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Coronavirus Pandemic

Secondary attack rates of COVID-19 in diverse contact settings, a meta-analysis

Ting Tian[1], Xiang Huo[1]

[1] *Jiangsu Provincial Center for Disease Control and Prevention, Nanjing, China*

Abstract

Introduction: The secondary attack rate (SAR) measures the transmissibility of an infectious agent. The reported SAR of COVID-19 varied in a broad range, and between different contact settings.

Methodology: We conducted a meta-analysis on the SAR of COVID-19 with adherence to the PRISMA guideline. We searched published literatures and preprints in international databases of PubMed and medRxiv, and in five major Chinese databases as of 20 April 2020, using the following search terms: ('COVID-19' and 'secondary attack rate') or ("COVID-19" and "close contact"). The random effect model was chosen for pooled analyses, using R (version 3.6.3).

Results: A total of 1,136 references were retrieved and 18 of them remained after screening. The pooled SAR of COVID-19 was 0.07 (95%: 0.03-0.12) in general. It differed significantly between contact settings, peaking in households (0.20, 95%: 0.15-0.28), followed by in social gatherings (0.06, 95%: 0.03-0.10). The point estimates of the pooled SARs in health facilities, transports, and work/study settings were all as low as 0.01. Among all the secondary cases, the proportion of asymptomatic infections was estimated to be 0.17 (95% CI: 0.09 – 0.34). The proportion was higher in households (0.26, 95% CI: 0.12-0.56), than in other contact settings.

Conclusions: The transmission risk of SARS-CoV-2 is much higher in households than in other scenarios. Identification of asymptomatic secondary infections should be enhanced in households.

Key words: COVID-19; SARS-CoV-2; secondary attack rate; contact setting; household; asymptomatic.

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Introduction

COVID-19 emerged in late 2019 and rapidly caused a global pandemic [1]. Human to human transmission occurs mainly through respiratory droplets and fomite [2]. Cluster infections have been frequently reported [3-5]. However, the reported secondary attack rates (SARs) varied in a broad range, and between different contact settings. The SAR is defined as the proportion of secondary infections among susceptible persons within a reasonable incubation period following known contact with the primary case [6]. It is a key epidemiological parameter, indicating the transmissibility of a causative agent. It is necessary to know the SAR of COVID-19, and its variability between different contact settings, informing the adaptive implementation of public health measures. Asymptomatic COVID-19 cases can cause onward transmission [7], as silent spreaders. However, the proportion of the asymptomatic infection is still unclear, which limits our insight into their contribution to transmission.

Methodology

Literature search, screening, and data extraction

We searched published literatures and preprints in English or in Chinese as of 20 April 2020, in two international databases of PubMed and medRxiv, and in five Chinese databases of Chinese National Knowledge Infrastructure (CNKI), WanFang databases, Chinese Journal of Epidemiology, Chinese Journal of Public Health and Chinese Journal of Preventive Medicine (Supplementary Table 1), using the following search terms: ("covid-19' and "secondary attack rate") or ("covid-19" and "close contact"). Literatures were firstly screened by title and abstract, and then assessed by the full text. Literature screening and data extraction were conducted by one investigator, and verified by another one. Any conflict was addressed through re-assessment till a consensus was agreed. The literature quality was assessed (Supplementary Table 2).

Inclusion and exclusion criteria

Literatures that clearly indicated the number of the secondary infections and of the close contacts of origin

were eligible for inclusion. Those using unverified media sourced data, or a subgroup data of another already-included study, were excluded.

Definitions

Confirmed cases: Laboratory confirmed COVID-19 cases, using PCR or equivalent nucleic acid amplification testing.

