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Sex difference in coronavirus disease (COVID-19): a systematic review and meta-analysis

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ABSTRACT

Objective To assess the sex difference in the prevalence of COVID-19 confirmed cases.

Design Systematic review and meta-analysis.

Setting PubMed, Cochrane Library and Google Scholar were searched for related information. The authors developed a data extraction form on an Excel sheet and the following data from eligible studies were extracted: author, country, sample size, number of female patients and number of male patients. Using STATA V.14 for analysis, the authors pooled the overall prevalence of men and/or women using a random-effect meta-analysis model. The authors examined the heterogeneity in effect size using Q statistics and I^2 statistics. Subgroup and sensitivity analyses were performed. Publication bias was also checked.

Participants Studies on COVID-19 confirmed cases were included.

Intervention Sex (male/female) of COVID-19 confirmed cases was considered.

Primary and secondary outcome measures The primary outcome was prevalence of COVID-19 among men and women.

Results A total of 57 studies with 221 195 participants were used in the analysis. The pooled prevalence of COVID-19 among men was found to be 55.00 (51.43–56.58, I^2=99.5%, p<0.001). Sensitivity analysis showed the findings were not dependent on a single study. Moreover, a funnel plot showed symmetrical distribution. Egger's regression test p value was not significant, which indicates absence of publication bias in both outcomes.

Conclusions The prevalence of symptomatic COVID-19 was found to be higher in men than in women. The high prevalence of smoking and alcohol consumption contributed to the high prevalence of COVID-19 among men. Additional studies on the discrepancies in severity and mortality rate due to COVID-19 among men and women and the associated factors are recommended.

Strengths and limitations of this study

- We used a prespecified protocol for search strategy and data abstraction.
- We used internationally accepted tools for critical appraisal to assess the quality of individual studies.
- Due to inclusion of studies published only in English, language bias is likely.
- Most of the included studies were from China due to lack of literature from other countries that reported on the outcome of interest.

BACKGROUND

COVID-19, first identified in Wuhan, China in late 2019, has rapidly evolved and has resulted in a pandemic by the first quarter of 2020, as indicated by the substantial rise in the number of cases and the fast geographical spread of the disease.[1–4] The WHO announced that the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19).[5 6] The virus has been named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses.[7] COVID-19 was declared by the WHO a public health emergency of international concern on 30 January 2020.[8] COVID-19 affects people differently, in terms of infection with SARS-CoV-2 and in mortality rate.[9 10]

Susceptibility to symptomatic COVID-19 seems to be associated with age, biological sex and comorbidities.[11] Although COVID-19 causes mild illness in a majority of cases, severe illness requiring hospital admission is not uncommon.[12] Moreover, it has the potential to trigger a life-threatening critical illness, characterised by respiratory failure, circulatory shock, sepsis or other organ failure, requiring intensive care.[13 14] According to Global Health 5050 data, the number of COVID-19 confirmed cases and the death rate due to the disease are high among men in different countries.[15–17]

A report in *The Lancet* and Global Health 5050 summary show that sex-disaggregated data are essential to understanding the distribution of risk, infection and disease in the population, and the extent to which sex and gender affect clinical outcomes.[18] Moreover, knowing the degree to which outbreaks affect

women and men in different ways is an important step in generating effective, equitable policies and interventions. Since the emergence of COVID-19 in Wuhan, China in December 2019,[19] it has quickly spread across China and numerous other countries.[20–24] To date, COVID-19 has affected more than 193 countries, with 2 733 591 confirmed cases, including 191 185 deaths and 751 404 recoveries.[25] While some previously published papers have shown sex variations, the findings are not conclusive due to inconsistencies in the prevalence of COVID-19 among men and women. Moreover, there is a lack of systematic review and meta-analysis that provides a worldwide clear picture of sex variations in the risk for COVID-19. Hence, this systematic review and meta-analysis was conducted to assess the pooled prevalence of COVID-19 among men and women.

Review question

The review question for this systematic review and meta-analysis is whether men are more susceptible to acquiring symptomatic COVID-19.

