ ■ ─ · · · · · · · · · · · · · · · ·	0.25 (95% CI: 0.15-0.37)
	Dong et al	China	26	53	259		0.20 (95% CI: 0.16-0.26)
	Xin et al	China	31	19	106	→	0.18 (95% CI: 0.11-0.27)
	Wu et al	China	35	48	148	·	0.32 (95% CI: 0.25-0.41)
	Zhang et al	China	38	10	62		0.16 (95% CI: 0.08-0.28)
	van der Hoek et al	Netherlands	54	49	174		0.28 (95% CI: 0.22-0.35)
	Cheng et al	Taiwan	100	10	151		0.07 (95% CI: 0.03-0.12)
	Li et al	China	105	64	392	⊢ ∎−−1	0.16 (95% CI: 0.13-0.20)
	Wang et al	China	124	77	355	→	0.22 (95% CI: 0.18-0.26)
	Zhang et al	China	136	339	956	⊢ ∎→	0.35 (95% CI: 0.32-0.39)
	Wuetal	China	144	50	280		0.18 (95% CI: 0.14-0.23)
	Sun et al	China	148	189	598		0.32 (95% CI: 0.28-0.35)
	Rosenberg et al		155	131	3/3		0.38 (95% CI: 0.33-0.44)
	Chen et al	China	187	37	270		0.13 (95% CI: 0.10-0.18)
		China	215	102	219		0.13 (95% CI: 0.10-0.18)
	Jing et al	China	215	103	704		
	fung et al	Singapore	223	13	213		0.06 (95% CI. 0.03-0.10)
	Luo et al	China	347	96	946		0.10 (95% CI: 0.08-0.12)
	Bietai	China	391	(1	686	F B -1	0.11 (95% CI: 0.09-0.14)
	vvang et al	China	602	111	714	-	0.16 (95% CI: 0.13-0.18)
	Dattner et al	Israel	637	873	2716		0.32 (95% CI: 0.30-0.34)
	Park et al	South Korea	a 5706	1248	10592	•	0.12 (95% CI: 0.11-0.12)
	Pollan et al	Spain		282	860		0.33 (95% CI: 0.30-0.36)
	Yousaf et al	USA		47	195		0.24 (95% CI: 0.18-0.31)
	Beta-Binomial Summary	/				•	0.21 (95% CI: 0.17-0.25)
	$\gamma = 0.054$						
						02 04 06 08	1
						Housheold Secondary Attack Rate	
_						·····,	
В			Index	Secondary	Total		
	Study	Country	cases	cases	contacts		Secondary Attack rate
	Up to 5 days exposure						
	Cheng et al	Taiwan	100	3	77		0.04 (95% Cl: 0.01-0.11)
	Li et al	China	105	24	139		0.17 (95% Cl: 0.11-0.25)
	Bohmer et al	Germany	16	2	20		0.10 (95% CI: 0.01-0.32)
	Chaw et al	Brunei	19	14	109	⊢	0.13 (95% CI: 0.07-0.21)
	Wu et al	China	35	31	93	••	0.33 (95% CI: 0.24-0.44)
	Burke et al	USA	9	0	7 •		0.00 (95% CI: 0.00-0.41)
	Beta-Binomial Summar γ = 0.064	у					0.15 (95% CI: 0.06-0.23)
	Over 5 days exposure						
	Cheng et al	Taiwan	100	7	74		0.09 (95% CI: 0.04-0.19)
	Li et al	China	105	40	253	⊢∎	0.16 (95% CI: 0.12-0.21)
	Bohmer et al	Germany	16	3	4	⊧∎	0.75 (95% CI: 0.19-0.99)
	Chaw et al	Brunei	19	2	14	⊢−−−−−	0.14 (95% CI: 0.02-0.43)
	Dawson et al	USA	26	16	64	—	0.25 (95% CI: 0.15-0.37)
	Wu et al	China	35	17	41	⊢	0.41 (95% CI: 0.26-0.58)
	Mahapure et al	India	4	22	43		0.51 (95% CI: 0.35-0.67)
	van der Hoek et al	Netherlands	s 54	49	174		0.28 (95% CI: 0.22-0.35)
	Burke et al	USA	9	2	8	• • • • • • • • • • • • • • • • • • •	0.25 (95% CI: 0.03-0.65)
	Beta-Binomial Summar	у					0.28 (95% CI: 0.18-0.38)
					r r		
					0	0.2 0.4 0.6 0.8 Household Secondary Attack Rate	1