Close contacts: A close contact is defined as anyone with the following exposures to a COVID-19 case, from 2 days before to 14 days after the case's onset of illness (or the day the asymptomatic case was sampled):

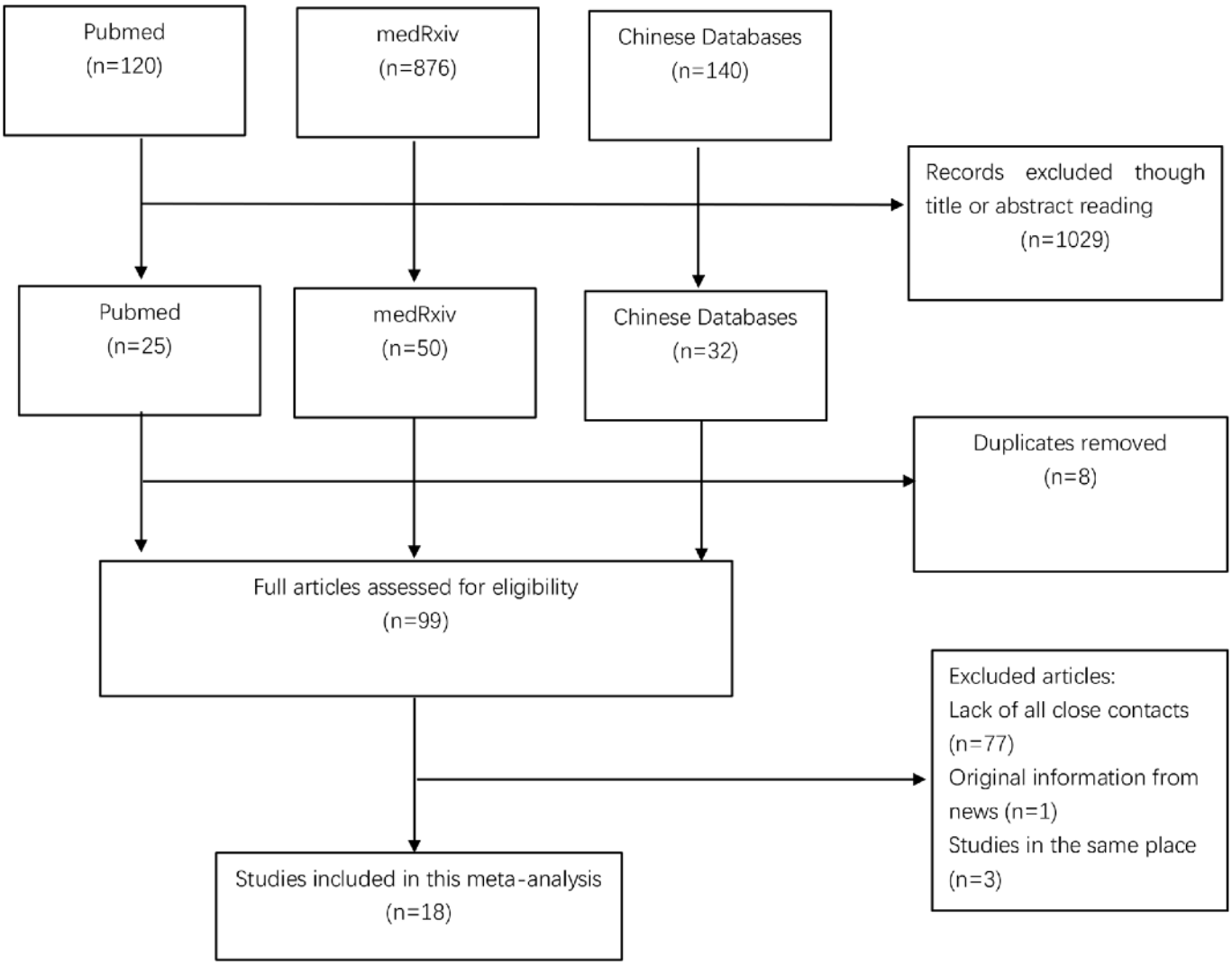
- Being within 1 metre of a COVID-19 case for >15 minutes;
- Direct physical contact with a COVID-19 case;
- Providing direct care for patients with COVID-19 disease without using proper personal protective equipment (PPE);
- Other definitions, as indicated by local risk assessments.