METHODS

Search strategy

This systematic review and meta-analysis identified studies that showed data on the proportion of men and women among COVID-19 confirmed cases. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines to search electronic databases, presented in online supplemental file 1. We retrieved studies from Google Scholar, PubMed, Scopus, Web of Science, Cochrane Library, Research Gate and institutional repositories, as described in detail previously.[26 27] The search included keywords which are combinations of population, condition/outcome and context. A snowball search for references of relevant papers was also performed. The following were the search terms and phrases included: 'Novel coronavirus', 'Novel coronavirus 2019', '2019 nCoV', 'COVID-19', 'Wuhan coronavirus', 'Wuhan pneumonia' and 'SARS-CoV-2'. Articles published in the English language from 1 January 2020 were considered. The search concluded on 27 March 2020, and four different researchers independently evaluated the search results. Using these key terms, the following search map was applied: (prevalence OR proportion OR magnitude) AND (Male OR Female) AND (Novel coronavirus OR Novel coronavirus 2019 OR 2019 nCoV OR COVID-19 OR Wuhan coronavirus OR Wuhan pneumonia OR SARS-CoV-2) AND COVID-19 confirmed patients, on PubMed database (online supplemental table S1). Thus, the PubMed search combines #1 AND #2 AND #3 AND #4, as shown in online supplemental table S1. The search date was from January 2000 to December 2019.

Study selection and screening

The retrieved studies were exported to EndNote V.8 reference managers to remove duplicate studies, as described in detail previously.[26 27] Two investigators (BBA and AMK) independently screened the selected studies using the article's title and abstract before retrieval of the full text. We used prespecified inclusion criteria to further screen full-text articles. Disagreements were discussed during a consensus meeting, and if necessary including the third and fourth researchers (MWA and TGA) to make the final decision on the studies to be included in the systematic review and meta-analysis.

Inclusion and exclusion criteria

Studies that reported on the proportion of men and/or women among confirmed patients with COVID-19 and published in the English language were included. Studies that did not report on the prevalence of men and/or women among confirmed patients with COVID-19 were excluded. Studies without abstract and/or full text, anonymous reports, editorials, and qualitative studies were excluded from the analysis. Prevalence was defined as the proportion of men and/or women among COVID-19 confirmed cases within a specific population, multiplied by 100.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Quality assessment

Using the Joanna Briggs Institute (JBI) Quality Appraisal Checklist, the authors appraised the quality of included studies.[28] The papers were split among a team of four reviewers. Each paper was then assessed by two reviewers and any disagreements were discussed with the third and fourth reviewers. A study was considered as low risk or of good quality when it scored 4 and above,[28] whereas a study that scored 3 and below was considered high risk or of poor quality, as described in detail previously[26 27] (online supplemental table S2).

Data extraction

The authors developed a data extraction form on an Excel sheet and the following data from eligible studies were extracted: author, country, sample size, number of female patients and number of male patients, as described in detail previously.[26 27] The data extraction sheet was piloted using four random papers, and it was adjusted after the template was piloted, as described in detail previously.[26 27] Two of the authors extracted data in collaboration using the extraction form. The third and fourth authors independently checked the correctness of data. Any disagreements between the reviewers were resolved through discussions with third and fourth reviewers, as described in detail previously.[26 27] Mistyping of data was resolved by crosschecking the included papers. Definitions of cases were as follows: (1) confirmed case: detection of SARS-CoV-2 nucleic acid in a clinical specimen; (2) possible case: any person with at least one of the following symptoms: cough, fever, shortness of breath,

or sudden onset of anosmia, ageusia or dysgeusia; and (3) probable case: any person with at least one of the following symptoms: cough, fever, shortness of breath, or sudden onset of anosmia, ageusia or dysgeusia, with close contact with a confirmed COVID-19 case in the 14 days prior to onset of symptom or having been a resident or a staff member in the 14 days prior to onset of symptoms in a residential institution for vulnerable people where ongoing COVID-19 transmission has been confirmed.

Synthesis of results

We transported the data to STATA V.14 for analysis after extracting the data in an Excel sheet, considering the reported prevalence of men and women. We pooled the overall prevalence of men and/or women using a random-effect meta-analysis model. We examined the heterogeneity in effect size using Q statistics and I^2 statistics. In this study, an I^2 statistic value of 0 indicates true homogeneity, whereas values of 25%, 50% and 75% represented low, moderate and high heterogeneity, respectively. Subgroup analysis was performed by study country and sample size. Sensitivity analysis was employed to examine the effect of a single study on the overall estimation. Publication bias was checked by a funnel plot and more objectively through Egger's regression test.