Figure 2. A) **Pooled overall household SARs.** Studies are ordered by the number of index cases reported in the study. Studies of large household contact tracing investigations were included irrespective of whether the number of index cases was reported in the study. B) **Stratified by duration of exposure to symptomatic index case.** Studies are ordered by the number of index cases reported in the study as this was not given by exposure duration. Study level point estimates and binomial confidence intervals are shown along with the pooled beta-binomial summary across studies. Exposure duration categories (<5 days and >5 days) were selected to maximize usage of data.

3.3 Healthcare Facilities

We identified 28 studies reporting healthcare-based contacts, 10 of which met our inclusion criteria for meta-analysis (Table S4)[30,33,39,42–46]. In six studies, the index cases were patients [30,33,39,42,44,45], two studies included both healthcare worker and patient index case populations [21,46], one study reported healthcare worker index cases [43] and in one study this information was not listed [26]. Study-level SARs varied from 0.0%-17.1% resulting in a pooled estimate among all healthcare contacts (patients and personnel combined) of 3.6% (95% CI: 1.0%-6.9%)(Figure 3B). There was no significant difference in the pooled SAR between patient or healthcare staff contact subgroups (p = 0.64; Figure 3B). The estimated R_{obs} in healthcare settings was 1.18 (95% CI: 0.65-2.04) but high levels of variation at the study level were observed, ranging from 0.0 to 4.5 (Figure S1, Table S10).

3.4 Social Settings

Twenty-two studies were identified that included social settings, varying from contact with an index case while travelling, at religious events, fitness classes, whilst shopping or at entertainment venues and other social events with family and friends (Table S6). Of these 22 studies, 13 fulfilled the criteria for meta-analysis [10,11,39,45,47,13,17,26–28,30,31,37]. We estimate low SARs in low-contact events with casual contacts or strangers, with a pooled SAR of 1.2% (95% CI: 0.3%-2.1%)(Figure 3C). In contrast, in settings with more familiar and prolonged contact such as small events with family and friends, the pooled SAR was 5.9% (95% CI: 3.8%-8.1%). A pooled R_{obs} of 0.38 (95% CI 0.18-0.64) was obtained from three of these studies with suitable reporting (Figure S1, Table S11). Travel-related contacts had an estimated SAR of 5.0% (95% CI: 0.3%-9.8%), similar to that in social events with family and friends (Figure 3C, Table S6). R_{obs} could not be estimated for any other contact groups due to insufficient data or study level information. Several other settings with high levels of transmission were identified but could not be pooled due to insufficient data, see Supplementary Results for further descriptions.

3.5 Exposure Location Summary

Table 1 summarises the pooled estimates of SAR and R_{obs} across different exposure locations. While the highest SARs were estimated for household contacts and in familial settings, the highest R_{obs} was estimated for healthcare settings. Pooled estimates for schools and care-homes were not possible due to a scarcity of studies reporting these locations (see Figure S4 and Supplementary Results for a review of the studies reporting on these settings).

Α	1	Index	Secondar	y Total		
Study	. Country of	cases	cases	contacts		Secondary Attack rate
Park et al	South Korea	2	0	84		0.00 (95% CI: 0.00-0.04)
Chaw et al	Brunei	19	6	848		0.01 (95% CI: 0.00-0.02)
Zhang et al	China	38	0	119		0.00 (95% CI: 0.00-0.03)
Chen et al	China	187	1	47	+	0.02 (95% CI: 0.00-0.11)
Pollan et al	Spain		118	1461		0.08 (95% CI: 0.07-0.10)
Beta-Binomial Summary						0.02 (95% CI: 0.00-0.04)
1 0.021					1	
				(0.05 0.1 Secondary Attack Rate	0.15