Asymptomatic cases: An asymptomatic case is a person with laboratory confirmed infection of COVID-19, who does not develop symptoms.

Statistical analyses

SAR was calculated as the proportion of secondary cases in close contacts of origin. The heterogeneity between studies was evaluated using the Higgins' I^2 test. Sensitivity analysis was conducted by omitting one study each time to evaluate its influence on the pooled estimate of SAR. Subgroup analyses were conducted by study regions and contact settings. Random effect meta-regression was performed to identify significant moderators of SAR. Results are reported as summary point estimate and 95% confidence interval (CI). The Funnel and Egger's test were used to address

Figure 1. Flow chart of the literature search and selection (as of April 20, 2020).



publication bias. Statistical significance was set at $p < 0.05$ (two-tailed). All statistical analyses were performed using R (version 3.6.3 for Windows), including the "metafor" package [8].

Results

Literature search and selection

We retrieved 120 articles from PubMed, 876 articles from medRxiv and 140 articles from Chinese databases. After screened by titles and abstracts, 1,037 of them were excluded, due to irrelevance or duplication. The remained were assessed by full text, and 18 studies were included in the meta-analysis (Figure 1) [9-26].

Study characteristics

Most of the literatures (14/18) came from mainland China. No publication bias was indicated (Egger's test, $p = 0.865$) (Supplementary Figure 1). However, there was a significant heterogeneity between studies ($I^2 = 99\%$, $p < 0.0001$). A total of 32,149 close contacts were documented. The reported SAR ranged from 0.00 (95% CI: 0.00 - 0.02) to 0.80 (95% CI: 0.28 - 0.99). Seven studies (all from mainland China) presented the number of asymptomatic secondary cases. For studies including multiple contact settings, the SAR and the proportion of asymptomatic secondary cases were extracted for each setting as well (Table 1).

Table 1. Characteristics of studies included in the meta-analysis.

Study	Authors	Geographical locations	Settings	Close contacts	Secondary infections	Asymptomatic secondary infections
1	Response Center [9]	Republic of Korea	multiple	2,370	13	unclear
1.1	Response Center [9]	Republic of Korea	household	119	9	unclear
2	Kostas et al. [10]	France	household	15	11	unclear
3	Burke RM et al. [11]	United States of America	multiple	445	2	unclear
3.1	Burke RM et al. [11]	United States of America	household	19	2	unclear
4	Li P et al. [12]	Zhoushan, China	household	5	4	1
5	Li W et al. [13]	Hubei, China	household	392	64	9
6	Wang Z et al. [14]	Wuhan, China	household	155	47	unclear
7	Yang L et al. [15]	Jinan, China	multiple	1,455	28	3
7.1	Yang L et al. [15]	Jinan, China	work/study together	963	1	0
7.2	Yang L et al. [15]	Jinan, China	household	169	24	2
7.3	Yang L et al. [15]	Jinan, China	transport exposure	259	0	0
7.4	Yang L et al. [15]	Jinan, China	healthcare setting	43	1	1
7.5	Yang L et al. [15]	Jinan, China	social gathering	21	0	0
8	Tian Y et al. [16]	Yangzhou, China	multiple	36	2	2
8.1	Tian Y et al. [16]	Yangzhou, China	household	12	2	2
8.2	Tian Y et al. [16]	Yangzhou, China	work/study together	24	0	0
9	Jiang Z et al. [17]	Nanning, China	multiple	116	10	unclear
10	Bi Q et al. [18]	Shenzhen, China	multiple	1,142	84	unclear
10.1	Bi Q et al. [18]	Shenzhen, China	household	686	77	unclear
10.2	Bi Q et al. [18]	Shenzhen, China	transport exposure	318	18	unclear
10.3	Bi Q et al. [18]	Shenzhen, China	social gathering	707	61	unclear
11	Cheng H et al. [19]	Taiwan, China	multiple	1,043	12	3
11.1	Cheng H et al. [19]	Taiwan, China	household	36	7	2
11.2	Cheng H et al. [19]	Taiwan, China	healthcare setting	301	0	0
11.3	Cheng H et al. [19]	Taiwan, China	social gathering	47	5	1
12	Luo L et al. [20]	Guangzhou, China	multiple	4,950	129	8
12.1	Luo L et al. [20]	Guangzhou, China	household	946	96	unclear
12.2	Luo L et al. [20]	Guangzhou, China	healthcare setting	679	7	unclear
12.3	Luo L et al. [20]	Guangzhou, China	transport exposure	818	1	unclear
13	Zeng J et al. [21]	Sichuan, China	multiple	13,990	226	unclear
14	Zhang R et al. [22]	Liaoning, China	multiple	2,784	67	9
14.1	Zhang R et al. [22]	Liaoning, China	household	171	39	unclear
14.2	Zhang R et al. [22]	Liaoning, China	social gathering	655	11	unclear
14.3	Zhang R et al. [22]	Liaoning, China	transport exposure	731	4	unclear
14.4	Zhang R et al. [22]	Liaoning, China	work/study together	1,211	13	unclear
15	Chen Y et al. [23]	Ningbo, China	multiple	2,147	132	22
15.1	Chen Y et al. [23]	Ningbo, China	household	279	37	10
15.2	Chen Y et al. [23]	Ningbo, China	social gathering	724	52	6
15.3	Chen Y et al. [23]	Ningbo, China	work/study together	47	1	0
15.4	Chen Y et al. [23]	Ningbo, China	transport exposure	235	28	4
15.5	Chen Y et al. [23]	Ningbo, China	healthcare setting	297	4	0
15.6	Chen Y et al. [23]	Ningbo, China	occasional work/life contact	83	5	1
15.7	Chen Y et al. [23]	Ningbo, China	public setting exposure	482	5	1
16	Dong X et al. [24]	Tianjin, China	household	259	53	unclear
17	Sun W et al. [25]	Zhejiang, China	household	598	189	unclear
18	Deng Z et al. [26]	Nanchang, China	multiple	247	25	unclear