RESULTS

Study selection

A total of 2574 studies were identified using electronic search (databases, n=2560; other sources, n=12). After removal of duplicates, a total of 1352 articles remained (1222 duplicates). Finally, 86 studies were screened for full-text review, and 57 articles (n=221 195 patients) were selected for analysis (figure 1). The citation manager automatically identifies duplicates and creates a separate group among the imported references which can be deleted. For different citations of the same paper, we screened and de-duplicated the citations by hand and recorded them on a Microsoft Excel spreadsheet after assessment of whether they have the same author, title, publication date, volume, issue, sample size and so on. The duplicate one was then removed.

Characteristics of the included studies

A total of 57 studies were included in the systematic review and meta-analysis.[1 10 13 14 24 29–75] All studies were published in 2020, with sample size ranging from 9[76] to 78 771[46] (table 1).

Meta-analysis

Prevalence of COVID-19 among men

All studies (n=57) with a total of 221 195 patients reported on the proportion of men and women with COVID-19.[1 10 13 14 24 29–75] The prevalence of COVID-19 among men ranges from 37.5 in Liu *et al*[32] to 77.08 in Chen *et al*.[58] Random-effects model analysis from these studies revealed that the pooled prevalence of COVID-19 confirmed cases was 55.00 (51.43–56.58, I^2=99.5%, p<0.001) (figure 2).

Subgroup analysis of COVID-19 confirmed cases among men

A subgroup analysis was performed through stratification by country, province, sample size and quality score. Based on this, the prevalence of COVID-19 was found to be 55.99 (51.99–59.99), 39.21 (34.85–43.84), 59.80 (59.16–60.44), 37.77 (36.31–39.24) and 50.00 (26.90–73.10) in China, Africa, Italy, Korea and Singapore, respectively (table 2 and online supplemental figure 1).

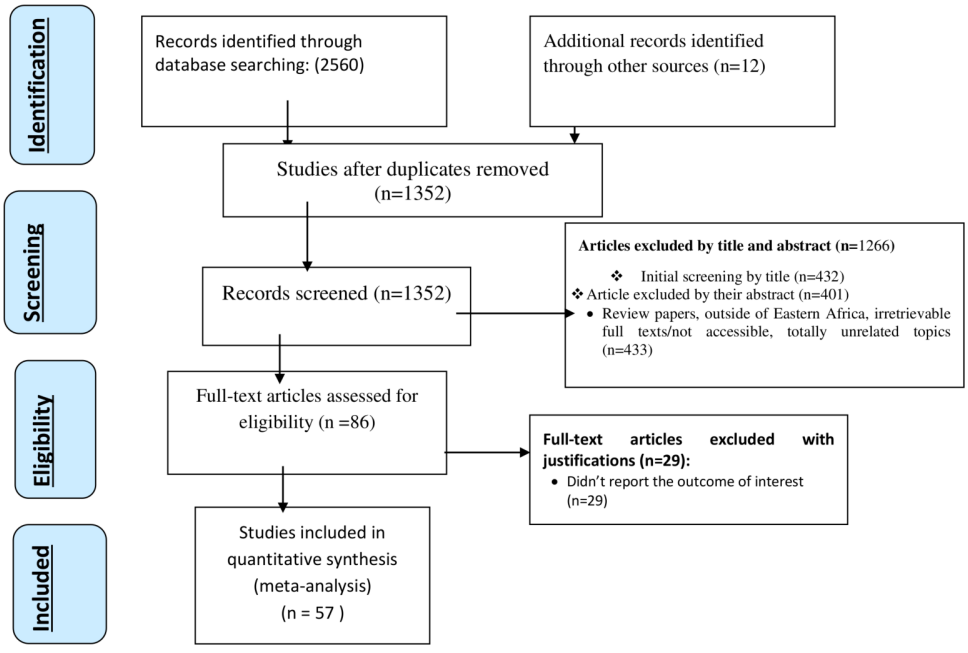

Figure 1 PRISMA flow diagram shows the results of the search and the reasons for exclusion. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Table 1 Characteristics of included studies of men and women among COVID-19 confirmed cases