В		Index	Secondar	y Total						
Study	Country	cases	cases	contacts	5					Secondary Attack rate
Patient contacts										
Wee et al	Singapore	5	1	13		· · ·				0.08 (95% CI: 0.00-0.36
Chen et al	China	187	4	225						0.02 (95% CI: 0.00-0.04
Beta-Binomial Summary γ = 0.000					•					0.02 (95% CI: 0.01-0.03
Healthcare staff contacts										
Pini et al	Italy	2	0	14						0.00 (95% CI: 0.00-0.23
Chen et al	China	4	18	105		-	· · ·			0.17 (95% CI: 0.10-0.26
Chen et al	China	187	0	72	•					0.00 (95% CI: 0.00-0.05
Luo et al	China	347	7	679	HE-I					0.01 (95% CI: 0.00-0.02
Liu et al	China	1158	2	573						0.00 (95% CI: 0.00-0.01
Lombardi et al	Italy		139	1573						0.09 (95% CI: 0.07-0.10
Beta-Binomial Summary γ = 0.096										0.05 (95% CI: 0.00-0.10
Non-disaggregated contacts										
Cheng et al	Taiwan	100	6	698	HE -1					0.01 (95% CI: 0.00-0.02
Zhang et al	China	136	7	572						0.01 (95% CI: 0.00-0.03
Combined Beta-Binomial Summary	/				-					0.04 (95% CI: 0.01-0.07
					i	1		1	1	
					0	0.1		0.2	0.3	0.4
							Seconda	ry Attack Rate		

с		Index	Secondar	v Total	
Study	Country	cases	cases	contacts	Secondary Attack rate
Casual contacts					
Zhang et al	China	11	2	8224	0.00 (95% CI: 0.00-0.00)
Chaw et al	Brunei	19	4	445	• 0.01 (95% CI: 0.00-0.02)
Zhang et al	China	38	1	122	• 0.01 (95% CI: 0.00-0.04)
Chen et al	China	187	10	565	0.02 (95% CI: 0.01-0.03)
Luo et al	China	347	11	875	•••• 0.01 (95% CI: 0.01-0.02)
Wang et al	China	602	75	3363	••• 0.02 (95% CI: 0.02-0.03)
Liu et al	China	1158	41	3344	••• 0.01 (95% CI: 0.01-0.02)
Beta-Binomial Summary					• 0.01 (95% CI: 0.00-0.02)
γ = 0.010					
Family and friends					
Bohmer et al	Germany	16	11	217	0.05 (95% CI: 0.03-0.09)
Chaw et al	Brunei	19	5	144	0.03 (95% CI: 0.01-0.08)
Zhang et al	China	38	1	66	0.02 (95% CI: 0.00-0.08)
Chen et al	China	187	52	724	0.07 (95% CI: 0.05-0.09)
Jing et al	China	215	31	1314	0.02 (95% CI: 0.02-0.03)
Bi et al	China	391	61	707	0.09 (95% CI: 0.07-0.11)
Pollan et al	Spain		146	1284	0.11 (95% CI: 0.10-0.13)
Beta-Binomial Summary					0.06 (95% CI: 0.04-0.08)
Travel					
Zhang et al	China	136	22	326	0.07 (95% CI: 0.04-0.10)
Chen et al	China	187	28	235	• 0.12 (95% CI: 0.08-0.17)
Luo et al	China	347	1	818	→ 0.00 (95% CI: 0.00-0.01)
Bi et al	China	391	18	318	• 0.06 (95% CI: 0.03-0.09)
Liu et al	China	1158	31	2038	0.02 (95% CI: 0.01-0.02)
Beta-Binomial Summary $\gamma = 0.058$					0.05 (95% Cl: 0.00-0.10)
					0.05 0.1 0.15 0.2 0.25 Secondary Attack Rate

Figure 3. Secondary attack rates stratified by exposure locations. A) Workplace based contacts. B) Healthcare based contacts. B) Healthcare based contacts. Beta-binomial summary estimates are presented for patient and healthcare staff contacts of index-cases and a combined (non-disaggregated) contacts category. This combined contacts summary estimate was pooled across all studies in the healthcare setting and includes two studies where disaggregated contact groups were not reported. C) Social contact environments. Studies are ordered by the number of index cases reported at the study level. Large population-level studies were included irrespective of whether the number of index cases was reported by the study.

