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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-040129
Article Type:	Original research
Date Submitted by the Author:	06-May-2020
Complete List of Authors:	Abate, Biruk; Woldia University, Nursing; Woldia University, Nursing Kassie, Ayelign; Woldia University, Nursing; Wudu, Mesfin; Woldia University, Nursing; Woldia University, Nursing Mesafint, Teshome ; Nursing
Keywords:	INFECTIOUS DISEASES, Epidemiology < INFECTIOUS DISEASES, IMMUNOLOGY, Epidemiology < TROPICAL MEDICINE

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

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***Running title*:** Sex difference in coronavirus disease (COVID-19)

Abstract

Objective: To assess the sex difference in the prevalence of coronavirus disease (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 the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number female patients, and the number of male patients. Using STATA 14 for analysis authors pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I^2 statistics. Subgroup and sensitivity analysis was done Publication bias was also checked.

Participants: Studies with COVID-19 confirmed cases were included.

Intervention: sex (male/female) of COVID-19 confirmed cases were considered

Primary and secondary outcome measures: Primary outcomes were prevalence of COVID-19 among males and females.

Result: A total of 57 studies with 221195 participants were used for analysis. The pooled prevalence of COVID-19 among males was found to be 55.00(51.43-56.58; I2=99.5%; p<0.001). The 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 the absence of publication bias in both outcomes.

Conclusions: The prevalence of COVID-19 is higher among males than females. This can be explained with the hormonal and chromosomal variation between males and females. In addition the high prevalence of smoking and alcohol consumption has contributed for increased high prevalence of COVID-19 among males. Additional studies regarding discrepancy in severe illness and mortality due to COVID-19 among males and females and factors which determine the exposure, severity and mortality due to COVID-19 is recommended.

Keywords: COVID-19; sex difference; Systematic review; Meta-analysis

Background

A COVID-19, first identified in Wuhan, China in late 2019, has rapidly evolved 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 now been named Sever Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) (7). COVID-19 has now been declared as a Public Health Emergency of International Concern by the WHO on 30th January 2020(8). COVID-19 affects people differently, in terms of infection with the virus SARS-CoV-2 and mortality rates(9, 10).

Susceptibility to COVID-19 seems to be associated with age, biological sex, and comorbidities (11). Although the COVID-19 causes a mild illness in a majority of cases, severe illness requiring hospital admission is not uncommon (12). Besides, it has the potential to precipitate a life-threatening critical illness, characterized by respiratory failure, circulatory shock, sepsis or other organ failure, requiring intensive care(13, 14).

According to Global Health 5050 data gathering, the highest ratio of male to female deaths, as a result of COVID-19, is in Denmark and Greece: 2.1 to 1, in Republic of Ireland 2 to 1, Italy and Switzerland have a 1.9 to 1 ratio each, Iran, with 1.1 to 1, and Norway, with 1.2 to 1(15-17). Overall, 9/ 18 countries have more COVID-19 cases among women than they do among men. Six of the 18 countries have more cases among men than they do among women. Norway, Sweden, and Germany have a 50–50% case ratio while Switzerland (53% of women to 47% of men), Spain (51% to 49%),The Netherlands (53% to 47%),Belgium (55% to 45%),South Korea (60% to 40%),Portugal (57% to 43%),Canada (52% to 48%),Republic of Ireland (52% to 45%) and a higher number of confirmed cases have been observed among men than women in Greece, Italy, Peru, China, and Australia(16-17).

The report in The Lancet reads, "Knowing the degree to which outbreaks upsets women and men in different way is a important step for generating effective, equitable policies and interventions." Men and women tend to react differently to potential vaccines and treatments, so having access to sex-disaggregated data is crucial for conducting safe clinical trials(18).Understanding sex difference in world health is a core component of ensuring effective and equitable national and global health systems that work for everyone.

National governments and global health organizations must urgently face up to this reality.

Since the occurrence of COVID-19 infection in Wuhan, China, in December 2019 (19), it has quickly spread across China and numerous other countries(20-24). So far, 2019-nCoV has affected more than 210 countries with 2, 733,591 confirmed cases, including 191185 deaths and 751,404 recovery (25).Given the rapid spread of COVID-19 and its health related impacts, many research articles have been done already been published about this epidemic (26). Global Health 5050 summarize in their article, Sex-disaggregated data are essential for understanding the distributions of risk, infection, and disease in the population, and the extent to which sex and gender affect clinical outcomes. Even though, some previously published papers haven showed the sex variation, some indicates males are at high risk than female while others indicate females are at high risk for COVID-19. Therefore the findings are not conclusive due to inconsistency in prevalence of COVID-19 among males and females. Moreover, there is lack of systematic review and meta-analysis which indicated the worldwide clear picture of sex variation on the risk of COVID-19. Hence, this systematic review and meta-analysis was conducted to assess the pooled prevalence of COVID-19 among males and females.

Review question

The review questions of this systematic review and meta-analysis were:

Are men more susceptible to getting COVID-19?

Methods

Search strategy

This systematic review and meta-analysis identified studies that revealed data on the proportion of sex in COVID-19 confirmed case. We retrieved studies from Google Scholar, PubMed, Scopus, Web of Sciences Cochrane library, research gate, and institutional repositories. The search included keywords that are the combinations of population, condition/outcome, and context. A snowball searching for the references of relevant papers for linked articles was also performed. Those search terms or phrases including were: The search terms used were: "Novel coronavirus," "Novel coronavirus 2019", "2019 nCoV", "COVID-19", "Wuhan coronavirus," "Wuhan pneumonia," and "SARS-CoV-2." Articles published in English language were considered from January 1, 2020. The searches were concluded by March 27, 2020, and four different researchers independently evaluated search results. Using those 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 (Table S1). Thus, the PubMed search combines #1 AND #2 AND #3 AND #4 (Table S1). The searching date was January 2000 to December 2019.

Study selection and screening

The retrieved studies were exported to Endnote version 8 reference managers to remove duplicate studies. Two investigators (BB and AM) independently screened the selected studies using article's title and abstracts before retrieval of full-text papers. We used pre-specified inclusion criteria to further screen the full-text articles. Disagreements were discussed during a consensus meeting or, if necessary, by including the third and fourth researchers (MW and TG) to make the final decision for the selection of studies to be included in the systematic review and meta-analysis.

Inclusion and exclusion criteria

Those studies had reported the proportion of male and/or female among COVID-19 confirmed patients and published in the English language. Studies which didn't report the prevalence of male and/or female among COVID-19 confirmed patients were excluded. Citations without abstract and/or full-text, anonymous reports, editorials, and qualitative studies were excluded from the analysis. The Prevalence of male and female as the proportion of male and/or female among COVID-19 confirmed cases within a specific population and multiply by 100 to be prevalence report in both case.

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 (27). There was a team of four reviewers and the papers were split amongst the team. Each paper was then assessed by two reviewers and any disagreements were discussed with the third and the fourth reviewers. Studies were considered as low risk or good quality when it scored 4 and above (27), whereas the studies scored 3 and below were considered as high risk or poor quality (Table S2).

Data extraction

The authors developed a data extraction form on the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number female patients, and the number of male patients. The data extraction sheet was piloted using 4 papers randomly, and it was adjusted after piloted the template. Two of the authors extracted the data using the extraction form in collaboration. The third and fourth authors checked the correctness of the data independently. Any disagreements between reviewers were resolved through discussions with third and fourth reviewers when required. The mistyping of data was resolved through crosschecking with the included papers.