Sr no	Author	Country	Study period	Sample size	Male	Female	Quality score	Reference
1	Li *et al*	China	January–February	83	44	39	6/9	29
2	Liu *et al*	China	11–20 January	12	8	4	9/9	30
3	Li *et al*	China	23 January–8 February	109	59	50	6/9	31
4	Liu *et al*	China	January–February	40	15	25	8/9	32
5	Wu *et al*	China	22 January–14 February	80	39	41	8/9	33
6	Xu *et al*	China	10–26 January	62	36	26	8/9	10
7	Xu *et al*	China	January–February	50	29	21	6/9	34
8	Yao *et al*	China	1 January–7 February	195	115	80	8/9	35
9	Young *et al*	China	22–31 January	18	9	9	6/9	36
10	Zhang *et al*	China	16 January–3 February	140	71	69	8/9	37
11	Zhang *et al*	China	18 January–3 February	9	5	4	7/9	38
12	Zhao *et al*	China	16 January–3 February	101	56	45	8/9	39
13	Zhu *et al*	China	1 December–15 February	12	8	4	7/9	40
14	Yanping *et al*	China	February 2020	44 672	22 981	21 691	8/9	41
15	Guan *et al*	China	February 2020	1099	640	459	7/9	42
16	WHO	Africa	March 2020	482	189	177	7/9	43
17	Huang *et al*	China	January 2020	41	30	11	7/9	1
18	Chen *et al*	China	December 2020	99	67	32	6/9	44
19	Wang *et al*	China	March 2020	138	75	63	7/9	24
20	Kaiyuan *et al*	China	February 2020	507	281	201	6/9	45
21	Giwa and Desai	China	March 2020	78 771	57 482	21 289	9/9	46
22	Qian *et al*	China	March 2020	91	37	54	8/9	47
23	Livingston and Bucher	Italy	March 2020	22 512	13 462	9050	7/9	48
24	Wang *et al*	China	March 2020	110	48	62	6/9	49
25	KSID	Korea	February 2020	4212	1591	2621	9/9	50
26	Su and Lai	China	March 2020	10	7	3	6/9	51
27	Dowd *et al*	China	March 2020	59 600	30 000	29 600	8/9	52
28	Kui *et al*	China	March 2020	137	61	76	8/9	53
29	Deng *et al*	China	March 2020	33	17	16	8/9	54
30	Dong *et al*	China	March 2020	135	72	63	6/9	55
31	Xiaobo *et al*	China	March 2020	52	35	17	8/9	13
32	Zhou *et al*	China	March 2020	191	119	72	6/9	14
33	Wu *et al*	China	March 2020	297	147	150	8/9	56
34	Gao and Xia	China	January–February 2020	213	108	105	7/9	57
35	Chen *et al*	China	February 2020	291	145	146	8/9	58
36	Zhang *et al*	China	December 2019	221	108	113	7/9	59
37	Wu *et al*	China	March 2020	21	10	11	8/9	60
38	Cao *et al*	China	February 2020	128	60	68	7/9	61
39	Chung *et al*	China	March 2020	20	13	7	7/9	62
40	Xiao *et al*	China	March 2020	73	41	32	7/9	63
41	Qi *et al*	China	January–February 2020	267	149	118	6/9	64
42	Liang *et al*	China	February 2020	1590	911	679	7/9	65
43	Wang *et al*	China	February 2020	55	22	23	6/9	66
44	Easom *et al*	UK	April 2020	68	32	36	9/9	67
45	Mizumoto *et al*	Japan	March 2020	634	321	313	8/9	41

Continued

Table 1 Continued

Sr no	Author	Country	Study period	Sample size	Male	Female	Quality score	Reference
46	Chen *et al*	China	March 2020	48	37	11	7/9	68
47	Cheng *et al*	China	March 2020	1079	573	505	6/9	69
48	Li *et al*	China	March 2020	47	28	19	9/9	31
49	Tian *et al*	China	April 2020	262	127	135	8/9	70
50	Li *et al*	China	March 2020	425	240	185	7/9	71
51	Liu *et al*	China	February 2020	109	59	50	6/9	1
52	Cao	China	February 2020	198	101	97	9/9	72
53	Chaolin *et al*	China	February 2020	41	30	11	6/9	73
54	Yang *et al*	China	February 2020	52	35	17	8/9	13
55	Liu *et al*	China	February 2020	51	32	19	8/9	74
56	Huang *et al*	China	February 2020	41	30	11	8/9	1
57	Wang *et al*	China	February 2020	138	75	63	6/9	75

KSID, Kerala State Institute of Design; Sr no, Serial number.