Setting	Pooled SAR	95% Confidence Interval	Pooled R _{obs}	95% Confidence Interval
Households	21.1%	17.4% - 24.8%	0.96	0.67 - 1.32
Social gatherings with family and friends	5.9%	3.8% - 8.1%	0.38	0.18 - 0.64
Travel	5.0%	0.3% - 9.8%	-	-
Healthcare	3.6%	1.0% - 6.9%	1.18	0.65 - 2.04
Workplace	1.9%	0.0% - 3.9%	-	-
Casual close contacts	1.2%	0.3% - 2.1%	-	-

Table 1 Summary table of the pooled SAR and R_{obs} for the exposure locations considered in this study. Where values are missing there was not enough data available to estimate a pooled value.

3.6 Age Effects

In total 10 studies provided age break downs of index cases and contacts [10,12,16,22,25,31,33,37,45,48]. Across all exposure locations we found no significant differences in SARs or R_{obs} in index cases aged under 20 and those over 20 (p = 0.12, p = 0.15 respectively) (Figure 4A, Figure S5, Table S12). Similar patterns were observed when comparing SARs by age of contacts with no significant differences between the two age groupings (p = 0.43) (Figure 4C, Figure S6). R_{obs} for contact age group categories were not estimated due to insufficient data.

Due to a lack of data in other settings we were able to stratify these estimates for household exposure only. We observed a marginally significant difference in transmissibility and significant difference susceptibility by age in this setting (index 0-19 years: 4.4% [95% CI: 0.0%-10.8%] vs. index \geq 20 years: 10.0% [95% CI: 8.2%-11.8%], p = 0.07 and contact 0-19 years: 6.16% [95% CI 4.1%-8.2%] vs. contact \geq 20 years: 13.7% [95% CI: 8.7%-18.7%], p = 0.01)(Figure 4A, Figure 4C). When further disaggregating age groups, the trend for SARs to increase with increasing age of index cases and contacts was maintained (Figure 4B, Figure 4D). However, we note that across contact age groups the SARs increase at a higher rate for household contacts (Figure 4D).



Figure 4. Pooled estimates of SARs by age of the index case and contacts stratified by contact location. (A) Index cases stratified by 0-19 and 20+ age brackets and exposure location to the index case **(B)** index cases stratified by 10-,20- and 40-year age brackets. **C)** Contacts stratified by 0-19 and 20+ age brackets and exposure location **(D)** contacts stratified by 10, 20- and 40- year age brackets. Point estimates were obtained from fitting a beta-binomial model to pooled study data, with 95% Confidence Intervals shown by horizontal and vertical bars. All contacts combine studies regardless of exposure locations, and household only those studies relating to household transmission. The pooled household SAR for ages 60+ is not shown as there was insufficient data for this age group.

3.7 Symptom Status of Index Case

Symptom status definitions were broadly consistent across studies. Among 19 studies included in the pooling [18,19,45,47,49–55,27,29–31,33,39,40,44] SAR was lowest for asymptomatic index cases at 3.5% (95% CI: 0.0%-6.4%) (Figure 5). The SAR was significantly higher for pre-symptomatic and symptomatic index cases, estimated at 9.3% (95% CI: 4.5%-14.0%, p = 0.03) and 12.8% (95% CI: 8.9%-16.7%, p = <0.001), respectively (Figure 5). This increasing transmission potential with presence of symptoms was mirrored in the pooled R_{obs} estimates per category. Asymptomatic index cases resulted in the lowest R_{obs} of 0.29 (95% CI: 0.10-0.71), followed by pre-symptomatic index cases (R_{obs}=0.78, 95% CI: 0.36-1.44, p = 0.07) and symptomatic index cases (R_{obs}=1.01, 95% CI: 0.57-1.61, p = 0.01) (Figure S1, Table S13). The R_{obs} from pre-symptomatic index cases was highly sensitive to the inclusion of a single study in a fitness class setting, which increased the pre-symptomatic R_{obs} to 1.95 (95% CI: 1.28-2.87) (Figure S1, Table S13).