SAR and proportion of asymptomatic secondary infections

We employed the random effects model for meta-analyses, considering the big heterogeneity between studies. The pooled SAR of COVID-19 was 0.07 (95%: 0.03-0.12) in general (Figure 2). Sensitivity analyses showed that no single study had significant influence on the pooled estimate. The SAR differed significantly among contact settings. It peaked in households (0.20, 95% CI: 0.15-0.28), followed by in social gatherings (0.06, 95% CI: 0.03-0.10), and was low in healthcare facilities, transports and work/study settings (Figure 3 and 4). Meta-regression analyses indicated that household setting and social gathering setting were associated with significantly elevated SARs, and could jointly explain 51.0% of the total heterogeneity among studies. The pooled proportion of asymptomatic secondary cases was 0.17 (95% CI: 0.09 – 0.34) in general and 0.26 (95%CI: 0.12 - 0.56) in households (Figure 5 and 6).

Figure 2. Overall pooled SAR of COVID-19.

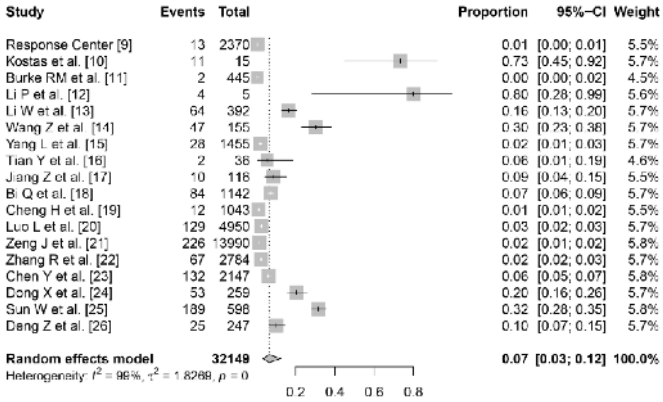


Figure 3. Pooled SARs in healthcare setting, households and social gatherings.