Synthesis of results

The authors transformed the data to STATA 14 for analysis after it was extracted in an excel sheet considering prevalence male and female reported. We pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I^2 statistics. In this study, the I^2statistic value of zero indicates true homogeneity, whereas the value 25, 50, and 75% represented low, moderate and high heterogeneity, respectively. Subgroup analysis was done by the 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 the funnel plot and more objectively through Egger's regression test.

Result

Study selection

A total of 2574 studies were identified using electronic searches (through Database searching (n = 2560)) and other sources (n =12)). After duplication removal, a total of 1352 articles remained (1222 duplicated). Finally, 86 studies were screened for full-text review and, 57 articles (n=221195 patients) were selected for the analysis (Fig.1).

Characteristics of included studies

A total of 57 studies included in the systematic review and meta-analysis (1, 10, 13, 14, 24, 28-74). All studies published in 2020 G.C The studies included participants ranging from 9 (75)to 78771 (45) (Table1).

Meta-analysis

Prevalence of COVID-19 among male

All studies (n=57) had reported the sex proportion of COVID-19 (1, 10, 13, 14, 24, 28-74).The prevalence of COVID-19 among male ranges from 37.5 Liu J et al (31) to 77.08 Chen X et al (57) random-effects model analysis from those studies revealed that, the pooled prevalence of severe illness is 55.00(51.43-56.58; I^2=99.5%; p<0.001) (Fig.2).

Subgroup analysis of COVID-19 confirmed cases among male

The subgroup analysis was done through stratification by country. Based on this, the prevalence of severe illness was found to be 61.34 in china and 29.9 in Italy (Supplementary Fig 1).

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-19confirmed cases. The results of 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) Li J ET al and 25.0 (19.87-30.13) Yanping Z ET al after the deletion of a single study (Figure 3).

Publication Bias

We have also checked publication bias and, a funnel plot showed symmetrical distribution. Egger's regression test p-value was 0.599, which indicates the absence of publication bias (Figure 4).

Discussion

Recently, following the COVID-19 outbreak, numerous questions have been raised; comprising what is their sex difference in getting COVID-19?. This systematic review and meta-analysis were conducted to assess the sex difference in getting COVID -19 disease and this review revealed the pooled prevalence of COVID-19 among males and females.

Fifty seven studies were included in the final analysis. The pooled prevalence COVID -19 confirmed cases among males and females was found to be 55.00(51.43-56.58; I2=99.5%; p<0.001) and 45.00(41.42-48.57). This finding is supported by other studies finding (76, 77).

Biological sex variation is said to be one of the reason for the sex discrepancy of COVID-19(78). Women's innate immune response affected by sex chromosomes and sex hormones plays a role. As a result, women are in general able to mount a more vigorous immune response to infections [and] vaccinations(79).

Some previous studies on coronaviruses in mice have suggested that the hormone estrogen may have a protective role. Estrogens suppress the escalation phase of the immune response that leads to increased cytokine release(80). The authors showed that female mice treated with an estrogen receptor antagonist died at close to the same rate as the male mice(81).

In addition behavioral factors, like smoking and alcohol consumption, which tend to occur more among men, those behaviors predisposes males for cardiac and respiratory diseases. This may also explain the overall higher mortality rates among men (82-84).

A systematic review and meta-analysis revealed that comorbid disease, such as respiratory system disease, hypertension, and cardiovascular disease as risk a risk factors for death compared with patients without comorbidity(85).

Strength and limitations

This systematic review and meta- analysis has several strengths: we used a pre-specified protocol for search strategy and data abstraction and used internationally accepted tools for a critical appraisal system for quality assessment of individual studies. Besides we employed subgroup analysis, publication bias and sensitivity analysis Nevertheless, this review had some limitations: because of the inclusion of studies which are published in English only, language bias is likely. In addition most included are from China due to lack of literatures from other countries in the world which reported the outcome of interest. However, the data in this review permit to systematically review and analyze the pooled prevalence of severe illness and mortality among COVID-19 confirmed patients

Conclusions

The prevalence of COVID-19 is higher among males than females. This can be explained with the hormonal and chromosomal variation between males and females. In addition the high prevalence of smoking and alcohol consumption has contributed for increased high prevalence of COVID-19 among males. Although there has been a rapid surge in research in response to the outbreak of COVID-19, additional studies regarding discrepancy in severe illness and mortality due to COVID-19 among males and females and factors which determine the exposure, severity and mortality due to COVID-19 is recommended. Everyone should take actions, such as hand washing with sanitizer, social distancing, avoid crowding (2m apart if coming together is must), avoid smoking and alcohol consumption especially among men to help slow the spread of COVID-19.

Abbreviations

COVID-19: coronavirus disease 2019; WHO: World Health Organization; ICTV: International Committee of Taxonomy of Viruses; SARS-CoV-2: Sever Acute Respiratory Syndrome Coronavirus 2; CI: Confidence Interval; AOR: Adjusted odds ratio; ARTI: Acute Respiratory Tract Infections

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and material

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

We have confirmed that we have no competing interests.

Funding

No funding was obtained for this study

Authors' contributions

BB, AM, MW, and TG: developed the study design and protocol, literature review, selection of studies, quality assessment, data extraction, statistical analysis, interpretation of the data and developing the initial drafts of the manuscript and prepared the final draft of the manuscript. All authors read and approved the final manuscript.

Acknowledgments

We would like to thank the authors of the included primary studies.

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Figure and Table Legend

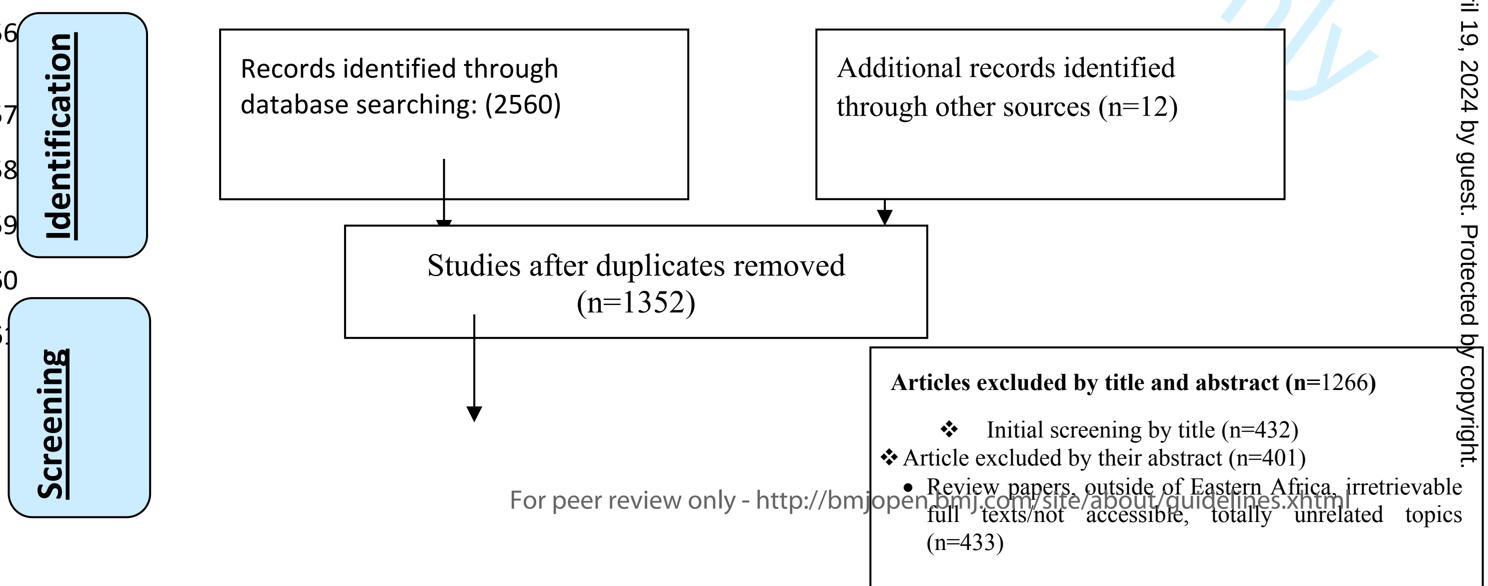
Figure 1: PRISMA flow diagram showed the results of the search and reasons for exclusion