		Exposure	Index S	Secondar	y Total		
Study	Country	Location	cases	cases	contac	S	Secondary Attack rate
Asymptomatic	•						
Jiang et al	China	combined	8	1	174	-	0.01 (95% CI: 0.00-0.03)
Zhang et al	China	combined	14	1	36		0.03 (95% CI: 0.00-0.15)
Han et al	China	combined	18	0	41	•	0.00 (95% CI: 0.00-0.09)
Chaw et al	Brunei	household	19	2	32		0.06 (95% CI: 0.01-0.21)
Chen et al	China	combined	30	22	146		0.15 (95% CI: 0.10-0.22)
Zhang et al	China	combined	83	1	119		0.01 (95% CI: 0.00-0.05)
Park et al	South Korea	household	97	0	4		0.00 (95% CI: 0.00-0.60)
Liu et al	China	combined	147	24	914	-	0.03 (95% CI: 0.02-0.04)
Luo et al	China	combined	347	1	305	-	0.00 (95% CI: 0.00-0.02)
Beta-Binomial Sumr γ = 0.047	nary					•	0.03 (95% CI: 0.00-0.06)
Pre-symptomatic							
Jang et al	South Koreaso	ocial - fitness cla	ss 6	57	217	_	0.26 (95% CI: 0.21-0.33)
Jiang et al	China	combined	8	4	111		0.04 (95% CI: 0.01-0.09)
Hong et al	China	combined	13	14	74		0.19 (95% CI: 0.11-0.30)
Chaw et al	Brunei	household	19	4	50		0.08 (95% CI: 0.02-0.19)
Zhang et al	China	combined	83	11	250		0.04 (95% CI: 0.02-0.08)
Park et al	South Korea	household	97	0	11		0.00 (95% CI: 0.00-0.28)
Cheng et al	Taiwan	household	100	4	100	_ 	0.04 (95% CI: 0.01-0.10)
Liu et al	China	combined	147	23	236	_ -	0.10 (95% Cl: 0.06-0.14)
Liu et al	China	combined	1158	72	2211		0.03 (95% CI: 0.03-0.04)
Beta-Binomial Sumr γ = 0.053	nary					•	0.09 (95% Cl: 0.05-0.14)
Symptomatic							
Stein-Zamir et al	Israel	school	2	178	1312		0.14 (95% CI: 0.12-0.16)
Chen et al	China	healthcare	4	18	105	-	0.17 (95% CI: 0.10-0.26)
Jiang et al	China	combined	8	2	15		0.13 (95% CI: 0.02-0.40)
Burke et al	USA	household	9	2	15	e	0.13 (95% CI: 0.02-0.40)
Zhang et al	China	combined	14	9	238		0.04 (95% CI: 0.02-0.07)
Chaw et al	Brunei	household	19	10	41		0.24 (95% CI: 0.12-0.40)
Wang et al	China	household	25	10	42		0.24 (95% CI: 0.12-0.39)
Park et al	South Korea	household	97	34	210	_	0.16 (95% CI: 0.11-0.22)
Cheng et al	Taiwan	household	100	3	51	_	0.06 (95% CI: 0.01-0.16)
Li et al	China	household	105	64	392	_ -	0.16 (95% CI: 0.13-0.20)
Wang et al	China	household	124	77	355	_	0.22 (95% CI: 0.18-0.26)
Chen et al	China	combined	157	126	2001	.	0.06 (95% CI: 0.05-0.07)
Luo et al	China	combined	347	117	2305		0.05 (95% CI: 0.04-0.06)
Liu et al	China	combined	1158	411	5904		0.07 (95% CI: 0.06-0.08)
Beta-Binomial Sum	nary					•	0.13 (95% CI: 0.09-0.17)
γ = 0.037							
						0 0.2 0.4 Secondary Attack Rate	0.6