The pooled prevalence of COVID-19 among men in Wuhan, Shanghai, Hubei, Zhonghua, outside China, Zhejiang, Shenzhen, Jiangsu and Chongqing was 72.05 (95% CI 71.71 to 72.35, I^2=96.6, p=0.00), 51.01 (95% CI 44.05 to 57.97), 50.40 (95% CI 50.1 to 50.80, I^2=66.7, p=0.001), 54.07 (95% CI 51.63 to 56.51, I^2=37.9, p=0.139), 53.17 (95% CI 52.81 to 53.53, I^2=99.4, p=0.00), 46.45 (95% CI 39.10 to 53.81, I^2=99.4, p=0.00), 63.52 (95% CI 51.64 to 75.40, I^2=0.0, p=0.796), 44.84 (95% CI 35.99 to 53.68, I^2=29, p=0.235) and 52.20 (95% CI 47.95 to 56.44, I^2=65.1, p=0.09), respectively (table 2 and online supplemental figure 2).

With regard to quality score, the pooled prevalence of COVID-19 among men in studies which scored greater than or equal to 7 on the JBI Quality Appraisal Checklist was 53.66 (95% CI 49.23 to 58.09, I^2=99.5, p=0.00), and 56.79 (95% CI 52.79 to 60.990, I^2=94.7, p=0.00) among studies that scored less than 7 (table 2 and online supplemental figure 3).

With regard to sample size, the pooled prevalence of COVID-19 among men in studies with sample size greater than or equal to 384 was 53.86 (95% CI 47.09 to 60.63, I^2=99.9, p=0.00) and 54.96 (95% CI 52.35 to 57.57, I^2=64.5, p=0.00) among studies that scored less than 7 from the JBI Quality Appraisal Checklist (table 2 and online supplemental figure 4).

Sensitivity analysis

We employed a leave-one-out sensitivity analysis to identify the impact of individual research on the pooled prevalence of severe illness among COVID-19 confirmed cases. This sensitivity analysis showed that our findings were not dependent on a single study. Our pooled estimated prevalence of severe illness varied between 22.83 (19.12–26.53) in Li *et al*[29] and 25.0 (19.87–30.13) in Yanping *et al* after deletion of a single study (figure 3).

Publication bias

We also checked for publication bias and a funnel plot showed symmetrical distribution. Egger's regression test p value was 0.599. Both the symmetric funnel plot and the insignificant p value (<0.05) indicate absence of publication bias.

Meta-regression

Univariate meta-regression analyses revealed that the prevalence of smoking was found to be high among men. This contributed to the high prevalence of COVID-19 among men (p=0.002). Comorbidities such as hypertension (0.042), diabetes mellitus (0.012), chronic respiratory disease (0.021) and cardiovascular disease (0.001) were also found to be higher among men, and these significantly increased the prevalence of COVID-19. A higher proportion of severe/critical illness (0.003) and death (0.001) was also observed among men (table 3).

DISCUSSION

This systematic review and meta-analysis was conducted to assess the sex difference in acquiring COVID-19. Fifty-seven studies were included in the final analysis. This systematic review and meta-analysis revealed that the pooled prevalence of COVID-19 confirmed cases among men and women was 55.00 (51.43–56.58, I^2=99.5%, p<0.001) and 45.00 (41.42–48.57), respectively. This indicates COVID-19 is more prevalent in men than in women.