Table 1: Characteristics of included studies for male/female among COVID-19 confirmed cases

Figure 2: Forest plot showing the pooled prevalence of COVID-19 confirmed cases among male

Figure 3: sensitivity analysis for severe illness among COVID-19 confirmed cases

Figure 4: Publication bias for severe illness among COVID-19 confirmed cases



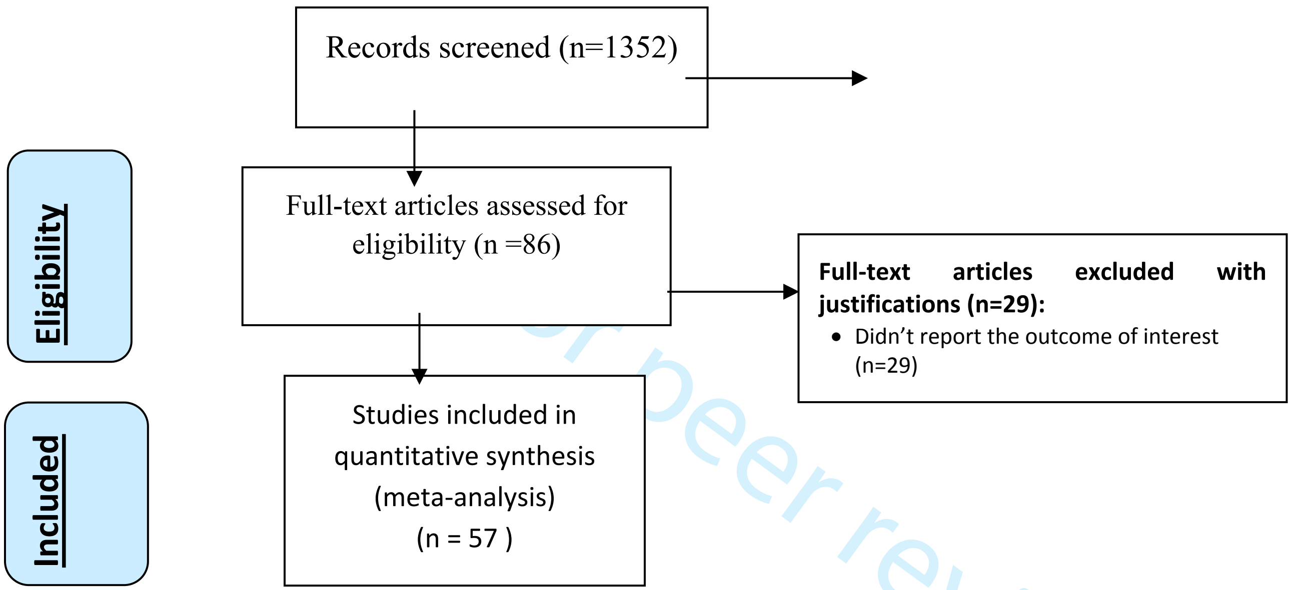


Figure 1

Table 1

Sr no	Author	Country	Study Period	Sample Size	Male	Female	Reference
1.	Li K et al	China	Jan-Feb	83	44	39	(28)
2.	Liu Y et al	China	Jan11-Jan20	12	8	4	(29)
3.	Liu Y et al	China	Jan23-Feb8	109	59	50	(30)
4.	Liu J et al	China	Jan-Feb	40	15	25	(31)
5.	Wu J et al	China	Jan22-Feb14	80	39	41	(32)
6.	Xu X et al	China	Jan10-Jan26	62	36	26	(10)

7.	Xu Y et al	China	Jan-Feb	50	29	21	(33)
8.	Yao et al	China	Jan01-Feb07	195	115	80	(34)
9.	Young et al	China	Jan22-Jan31	18	9	9	(35)
10.	Zhang J et al	China	Jan16-Feb03	140	71	69	(36)
11.	Zhang M et al	China	Jan18-Feb03	9	5	4	(37)
12.	Zhao et al	China	Jan16-Feb03	101	56	45	(38)
13.	Zhu et al	China	Dec01-Feb15	12	8	4	(39)
14.	Yanping Z et al	China	February 2020	44672	22981	21691	(40)
15.	W. Guan et al	China	February 2020	1099	640	459	(41)
16.	WHO ,2020	Africa	March 2020	482	189	177	(42)
17.	Huang et al	China	Jan, 2020	41	30	11	(1)
18.	Chen et al	China	December 2020	99	67	32	(43)
19.	Wang et al	China	March 2020	138	75	63	(24)
20.	Kaiyuan S et al		February, 2020	507	281	201	(44)
21.	AL Giwa et al	China	March, 2020	78771	57482	21289	(45)
22.	Qian G et al	China	March, 2020	91	37	54	(46)
23.	Livingston E et al	Italy	March, 2020	22512	13462	9050	(47)
24.	Wang Y et al	China	March, 2020	110	48	62	(48)
25.	KSID,2020	Korea	February, 2020	4212	1591	2621	(49)
26.	Su YJ et al	China	March, 2020	10	7	3	(50)
27.	Jennifer B et al	China	March, 2020	59600	30000	29600	(51)
28.	Kui et al	China	March, 2020	137	61	76	(52)
29.	Deng L et al	China	March, 2020	33	17	16	(53)
30.	Dong X et al	China	March, 2020	135	72	63	(54)
31.	Xiaobo et al	China	March, 2020	52	35	17	(13)
32.	Zhou F et al	China	March, 2020	191	119	72	(14)
33.	Wu Y et al	China	March, 2020	297	147	150	(55)
34.	Gao Q et al	China	January to February ,2020	213	108	105	(56)
35.	Chen X et al	China	February 2020	291	145	146	(57)
36.	Zhang G et al	China	December 2019	221	108	113	(58)
37.	Wu W et al	China	March, 2020	21	10	11	(59)
38.	Cao M et al	China	February, 2020	128	60	68	(60)
39.	Chung et al	China	March, 2020	20	13	7	(61)
40.	Xiao F et al	China	March, 2020	73	41	32	(62)
41.	Qi D et al	China	January to February ,2020	267	149	118	(63)
42.	Liang et al	China	China	1590	911	679	(64)
43.	Wang Y et al	China	February, 2020	55	22	23	(65)
44.	Nicholas E et al	UK	April 2020	68	32	36	(66)
45.	Mizumoto K et al	Japan	March, 2020	634	321	313	(40)
46.	Chen X et al	China	March, 2020	48	37	11	(67)
47.	Cheng J et al	China	March, 2020	1079	573	505	(68)
48.	Li J et al	China	March, 2020	47	28	19	(30)