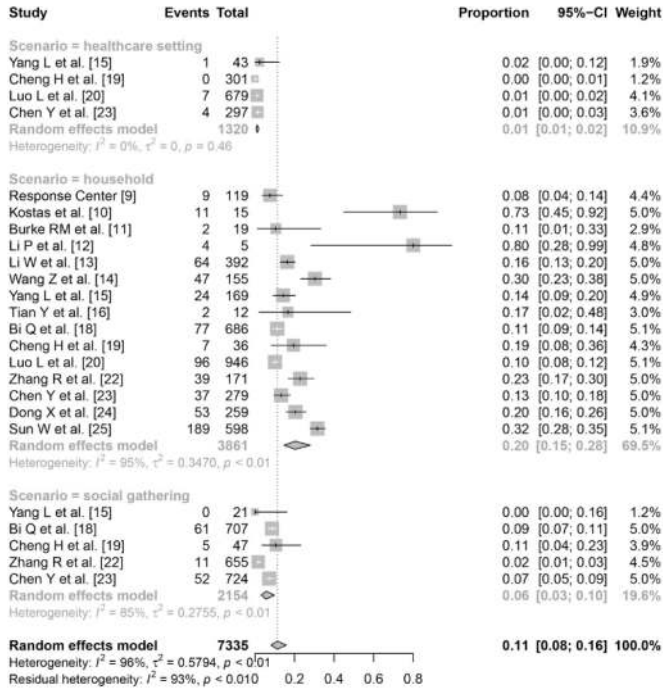


Figure 4. Pooled SARs in transports and work/study settings.

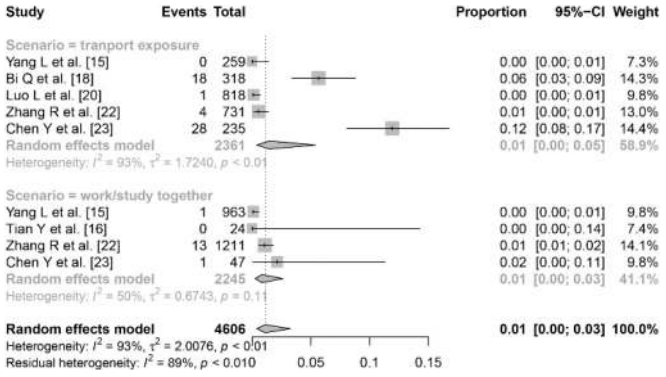


Figure 5. Overall pooled proportion of asymptomatic secondary cases.

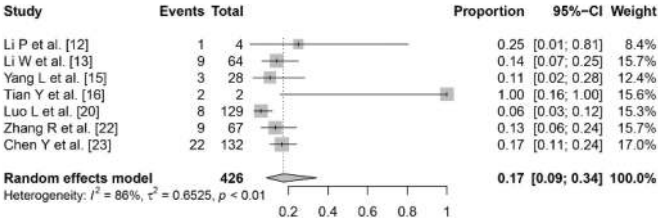
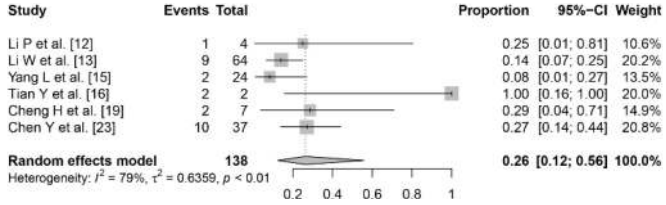


Figure 6. Pooled proportion of asymptomatic secondary cases in households.



Discussion

Our pooled SAR of COVID-19 is similar with the SARs reported by later published studies [27, 28]. Household SAR varied widely across literature in this study, which is also observed in another systematic review on SAR in household contacts [29]. The pooled SAR in household setting in this study is comparable

with that from a later published retrospective study from Guangzhou, China (17.1%, 95% CI: 13.3% - 21.8%) [30], and those from other meta-analysis studies on SAR in households [31,32].