Similar finding was reported in other studies.[77 78] A study in Ontario, Canada showed that men were more likely to test positive.[79 80] In Pakistan 72% of COVID-19 cases were male.[81] According to Global Health 5050 data, the number of COVID-19 confirmed cases and the death rate due to the disease are high among men in different countries.[15–17]

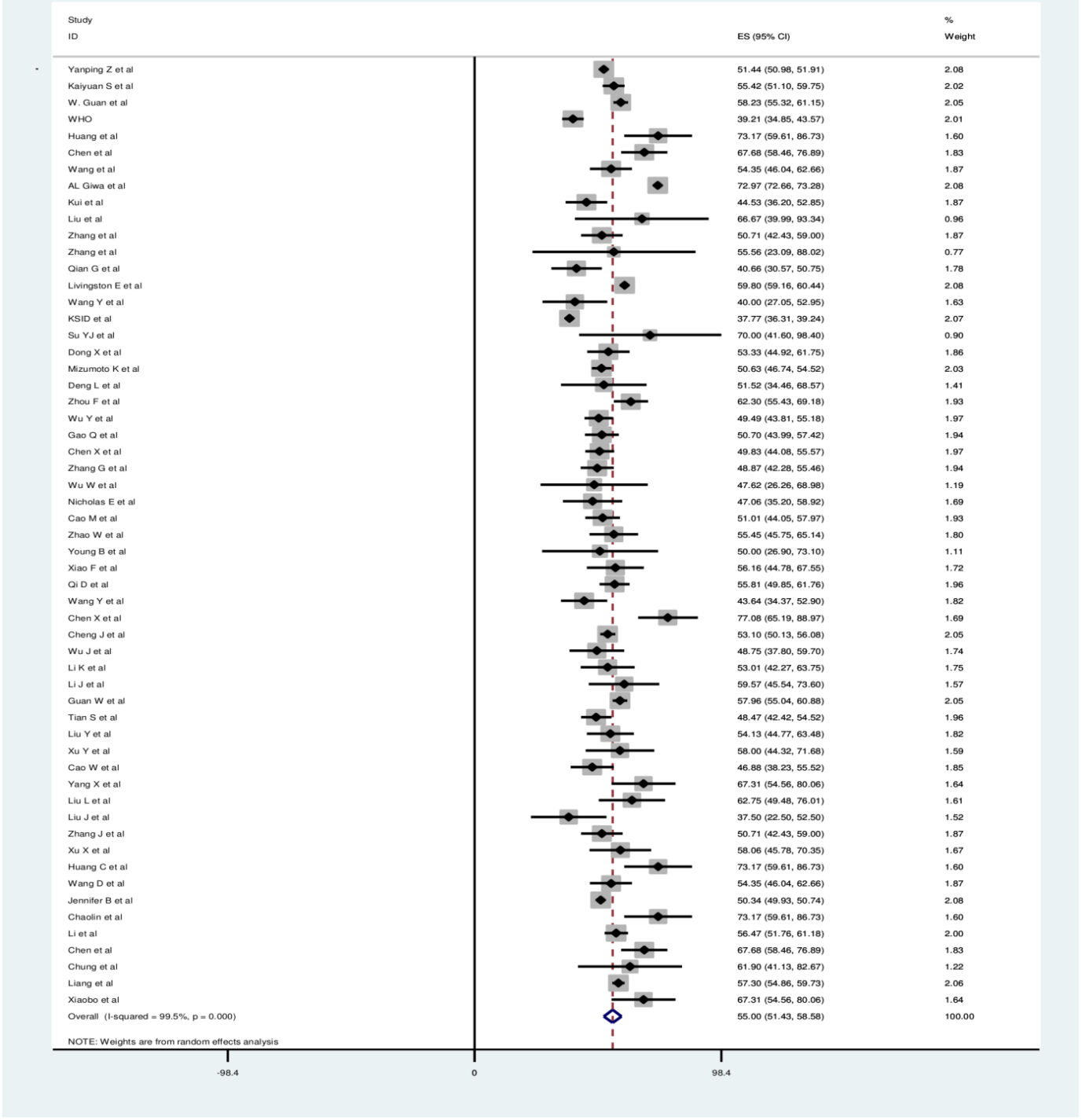

Figure 2 Forest plot showing the pooled prevalence of COVID-19 confirmed cases among men. ES, Estimate.