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49.	Tian S et al	China	April 2020	262	127	135	(69)
50.	Li et al	China	March, 2020	425	240	185	(70)
51.	Liu Y et al	China	February, 2020	109	59	50	(1)
52.	Cao W et al	China	February, 2020	198	101	97	(71)
53.	Chaolin et al	China	February, 2020	41	30	11	(72)
54.	Yang X et al	China	February, 2020	52	35	17	(13)
55.	Liu L et al	China	February, 2020	51	32	19	(73)
56.	Huang C et al	China	February, 2020	41	30	11	(1)
57.	Wang D et al	China	February, 2020	138	75	63	(74)

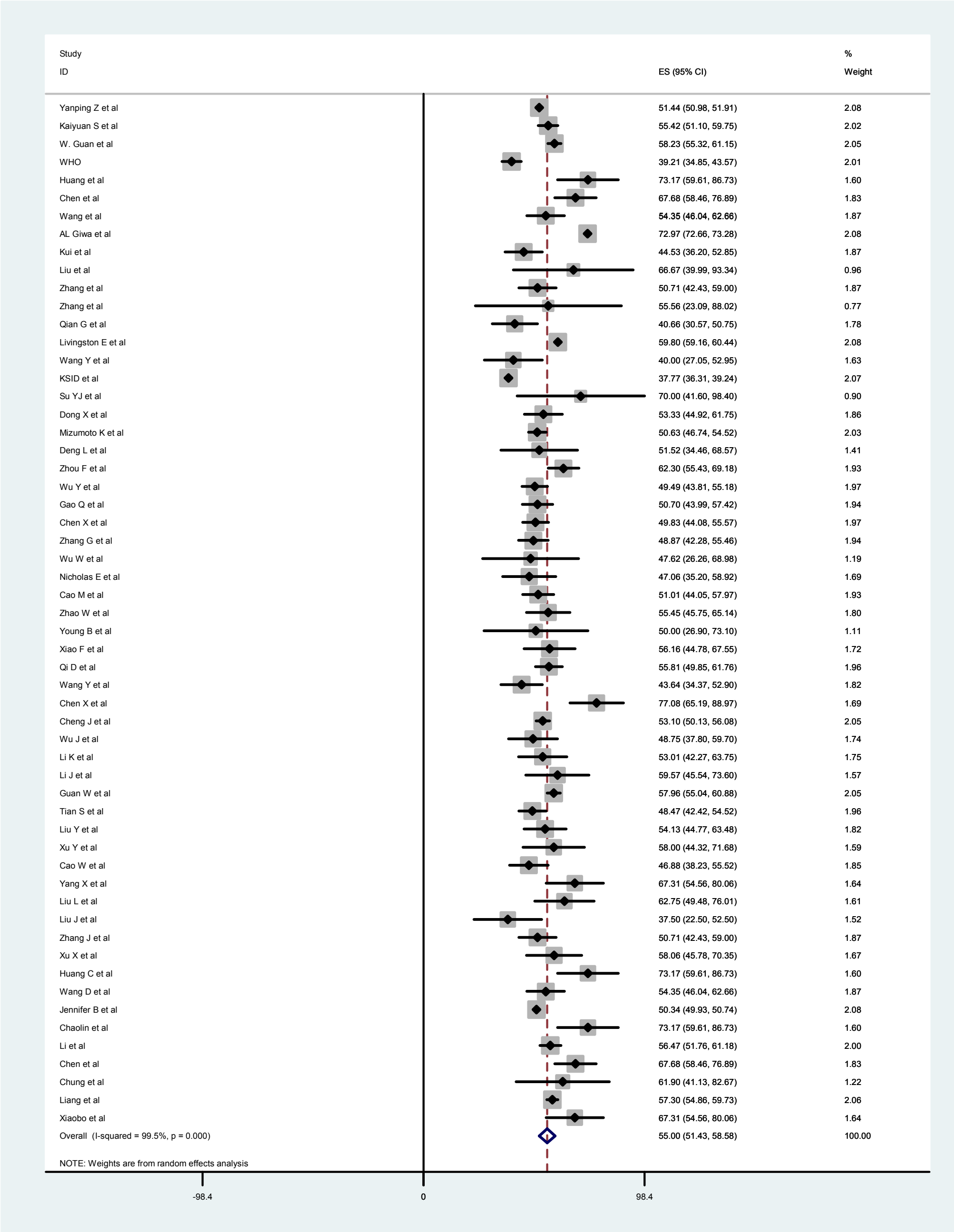

Study
ID
ES (95% CI)
%
Weight
Yanping Z et al 51.44 (50.98, 51.91) 2.08
Kaiyuan S et al 55.42 (51.10, 59.75) 2.02
W. Guan et al 58.23 (55.32, 61.15) 2.05
WHO 39.21 (34.85, 43.57) 2.01
Huang et al 73.17 (59.61, 86.73) 1.60
Chen et al 67.68 (58.46, 76.89) 1.83
Wang et al 54.35 (46.04, 62.66) 1.87
AL Giwa et al 72.97 (72.66, 73.28) 2.08
Kui et al 44.53 (36.20, 52.85) 1.87
Liu et al 66.67 (39.99, 93.34) 0.96
Zhang et al 50.71 (42.43, 59.00) 1.87
Zhang et al 55.56 (23.09, 88.02) 0.77
Qian G et al 40.66 (30.57, 50.75) 1.78
Livingston E et al 59.80 (59.16, 60.44) 2.08
Wang Y et al 40.00 (27.05, 52.95) 1.63
KSID et al 37.77 (36.31, 39.24) 2.07
Su YJ et al 70.00 (41.60, 98.40) 0.90
Dong X et al 53.33 (44.92, 61.75) 1.86
Mizumoto K et al 50.63 (46.74, 54.52) 2.03
Deng L et al 51.52 (34.46, 68.57) 1.41
Zhou F et al 62.30 (55.43, 69.18) 1.93
Wu Y et al 49.49 (43.81, 55.18) 1.97
Gao Q et al 50.70 (43.99, 57.42) 1.94
Chen X et al 49.83 (44.08, 55.57) 1.97
Zhang G et al 48.87 (42.28, 55.46) 1.94
Wu W et al 47.62 (26.26, 68.98) 1.19
Nicholas E et al 47.06 (35.20, 58.92) 1.69
Cao M et al 51.01 (44.05, 57.97) 1.93
Zhao W et al 55.45 (45.75, 65.14) 1.80
Young B et al 50.00 (26.90, 73.10) 1.11
Xiao F et al 56.16 (44.78, 67.55) 1.72
Qi D et al 55.81 (49.85, 61.76) 1.96
Wang Y et al 43.64 (34.37, 52.90) 1.82
Chen X et al 77.08 (65.19, 88.97) 1.69
Cheng J et al 53.10 (50.13, 56.08) 2.05
Wu J et al 48.75 (37.80, 59.70) 1.74
Li K et al 53.01 (42.27, 63.75) 1.75
Li J et al 59.57 (45.54, 73.60) 1.57
Guan W et al 57.96 (55.04, 60.88) 2.05
Tian S et al 48.47 (42.42, 54.52) 1.96
Liu Y et al 54.13 (44.77, 63.48) 1.82
Xu Y et al 58.00 (44.32, 71.68) 1.59
Cao W et al 46.88 (38.23, 55.52) 1.85
Yang X et al 67.31 (54.56, 80.06) 1.64
Liu L et al 62.75 (49.48, 76.01) 1.61
Liu J et al 37.50 (22.50, 52.50) 1.52
Zhang J et al 50.71 (42.43, 59.00) 1.87
Xu X et al 58.06 (45.78, 70.35) 1.67
Huang C et al 73.17 (59.61, 86.73) 1.60
Wang D et al 54.35 (46.04, 62.66) 1.87
Jennifer B et al 50.34 (49.93, 50.74) 2.08
Chaolin et al 73.17 (59.61, 86.73) 1.60
Li et al 56.47 (51.76, 61.18) 2.00
Chen et al 67.68 (58.46, 76.89) 1.83
Chung et al 61.90 (41.13, 82.67) 1.22
Liang et al 57.30 (54.86, 59.73) 2.06
Xiaobo et al 67.31 (54.56, 80.06) 1.64
Overall (I-squared = 99.5%, p = 0.000) 55.00 (51.43, 58.58) 100.00
NOTE: Weights are from random effects analysis
-98.4
0
98.4