Household contacts were supposed to have a significantly elevated risk for being infected than other close contacts [18]. Our results indicate a significantly higher transmission risk in household setting than in social gathering, healthcare, public transport and work/study settings, which is echoed with recent studies from Singapore and China [28,33]. SARS-CoV-2 mainly transmits via respiratory droplets and fomite [2]. Close and prolonged contact could facilitate the viral transmission. Settings characterized with this kind of contact, such as households, bars and restaurants are expected to associate with high transmission risk. Less adherence to social distance, mask wearing, and hand hygiene, could also contribute to the higher SAR in households. In contrast, the comprehensive implementation of precautions could be attributed to the low SARs observed in healthcare facilities, transports and work/study settings.

The SAR of COVID-19 in households is higher than that of SARS (10.2%) [34] and pandemic influenza 2009 (13%) [35], which indicates a higher transmission capability of SARS-CoV-2. Infectiousness is suggested to peak on or before symptom onset of COVID-19 cases, while the peak is on 10 days and 1 day after symptom onset of SARS and influenza cases, respectively. It is estimated that 44% of secondary cases were infected during the index cases' pre-symptomatic stage [36]. This could jeopardize the effectiveness of symptom-based case isolation strategy badly.

Our pooled proportion of asymptomatic secondary cases is in line with the estimate from the Diamond Princess cruise ship [37], and the pooled estimate of another meta-analysis [38]. However, it is lower than the estimate (36%, 95% CI: 27% - 45%) from a Singaporean study using a Bayesian model [33]. The serology testing used in that study contributed to finding more asymptomatic infections, compared with PCR testing used in other studies. The suggested high proportion of asymptomatic cases underscores the importance of placing targeted countermeasures to this population, although the transmission potential of them is lower than that of the symptomatic cases [38]. It is not clear why the proportion of asymptomatic secondary cases is higher in households compared with other contact settings. A possible explanation is that children usually get infected from family members in households at the early stage of the pandemic, and they are likely to present mild or no symptoms [39]. Active viral screening conducted in family contacts could also be responsible for finding more asymptomatic cases.

Given the high transmission risk within households, isolating mild COVID-19 patients and asymptomatic cases in designated isolation facilities is recommended rather than at homes. Aggressive move restriction could curb the inter-household transmission. Lift or ease of lock down measures should be cautious and step-wise, with essential social distancing measures maintained, to prevent the introduction of virus to unaffected households.

Conclusions

The SAR of COVID-19 in households is higher than that of SARS and pandemic influenza 2009. The transmission risk of SARS-CoV-2 is much higher in households than in other scenarios. Identification and management of asymptomatic secondary cases should be enhanced in households.

Acknowledgements

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Authors' contributions

XH conceived the study. TT searched, screened, assessed the literature, and extracted the data. XH participated in literature screening and data extraction. XH and TT conducted data analyses, drafted and reviewed the manuscript.

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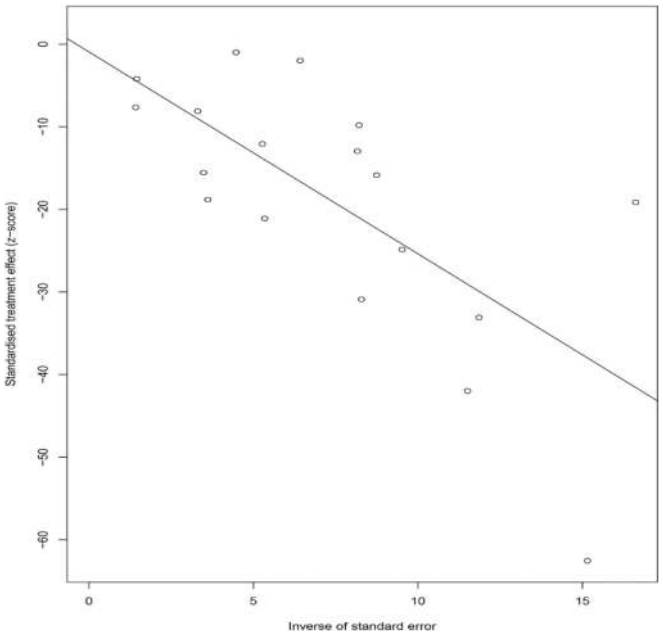
Corresponding author