This might be because behavioural factors and roles which increase the risk of acquiring COVID-19 tend to be more common among men. Men are more involved in various risky behaviours, such as alcohol consumption,[82–84] being involved in key activities during burial rites, and working in basic sectors and occupations that require them to continue being active, to work outside their homes and to interact with other people even during the containment phase (eg, food or pharmacy manufacturing and sales, agriculture or food production and distribution, transportation, and security). Because of this, men mostly do not stay at home, and sit together with other people and remove their mask to drink and smoke. This increased level of exposure predisposes men to a high risk of acquiring COVID-19. In China 50% of men smoke, and because it is considered not acceptable for women to smoke only 2% of them do so. Smoking is associated with adverse

Table 2 Subgroup analysis of the pooled prevalence of COVID-19 by country, province, quality score and sample size

Variables	Characteristics	Pooled prevalence (95% CI)	I^2 (p value)
By province in China	Wuhan	72.05 (71.71 to 72.35)	96.6 (0.00)
	Shanghai	51.01 (44.05 to 57.97)	–
	Hubei	50.40 (50.1 to 50.80)	66.7 (0.001)
	Zhonghua	54.07 (51.63 to 56.51)	37.9 (0.139)
	Zhejiang	46.45 (39.10 to 53.81)	99.4 (0.00)
	Shenzhen	63.52 (51.64 to 75.40)	0.0 (0.796)
	Jiangsu	44.84 (35.99 to 53.68)	29 (0.235)
	Chongqing	52.20 (47.95 to 56.44)	65.1 (0.09)
	Outside China	53.17 (52.81 to 53.53)	99.4 (0.00)
By country	China	55.99 (51.99 to 59.99)	99.5 (0.00)
	Africa	39.21 (34.85 to 43.84)	–
	Italy	59.80 (59.16 to 60.44)	–
	Korea	37.77 (36.31 to 39.24)	–
	Singapore	50.00 (26.90 to 73.10)	–
By JBI quality score	≥7	53.66 (49.23 to 58.09)	99.5 (0.00)
	<7	56.79 (52.79 to 60.990)	94.7 (0.00)
By sample size	≥384	53.86 (47.09 to 60.63)	99.9 (0.00)
	<384	54.96 (52.35 to 57.57)	64.5 (0.00)

JBI, Joanna Briggs Institute.

outcomes of COVID-19. For instance, the combined results of five studies showed that smokers were 1.4 times more likely than non-smokers to have severe symptoms of COVID-19.[85] Smoking is also related to a higher expression of ACE2 (the receptor for SARS-CoV-2), which might be the reason for the higher prevalence of COVID-19 in this subgroup of patients.[86]

Men tended to develop more symptomatic and serious disease than women, according to the clinical classification of severity. Similar incidence occurred during the previous coronavirus epidemics: men had worse outcomes of illness from severe acute respiratory syndrome[87] and a higher risk of dying from the Middle East respiratory syndrome.[88] Biological sex variation is said to be one of the reasons for the sex discrepancy in COVID-19 cases, severity and mortality.[89] Women are in general able to mount a more vigorous immune response to infections and vaccinations.[90] Some previous studies on coronaviruses in mice have suggested that oestrogen may have a protective role. Oestrogens suppress the escalation phase of the immune response that leads to increased cytokine release.[91] Authors also showed that female mice treated with an oestrogen receptor antagonist died at close to the same rate as male mice.[92]

The X chromosome is known to contain the largest number of immune-related genes in the whole genome.[88] With their XX chromosome, women have a double copy of key immune genes compared with a single copy in XY in men. This boost extends both to the general reaction to infections (the innate response) and to the more specific response to microbes, including antibody formation (adaptive immunity).[88] Thus women's immune systems are generally more responsive to infections. This might mean women are able to tackle the novel coronavirus more effectively, but this has not yet been proven.