Figure 2

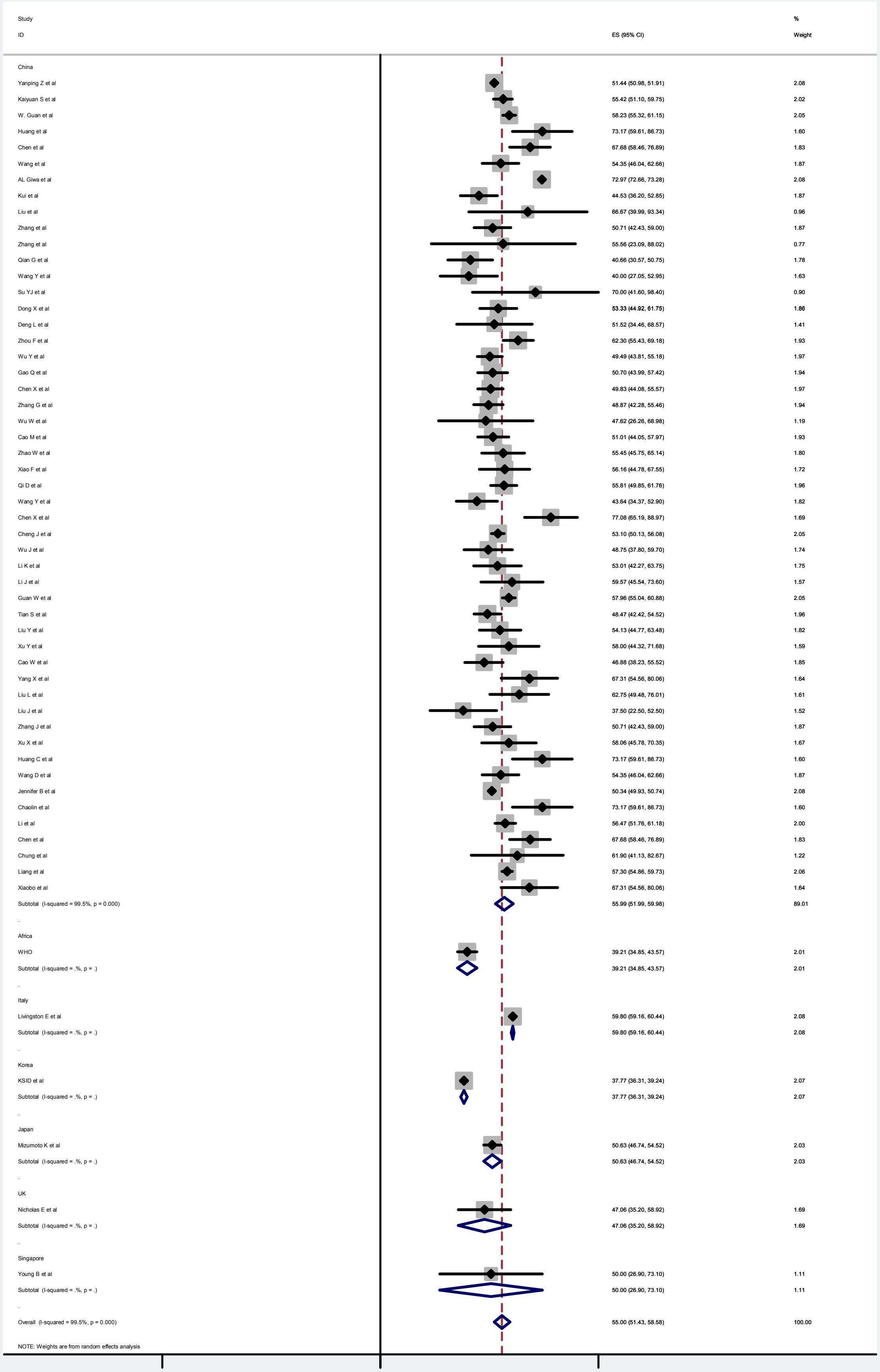
Study ommited	Coef.	[95% Conf.	Interval]
Cheng J et al	20.732838	20.445127	21.020546
Xu X et al	17.418531	17.156216	17.680845
Liu L et al	17.381458	17.119438	17.643478
Yao et al	17.516275	17.25304	17.77951
Wang Yet al	17.346966	17.085199	17.608732
Wu J et al	17.362354	17.100435	17.624273
Xia W et al	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

```
Tests for Publication Bias

Begg's Test

  adj. Kendall's Score (P-Q) =      305
          Std. Dev. of Score =   105.62 (corrected for ties)
           Number of Studies =       46
                           z =     2.89
                    Pr > |z| =    0.004
                           z =     2.88 (continuity corrected)
                    Pr > |z| =    0.004 (continuity corrected)

Egger's test
```

Std_Eff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
slope	16.85592	1.704925	9.89	0.000	13.41986	20.29197
bias	.9970979	1.884806	0.53	0.599	-2.801478	4.795674