Figure 5. **Estimated SARs from asymptomatic, pre-symptomatic and symptomatic index cases.** Studies are ordered by the number of index cases reported in the study as shown in the figure. Pooled estimates combine all exposure locations listed. Combined exposure locations relate to contact tracing studies where close contacts were not disaggregated by exposure location. Asymptomatic index cases were defined as those with a positive SARS-CoV-2 RT-PCR test and no reported clinical symptoms up to discharge or end of follow-up. Pre-symptomatic index cases were defined as those not reporting symptoms at the time of testing or during exposure but later developed symptoms. Symptomatic index cases reported COVID-19-associated symptoms at the time of sampling and/or during exposure.

4. Discussion

Despite the global extent of SARS-CoV-2 transmission, there remains relatively few detailed epidemiological studies (especially outside China) within defined contact groups. This systematic review provides an indication of the types and places of contacts that facilitate SARS-CoV-2 transmission. We found evidence to suggest that more familiar prolonged contact increases the potential for transmission, as does the presence of symptoms with moderate age-dependent effects observed at the household level. Crucially however, there was limited data identified in this review which did not allow for exploration of transmission patterns in workplaces, schools, and care-homes, and resulted in considerable uncertainty around the estimates in settings where data was available.

Sustained daily contact within households may explain the high pooled SAR estimated (21.1%) which is comparable to the pooled estimate of an earlier systematic review (18.1%) [5]. Our estimate hides substantial heterogeneity between studies, with reported SARs ranging between 0% and 51%. This range is similar to that identified in systematic reviews of household transmission of influenza, where SARs ranged from 1% to 38% [56,57], but higher than those for SARS-1 (6-8%)[58][59]. We found evidence of reduced SARs and R_{obs} when index cases were isolated outside the household within 5 days of symptom onset, suggesting that household transmission characteristics are influenced by contact tracing and isolation policies. While SARs could not be estimated in other residential settings, it is not unexpected that these locations report high study-specific attack rates. Elderly residents living in care homes are particularly vulnerable populations with high risk of severe outcomes and COVID-19-related mortality [2,3], therefore it is vital to further understand dynamics of transmission in these environments, to prevent further outbreaks. With many countries continuing to recommend "stay at home" measures, with cases isolating inside households, it is likely that this location will continue to be important in sustaining transmission.

We estimated a relatively low SAR (3.7%) in healthcare settings, substantially lower than that observed during the early stages of the SARS-1 epidemic in which healthcare workers were disproportionately affected [60–62]. This is potentially driven by the large number of identified and tested contacts per index case, which may also explain the highest R_{obs} (1.18) in this setting. In addition, it is plausible that lessons on the importance of infection control and personal protective equipment (PPE) has limited spread in these settings. However, it is important to note that all studies took place in high- and middle-income countries where PPE equipment is likely more widely available, however there was insufficient information provided to explore differences in transmission rates in relation to differential PPE use. This, in addition to the diversity of these healthcare systems, make generalisations about SARS-CoV-2 transmission rates in healthcare facilities difficult.

Our findings suggest that the SAR resulting from exposure to pre-symptomatic index cases is similar to that of symptomatic cases (10% vs 13%). Transmission potential from asymptomatic cases, while significantly lower than symptomatic cases (4%), was not insignificant. A previous systematic review has estimated that 20% of cases remain asymptomatic throughout infection but individual study estimates ranged between 3% to 67% [63]. Asymptomatic and pre-symptomatic cases could therefore account for a significant proportion of onward transmission, which has previously been estimated to be 6.6% and 47%, respectively [64]. If a large proportion of cases remain asymptomatic, transmission could be sustained even if all symptomatic cases are immediately isolated and therefore is particularly

challenging for control policies. Our findings highlight the need for rapid contact tracing and testing in contacts both with without symptoms.