Study ommited	Coef.	[95% Conf.	Interval]
Cheng J et al	20.732838	20.445127	21.020546
Xu X et al	17.418531	17.156216	17.680845
Liu L et al	17.381458	17.119438	17.643478
Yao et al	17.516275	17.25304	17.77951
Wang Yet al	17.346966	17.085199	17.608732
Wu J et al	17.362354	17.100435	17.624273
Xia W et al	17.317913	17.056414	17.579412
Xiao F et al	17.338419	17.076689	17.600149
Cao M	17.340126	17.078194	17.60206
Qian G et al	17.322186	17.060547	17.583824
Liu C et al	17.311192	17.049721	17.57266
Zhao et al	17.313881	17.052284	17.57548
Yang et al	17.312496	17.050829	17.574163
Gao Q et al	17.313957	17.052176	17.575737
Guan W	17.332129	17.068779	17.595478
Cao W et al	17.310188	17.048569	17.571806
Chen X	17.309149	17.04727	17.571028
Tian et al	17.307884	17.046061	17.569708
Tian S et al	17.307884	17.046061	17.569708
Yanping Z et al	16.002106	15.621832	16.382381
Qi D et al	17.304249	17.042439	17.566059
W. Guan et al	17.256212	16.993301	17.519123
Liu K et al	17.298866	17.037294	17.56044
Liu W et al	17.30262	17.041122	17.564116
Li Y et al	17.304375	17.042908	17.565842
Xu Y et al	17.304667	17.043205	17.56613
Wang D et al	17.297497	17.035929	17.559065
Wang D et al	17.297497	17.035929	17.559065
Wu Y et al	17.280704	17.018961	17.54245
Livingston E et al	14.335077	14.044443	14.625712
Li K et al	17.299694	17.0382	17.561188
Li K et al	17.299694	17.0382	17.561188
Chen W et al	17.301987	17.040525	17.56345
Huang C et al	17.303835	17.042391	17.565281
Wu W et al	17.305992	17.044569	17.567415
Young et al	17.306377	17.044958	17.567799
Wang Y et al	17.293758	17.032244	17.555273
Zhang J et al	17.283909	17.022371	17.545444
Zhang J et al	17.283909	17.022371	17.545444
Wu W et al	17.30135	17.039911	17.56279
Chen L et al	17.302288	17.040859	17.563717
Liu Y et al	17.284363	17.02286	17.545866
Chen X et al	17.295172	17.033726	17.556618
Zhou F et al	17.243504	16.981913	17.505095
Liu Y et al	17.302118	17.040703	17.563536
Li J et al	17.256153	16.994654	17.517653
Yang X et al	17.308687	17.047285	17.570087
Combined	17.308687	17.047285	17.570088

Figure 3 Sensitivity analysis of the pooled prevalence of COVID-19 confirmed cases among men.

Table 3 Meta-regression analysis showing factors which have an effect on sex difference in COVID-19

Variable	Event	Total	Male	Studies	Male (%)	Female (%)	P value
Smoking	2863	11 590	8693	19	75	25	0.002
Comorbidities							
Hypertension	46 546	169 694	101 410	46	59.7	40.3	0.042
Diabetes mellitus	24 773	176 952	125 768	48	71.1	28.9	0.012
Chronic respiratory disease	15 883	171 707	135 902	36	79	21	0.021
Cardiovascular disease	4352	174 085	152 276	39	81.7	18.3	0.001
Patient condition							
Severe/critical illness	38 128	158 870	105 322	49	66.3	33.7	0.003
Death	699 028	158 870	125 322	46	78.8	21.2	0.001

Moreover, the above-listed behavioural factors, such as smoking and alcohol consumption, tend to be more common among men, and these behaviours predispose men to cardiac and respiratory diseases. This may also explain the overall higher mortality rate among men.[86 93 94] A systematic review and meta-analysis revealed that comorbid diseases such as respiratory system disease, hypertension and cardiovascular disease are risk factors for death.[95]

CONCLUSIONS

The prevalence of symptomatic COVID-19 was found to be higher in men than in women. The high prevalence of smoking and alcohol consumption contributed to the high prevalence of COVID-19 among men,[3–5] along with occupational exposures which prevent men from staying at home, as well as sitting together with other people and removing their mask to drink and smoke. This increased level of exposure predisposes men to a high risk of acquiring COVID-19, making it more prevalent among men. Smoking and drinking alcohol reduce overall health and therefore make an individual more susceptible to symptomatic COVID-19 infection. Although there has been a rapid surge in research in response to the COVID-19 outbreak, additional studies with regard to discrepancies in severe illness and mortality due to COVID-19 among men and women and the factors that determine exposure, severity and mortality due to COVID-19 are recommended.

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