Figure 4


Study ID
ES (95% CI)
% Weight
China
Yanping Z et al 51.44 (50.98, 51.91) 2.08
Kaiyuan S et al 55.42 (51.10, 59.75) 2.02
W. Guan et al 58.23 (55.32, 61.15) 2.05
Huang et al 73.17 (59.61, 86.73) 1.60
Chen et al 67.68 (58.46, 76.89) 1.83
Wang et al 54.35 (46.04, 62.66) 1.87
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Wang Y et al 40.00 (27.05, 52.95) 1.63
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Zhou F et al 62.30 (55.43, 69.18) 1.93
Wu Y et al 49.49 (43.81, 55.18) 1.97
Gao Q et al 50.70 (43.99, 57.42) 1.94
Chen X et al 49.83 (44.08, 55.57) 1.97
Zhang G et al 48.87 (42.28, 55.46) 1.94
Wu W et al 47.62 (26.26, 68.98) 1.19
Cao M et al 51.01 (44.05, 57.97) 1.93
Zhao W et al 55.45 (45.75, 65.14) 1.80
Xiao F et al 56.16 (44.78, 67.55) 1.72
Qi D et al 55.81 (49.85, 61.76) 1.96
Wang Y et al 43.64 (34.37, 52.90) 1.82
Chen X et al 77.08 (65.19, 88.97) 1.69
Cheng J et al 53.10 (50.13, 56.08) 2.05
Wu J et al 48.75 (37.80, 59.70) 1.74
Li K et al 53.01 (42.27, 63.75) 1.75
Li J et al 59.57 (45.54, 73.60) 1.57
Guan W et al 57.96 (55.04, 60.88) 2.05
Tian S et al 48.47 (42.42, 54.52) 1.96
Liu Y et al 54.13 (44.77, 63.48) 1.82
Xu Y et al 58.00 (44.32, 71.68) 1.59
Cao W et al 46.88 (38.23, 55.52) 1.85
Yang X et al 67.31 (54.56, 80.06) 1.64
Liu L et al 62.75 (49.48, 76.01) 1.61
Liu J et al 37.50 (22.50, 52.50) 1.52
Zhang J et al 50.71 (42.43, 59.00) 1.87
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Huang C et al 73.17 (59.61, 86.73) 1.60
Wang D et al 54.35 (46.04, 62.66) 1.87
Jennifer B et al 50.34 (49.93, 50.74) 2.08
Chaolin et al 73.17 (59.61, 86.73) 1.60
Li et al 56.47 (51.76, 61.18) 2.00
Chen et al 67.68 (58.46, 76.89) 1.83
Chung et al 61.90 (41.13, 82.67) 1.22
Liang et al 57.30 (54.86, 59.73) 2.06
Xiaobo et al 67.31 (54.56, 80.06) 1.64
Subtotal (I-squared = 99.5%, p = 0.000) 55.99 (51.99, 59.98) 89.01
Africa
WHO 39.21 (34.85, 43.57) 2.01
Subtotal (I-squared = .%, p = .) 39.21 (34.85, 43.57) 2.01
Italy
Livingston E et al 59.80 (59.16, 60.44) 2.08
Subtotal (I-squared = .%, p = .) 59.80 (59.16, 60.44) 2.08
Korea
KSID et al 37.77 (36.31, 39.24) 2.07
Subtotal (I-squared = .%, p = .) 37.77 (36.31, 39.24) 2.07
Japan
Mizumoto K et al 50.63 (46.74, 54.52) 2.03
Subtotal (I-squared = .%, p = .) 50.63 (46.74, 54.52) 2.03
UK
Nicholas E et al 47.06 (35.20, 58.92) 1.69
Subtotal (I-squared = .%, p = .) 47.06 (35.20, 58.92) 1.69
Singapore
Young B et al 50.00 (26.90, 73.10) 1.11
Subtotal (I-squared = .%, p = .) 50.00 (26.90, 73.10) 1.11
Overall (I-squared = 99.5%, p = 0.000) 55.00 (51.43, 58.58) 100.00
NOTE: Weights are from random effects analysis
-98.4
0
98.4

Supplementary Figure 1: Sub group analysis for prevalence of COVID-19 among males

Table S1. Search strategy used for one of the databases

Medline/PubMed			
	Search terms		
Group	***Non-MeSH terms***	**MeSH (sub-terms in MeSH)**	**Citations**
#1	Magnitude Epidemiology proportion	Prevalence	
#2	Female	Male	
#3	Novel coronavirus Novel coronavirus 2019 2019 nCoV Wuhan coronavirus Wuhan pneumonia SARS-CoV-2	COVID-19	
#4		COVID-19 confirmed patients	
#1 AND #2 AND #3 AND #4			

(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 (MeSH term) on PubMed database (Table S1). Thus, the PubMed search combines #1 AND #2 AND #3 AND #4

Table S2: Quality appraisal result of included studies in East Africa, from 2002- 2019. Using Joanna Briggs Institute (JBI) quality appraisal checklist

Author	Quality assessment questions												
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Yes Total	Quality status	Overall appraisal
Cross-sectional studies														
1. Li K et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
2. Liu Y et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
3. Liu Y et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
4. Liu J et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
5. Wu J et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
6. Xu X et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
7. Xu Y et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
8. Yao et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
9. Young et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
10. Zhang J et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
11. Zhang M et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
12. Zhao et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
13. Zhu et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
14. Yanping Z et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
15. W. Guan et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
16. WHO ,2020	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
17. Huang et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
18. Chen et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
19. Wang et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included
20. Kaiyuan S et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
21. AL Giwa et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
22. Qian G et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
23. Livingston E et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
24. Wang Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
25. KSID,2020	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
26. Su YJ et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
27. Jennifer B et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
28. Kui et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
29. Deng L et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
30. Dong X et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
31. Xiaobo et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
32. Zhou F et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
33. Wu Y et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
34. Gao Q et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
35. Chen X et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
36. Zhang G et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
37. Wu W et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
38. Cao M et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
39. Chung et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included

40. Xiao F et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
41. Qi D et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
42. Liang et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included
43. Wang Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
44. Nicholas E et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
45. Mizumoto K et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
46. Chen X et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
47. Cheng J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
48. Li J et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
49. Tian S et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
50. Li et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
51. Liu Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
52. Cao W et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
53. Chaolin et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
54. Yang X et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
55. Liu L et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
56. Huang C et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
57. Wang D et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
58. Cheng J et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
59. Wu J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
60. Li K et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
61. Li J et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
62. Guan W et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
63. Tian S et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
64. Liu Y et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
65. Xu Y et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
66. Cao W et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
67. Yang X et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
68. Liu L et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
69. Zhang J et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included

Key: Y=yes, N=no, UC=unclear, Q=Question

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency	5

PRISMA 2009 Checklist

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Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions ateach stage, ideally with a flow diagram.	6
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	11
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	5
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	5
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	5
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
FUNDING			
Funding	27	N/A	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-040129.R1
Article Type:	Original research
Date Submitted by the Author:	13-Jun-2020
Complete List of Authors:	Abate, Biruk; Woldia University, Nursing; Woldia University, Nursing Kassie, Ayelign; Woldia University, Nursing; Wudu, Mesfin; Woldia University, Nursing; Woldia University, Nursing Aragie, Teshome ; Nursing
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Epidemiology, Global health, Infectious diseases, Nursing
Keywords:	INFECTIOUS DISEASES, Epidemiology < INFECTIOUS DISEASES, IMMUNOLOGY, Epidemiology < TROPICAL MEDICINE, EPIDEMIOLOGY

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

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***Running title*:** Sex difference in coronavirus disease (COVID-19)

Abstract

Objective: To assess the sex difference in the prevalence of coronavirus disease (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 the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number female patients, and the number of male patients. Using STATA 14 for analysis authors pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I^2 statistics. Subgroup and sensitivity analysis was done Publication bias was also checked.

Participants: Studies with COVID-19 confirmed cases were included.

Intervention: sex (male/female) of COVID-19 confirmed cases were considered

Primary and secondary outcome measures: Primary outcomes were prevalence of COVID-19 among males and females.

Result: A total of 57 studies with 221195 participants were used for analysis. The pooled prevalence of COVID-19 among males was found to be 55.00(51.43-56.58; I2=99.5%; p<0.001). The 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 the absence of publication bias in both outcomes.

Conclusions: The prevalence of symptomatic COVID-19 is higher among males than females. The high prevalence of smoking and alcohol consumption has contributed for increased high prevalence of COVID-19 among males. Additional studies regarding discrepancy in severe illness and mortality due to COVID-19 among males and females and factors which determine the exposure, severity and mortality due to COVID-19 is recommended.

Keywords: COVID-19; sex difference; Systematic review; Meta-analysis

Strength and limitations

This systematic review and meta- analysis has several strengths: we used a pre-specified protocol for search strategy and data abstraction and used internationally accepted tools for a critical appraisal system for quality assessment of individual studies. Besides we employed subgroup analysis, publication bias and sensitivity analysis. Nevertheless, this review had some limitations: because of the inclusion of studies which are published in English only, language bias is likely. In addition most included are from China due to lack of literatures from other countries in the world which reported the outcome of interest. However, the data in this review permit to systematically review and analyze the pooled prevalence of COVID-19 among males.