While studies reporting on the age breakdown of index cases and contacts were limited, we found evidence for age dependence in transmissibility and susceptibility in the household context, which was more limited when pooling across all settings. There is significant uncertainty around these estimates however, due to the sparsity of data. Therefore, understanding potential age-dependent effects in transmissibility and susceptibility remains challenging, and those effects we do see could relate to behavioural, contextual or biological factors which are as yet not fully understood [65]. There is growing evidence to suggest that children tend to experience mild or asymptomatic infections [66–70], which may explain the potential differences observed in transmission rates from index cases aged under 20 years old. Further to this, symptomatic testing policies may fail to detect childhood infections or identify children as index cases which could result in inaccuracies in estimates of transmission probability.

Understanding the importance of children's role in SARS-CoV-2 transmission especially with schools in many countries re-opening is crucial. In contrast to influenza in which schools are clearly important contributors to sustained transmission [71,72], school-based studies on SARS-CoV-2 are limited as many countries responded to the initial epidemic by closing schools. In addition to schools closing, many countries have and continue to encourage working from home practices. Furthermore, workplace settings vary greatly not just by country, but also between sectors, with some more able to facilitate Covid-19 safety measures, highlighting the difficulty in ascertaining a universal workplace sor SAR. Currently there is insufficient information to explore SARs in different types of workplaces or sectors.

We estimate relatively low R_{obs} across settings, suggesting that the use of contact tracing and isolation activities in these studies is an effective measure at reducing onward transmission. However, low numbers of studies were pooled and therefore there was considerable uncertainty in these estimates. Additionally, large cluster outbreaks can occur, as evidenced in several studies [28,31,38,40,41,47,73–76] and often, these events have the potential to overwhelm surveillance systems. The aggregate nature of the data used for our estimates of R_{obs} likely hides substantial individual level heterogeneity in transmission potential and meant we could not characterise the overdispersion factor relating to SARS-CoV-2 transmission. Therefore, characterising this overdispersion, or the potential for 'super spreading events' will be critical for further informing where to direct contact tracing efforts moving forwards. Early evidence suggests that transmission is overdispersed with around 19% of cases resulting in 80% of transmission in Hong Kong [77] and modelling studies based on reported global cluster sizes which suggested that as few as 10% of cases could account for 80% of all SARS-CoV-2 transmission [78]. The large cluster outbreaks identified in this review tend to be reported in indoor social or workplace settings potentially highlighting these locations as facilitating super-spreading events [79].

There are several limitations to this study. As in any active outbreak response, data collected from multiple teams under different country guidelines are subject to variations in definitions, follow-up time and testing protocols, limiting interpretation of pooled data. Furthermore, individual studies suffer from reporting and recall bias in identifying all contacts of a confirmed case. Across settings, index cases were commonly enrolled after presenting for medical attention and therefore can be biased towards infections that result in symptomatic or more serious illness and this could potentially

distort transmission pathways [56]. Without phylogenetic sequencing it is difficult to confidently resolve these pathways which could bias our estimates of SARs, for example if the index case was asymptomatic and is instead identified as a secondary case of the symptomatic case that first presented for testing or if transmission occurs outside the household but is attributed to a household index case. Globally, there is still a lack of detailed data from contact tracing studies to fully explore differing transmission potential by locations or individual characteristics. Throughout this review the majority of studies meeting the inclusion criteria to inform our pooled estimates came from China, where strict control policies were implemented which could limit the generalisability of estimates. Finally, evidence is continually emerging from newspaper articles, government reports and press-conferences that report on large outbreaks in care-homes, schools, workplaces and hospitals. Such sources cannot be systematically searched or reliably cited however, and currently this information is not translated into published contact tracing studies due to limited public health resources and the prioritisation of the ongoing emergency response.

In conclusion, early data suggest that transmission is highest in locations in which sustained and prolonged contacts are made – including households, and other residential locations. However, substantial onward transmission also appears to occur in social interactions with sustained duration of contacts such as family meals, celebrations and religious gatherings. Further research on transmission in these settings, as well as in schools and workplaces and age-dependent effects in all these settings, in which there are limited data to date, is urgently required to continue to inform transmission reduction strategies.

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