Xiang Huo, MD, MSc
Department of food safety and assessment
Jiangsu Provincial Center for Disease Control and Prevention
Jiangsu road 172, 210009, Nanjing, China
Tel: +86 025 83759541
Fax: +86 025 83759401
Email: huox@foxmail.com

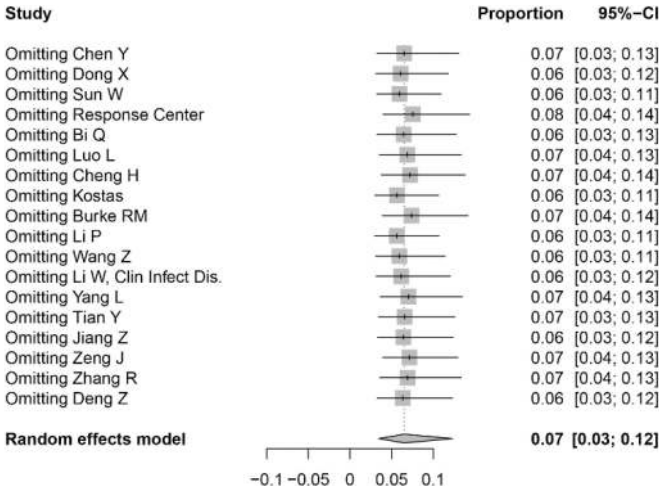
Conflict of interests: No conflict of interests is declared.

Annex – Supplementary Items

Supplementary Figure 1. Publication bias.



Supplementary Figure 2. Sensitivity analysis.



Supplementary Table 1. Database links.

Databases	Link addresses
PubMed	https://pubmed.ncbi.nlm.nih.gov/
medRxiv	https://www.medrxiv.org/
CNKI (Chinese National Knowledge Infrastructure)	https://www.cnki.net/
WanFang database	http://www.wanfangdata.com.cn/index.html
Chinese Journal of Epidemiology	http://chinaepi.icdc.cn/zhlxbx/ch/index.aspx
Chinese Journal of Public Health	http://www.zgggws.com/
Chinese Journal of Preventive Medicine	http://www.pubhealth.org.cn/

Supplementary Table 2. Agency for Healthcare Research and Quality (AHRQ) checklist to assess quality of the included studies.

ARHQ Methodology Checklist for Cross-sectional study	Chen Y	Dong X	Sun W	Response Center	Bi Q	Luo L	Cheng H	Kostas	Burke RM	Li P	Wang Z	Li W	Yang L	Tian Y	Jiang Z	Zeng J	Zhang R	Deng Z
1) Define the source of information (survey, record review)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2) List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
3) Indicate time period used for identifying patients	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
4) Indicate whether or not subjects were consecutive if not population-based	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
5) Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants	N	N	N	N	Y	Y	Y	N	N	N	Y	N	N	N	N	N	N	N
6) Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements)	Y	Y	Y	U	Y	Y	U	U	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
7) Explain any patient exclusions from analysis	NA	NA	NA	NA	NA	Y	Y	NA	NA	NA	Y	Y	Y	NA	NA	NA	NA	NA
8) Describe how confounding was assessed and/or controlled.	N	N	U	N	N	N	N	U	N	N	N	N	N	N	N	N	Y	N
9) If applicable, explain how missing data were handled in the analysis	NA	NA	NA	NA	Y	Y	NA	NA	NA	NA	Y	NA	N	NA	NA	NA	NA	NA
10) Summarize patient response rates and completeness of data collection	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
11) Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Total score	**7**	**7**	**7**	**6**	**9**	**10**	**8**	**6**	**7**	**7**	**10**	**8**	**8**	**7**	**7**	**7**	**8**	**7**

Y= Yes; N= No; U= Unclear; NA= Not Applicable.