Background

A COVID-19, first identified in Wuhan, China in late 2019, has rapidly evolved 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 now been named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) (7). COVID-19 has now been declared as a Public Health Emergency of International Concern by the WHO on 30th January 2020(8). COVID-19 affects people differently, in terms of infection with the virus SARS-CoV-2 and mortality rates(9, 10).

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

The report in the lancet and Global Health 5050 summarize, sex-disaggregated data are essential for understanding the distributions of risk, infection, and disease in the population, and the extent to which sex and gender affect clinical outcomes (18). Besides, knowing the degree to which outbreaks upsets women and men in different way is an important step for generating effective, equitable policies and interventions. Since the occurrence of COVID-19 infection in Wuhan, China, in December 2019 (19), it has quickly spread across China and numerous other countries(20-24). So far, 2019-nCoV has affected more than 193 countries with 2,733,591 confirmed cases, including 191185 deaths and 751,404 recovery (25). Even though, some previously published papers haven showed the sex variation, those findings are not conclusive due to inconsistency in prevalence of COVID-19 among males and females. Moreover, there is lack of systematic review and meta-analysis which indicated the worldwide clear picture of sex variation on the risk of

COVID-19. Hence, this systematic review and meta-analysis was conducted to assess the pooled prevalence of COVID-19 among males and females.

Review question

The review questions of this systematic review and meta-analysis were:

- Are men more susceptible to getting symptomatic COVID-19?

Methods

Search strategy

This systematic review and meta-analysis identified studies that revealed data on the proportion of sex in COVID-19 confirmed case. We retrieved studies from Google Scholar, PubMed, Scopus, Web of Sciences Cochrane library, research gate, and institutional repositories. The search included keywords that are the combinations of population, condition/outcome, and context. A snowball searching for the references of relevant papers for linked articles was also performed. Those search terms or phrases including were: The search terms used were: "Novel coronavirus," "Novel coronavirus 2019", "2019 nCoV", "COVID-19", "Wuhan coronavirus," "Wuhan pneumonia," and "SARS-CoV-2." Articles published in English language were considered from January 1, 2020. The searches were concluded by March 27, 2020, and four different researchers independently evaluated search results. Using those 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 (Table S1). Thus, the PubMed search combines #1 AND #2 AND #3 AND #4 (Table S1). The searching date was January 2000 to December 2019.

Study selection and screening

The retrieved studies were exported to Endnote version 8 reference managers to remove duplicate studies. Two investigators (BB and AM) independently screened the selected studies using article's title and abstracts before retrieval of full-text papers. We used pre-specified inclusion criteria to further screen the full-text articles. Disagreements were discussed during a consensus meeting or, if necessary, by including the third and fourth researchers (MW and TG) to make the final decision for the selection of studies to be included in the systematic review and meta-analysis.

Inclusion and exclusion criteria

Those studies had reported the proportion of male and/or female among COVID-19 confirmed patients and published in the English language. Studies which didn't report the prevalence of male and/or female among COVID-19 confirmed patients were excluded. Citations without abstract and/or full-text, anonymous reports, editorials, and qualitative studies were excluded from the analysis. The Prevalence of male and female as the proportion of male and/or female among COVID-19 confirmed cases within a specific population and multiply by 100 to be prevalence report in both case.

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 (26). There was a team of four reviewers and the papers were split amongst the team. Each paper was then assessed by two reviewers and any disagreements were discussed with the third and the fourth reviewers. Studies were considered as low risk or good quality when it scored 4 and above (26), whereas the studies scored 3 and below were considered as high risk or poor quality (Table S2).

Data extraction

The authors developed a data extraction form on the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number female patients, and the number of male patients. The data extraction sheet was piloted using 4 papers randomly, and it was adjusted after piloted the template. Two of the authors extracted the data using the extraction form in collaboration. The third and fourth authors checked the correctness of the data independently. Any disagreements between reviewers were resolved through discussions with third and fourth reviewers when required. The mistyping of data was resolved through crosschecking with the included papers. The case definition considered was as follows: confirmed case: detection of SARS-CoV-2 nucleic acid in a clinical specimen; possible case: any person with at least one of the following symptoms: cough, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia; probable case: any person with at least one of the following symptoms : cough, fever, shortness of breath, 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

The authors transformed the data to STATA 14 for analysis after it was extracted in an excel sheet considering prevalence male and female reported. We pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I^2 statistics. In this study, the I^2statistic value of zero indicates true homogeneity, whereas the value 25, 50, and 75% represented low, moderate and high heterogeneity, respectively. Subgroup analysis was done by the 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 the funnel plot and more objectively through Egger's regression test.

Result

Study selection

A total of 2574 studies were identified using electronic searches (through Database searching (n = 2560)) and other sources (n =12)). After duplication removal, a total of 1352 articles remained (1222 duplicated). Finally, 86 studies were screened for full-text review and, 57 articles (n=221195 patients) were selected for the analysis (Fig.1). This citation manager automatically identifies duplicates creates a separate group among imported references, which can be deleted. For those different citation for the same paper we screened and de-duplicated the citations by hand, which were recorded on a Microsoft Excel spreadsheet after assessing if they have the same author, title, publication date, volume, issue, sample size, etc we removed the duplicated one.

Characteristics of included studies

A total of 57 studies included in the systematic review and meta-analysis (1, 10, 13, 14, 24, 27-73). All studies published in 2020 G.C The studies included participants ranging from 9 (74)to 78771 (44) (Table1).

Meta-analysis

Prevalence of COVID-19 among male

All studies (n=57) with a total of 2,21195 patients had reported the sex proportion of COVID-19 (1, 10, 13, 14, 24, 27-73).The prevalence of COVID-19 among male ranges from 37.5 Liu J et al (30) to 77.08 Chen X et al (56) random-effects model analysis from those studies revealed that, the pooled prevalence of COVID-19 confirmed cases is 55.00(51.43-56.58; I^2=99.5%; p<0.001) (Fig.2).

Subgroup analysis of COVID-19 confirmed cases among male

The subgroup analysis was done through stratification by country, providences, 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), 50.00(26.90-73.10) in China, Africa, Italy, Korea, and Singapore respectively (Table 2 and Supplementary Fig 1).

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

Regarding quality score the pooled prevalence of COVID-19 among male in studies which scored greater than or equal to seven was 53.66(95% CI:49.23-58.09) ;I^2 =99.5, P= 0.00, and 56.79(95% CI:52.79-60.990) ;I^2 =94.7, P= 0.00 among studies scored less than seven from JBI quality appraisal checklist(Table 2 and Supplementary Fig 3).

Regarding sample size the pooled prevalence of COVID-19 among male in studies which have sample size greater than or equal to 384 was 53.86(95% CI:47.09-60.63) ;I^2 =99.9, P= 0.00, and 54.96(95% CI:52.35-57.57) ;I^2 =64.5, P= 0.00 among studies scored less than seven from JBI quality appraisal checklist(Table 2 and Supplementary 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-19confirmed cases. The results of 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) Li J ET al and 25.0 (19.87-30.13) Yanping Z ET al after the deletion of a single study (Figure 3).

Publication Bias

We have also checked 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) indicates the absence of publication bias.

Meta-regression

Univariate meta-regression analyses revealed that the prevalence of smoking was found to be high in males . This contributed for high prevalence of COVID-19 among males (P=0.002). Comorbidities like hypertension (0.042), diabetic mellitus (0.012, chronic respiratory disease (0.021), and cardio vascular disease (0.001) were also found to be higher in males and these significantly increases the prevalence of COVID-19. Besides, higher proportion of sever/critical illness (0.003) and death (0.001) were also observed among males (Table 3).

Discussion

This systematic review and meta-analysis were conducted to assess the sex difference in getting COVID -19 diseases. Fifty seven studies were included in the final analysis. The result of this systematic review and meta-analysis revealed that the pooled prevalence of COVID -19 confirmed cases among males and females was found to be 55.00(51.43-56.58; I2=99.5%; p<0.001) and 45.00(41.42-48.57) respectively. This indicates COVID -19 is prevalent in males than females.

This finding was also reported by other studies (75, 76). A study in Ontario, Canada showed that men were more likely to test positive(77, 78). In Pakistan 72% of COVID-19 cases were male(79). According to Global Health 5050 data gathering, the number of COVID-19 confirmed cases and the death rate due to COVID-19 is high among males in different countries (15-17).

This might be due to behavioral factors and roles which increase the risk of acquiring COVID-19 tend to occur more among men. Male are more involved in different risky behaviors like alcohol consumption (80-82), key activities in burial rites; as employees in basic sectors and occupations that continue being active and require them to work outside the home and interact with other people during the containment phase (e.g., food or pharmacy manufacturing and sales, agriculture or food production and distribution, transportation, and security). Because of such behaviors males mostly don't stay at home, sit together, and remove their mask while they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease. In China 50% of men in smoke, but because it is not considered acceptable for women to smoke, only 2% of them do so. Smoking is associated with adverse 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 (83). Besides, smoking is related to higher expression of ACE2 (the receptor for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), which might be the reason for the higher prevalence of COVID-19 in this subgroup of patients than in women (84).

Men tended to develop more symptomatic and serious cases than women, according to the clinical classification of severity. Similar occasions occurred during previous coronavirus epidemics: men had worse outcomes of illness from severe acute respiratory syndrome (SARS), (85)and a higher risk of dying from Middle East respiratory syndrome (MERS)(86). Biological sex variation is said to be one of the reason for the sex discrepancy of COVID-19 cases, severity and mortality(87). Women are in general able to mount a more vigorous immune response to infections and vaccinations(88). Some previous studies on coronaviruses in mice have suggested that the hormone estrogen may have a protective role. Estrogens suppress the escalation phase of the immune response that leads to

188 increased cytokine release(89). The authors showed that female mice treated with an estrogen receptor antagonist died at close to the
189 same rate as the male mice(90).

190 The X chromosome is known to contain the largest number of immune-related genes in the whole genome(86). With their XX
191 chromosome, women have a double copy of key immune genes compared to the single copy in XY men. This boost extends to both
192 the general reaction to infection (the innate response) and also to the more specific response to microbes including antibody formation
193 (adaptive immunity)(86). Thus women's immune systems are generally more responsive to infections. This might mean women are
194 able to tackle the novel coronavirus more effectively but this has not yet been proven.

195 Besides, the above listed behavioral factors like smoking and alcohol consumption tend to occur more among men, those behaviors
196 predisposes males for cardiac and respiratory diseases. This may also explain the overall higher mortality rates among men (84, 91,
197 92). A systematic review and meta-analysis revealed that comorbid disease, such as respiratory system disease, hypertension, and
198 cardiovascular disease as risk a risk factors for death compared with patients without comorbidity(93).

199 Conclusions

200 The prevalence of symptomatic COVID-19 is higher among males than females. This can be explained with prevalent behaviors
201 which increase the risk of acquiring COVID-19 are among males. Males are more involved in different risky behaviors like alcohol
202 consumption (3-5), and occupational exposures because of which males mostly don't stay at home, sit together, remove their mask
203 while they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease; that is why
204 it is more prevalent in male. Smoking and drinking alcohol reduce your overall health and therefore make you more susceptible to
205 symptomatic COVID-19 infection. Although there has been a rapid surge in research in response to the outbreak of COVID-19,
206 additional studies regarding discrepancy in severe illness and mortality due to COVID-19 among males and females and factors which
207 determine the exposure, severity and mortality due to COVID-19 is recommended.

208 Abbreviations

COVID-19: coronavirus disease 2019; WHO: World Health Organization; ICTV: International Committee of Taxonomy of Viruses; SARS-CoV-2: Sever Acute Respiratory Syndrome Coronavirus 2; CI: Confidence Interval; AOR: Adjusted odds ratio; ARTI: Acute Respiratory Tract Infections

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and material

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

We have confirmed that we have no competing interests.

Funding

No funding was obtained for this study

Authors' contributions

BB, AM, MW, and TG: developed the study design and protocol, literature review, selection of studies, quality assessment, data extraction, statistical analysis, interpretation of the data and developing the initial drafts of the manuscript and prepared the final draft of the manuscript. All authors read and approved the final manuscript.

Acknowledgments

We would like to thank the authors of the included primary studies.

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Table Legend

Table 1: Characteristics of included studies for male/female among COVID-19 confirmed cases

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

Table 3: **a meta-regression analysis showing factors which have effect on the sex difference of COVID-19**

410 Table 1

Sr no	Author	Country	Study Period	Sample Size	Male	Female	Quality score	Reference
1.	Li K et al	China	Jan-Feb	83	44	39	6/9	(27)
2.	Liu Y et al	China	Jan11-Jan20	12	8	4	9/9	(28)
3.	Liu Y et al	China	Jan23-Feb8	109	59	50	6/9	(29)
4.	Liu J et al	China	Jan-Feb	40	15	25	8/9	(30)
5.	Wu J et al	China	Jan22-Feb14	80	39	41	8/9	(31)
6.	Xu X et al	China	Jan10-Jan26	62	36	26	8/9	(16)
7.	Xu Y et al	China	Jan-Feb	50	29	21	6/9	(32)
8.	Yao et al	China	Jan01-Feb07	195	115	80	8/9	(33)
9.	Young et al	China	Jan22-Jan31	18	9	9	6/9	(34)
10.	Zhang J et al	China	Jan16-Feb03	140	71	69	8/9	(35)
11.	Zhang M et al	China	Jan18-Feb03	9	5	4	7/9	(36)
12.	Zhao et al	China	Jan16-Feb03	101	56	45	8/9	(37)
13.	Zhu et al	China	Dec01-Feb15	12	8	4	7/9	(38)
14.	Yanping Z et al	China	February 2020	44672	22981	21691	8/9	(39)
15.	W. Guan et al	China	February 2020	1099	640	459	7/9	(40)
16.	WHO ,2020	Africa	March 2020	482	189	177	7/9	(41)
17.	Huang et al	China	Jan, 2020	41	30	11	7/9	(1)
18.	Chen et al	China	December 2020	99	67	32	6/9	(42)
19.	Wang et al	China	March 2020	138	75	63	7/9	(24)
20.	Kaiyuan S et al	China	February, 2020	507	281	201	6/9	(43)
21.	AL Giwa et al	China	March, 2020	78771	57482	21289	9/9	(44)
22.	Qian G et al	China	March, 2020	91	37	54	8/9	(45)
23.	Livingston E et al	Italy	March, 2020	22512	13462	9050	7/9	(46)
24.	Wang Y et al	China	March, 2020	110	48	62	6/9	(47)
25.	KSID,2020	Korea	February, 2020	4212	1591	2621	9/9	(48)
26.	Su YJ et al	China	March, 2020	10	7	3	6/9	(49)
27.	Jennifer B et al	China	March, 2020	59600	30000	29600	8/9	(50)
28.	Kui et al	China	March, 2020	137	61	76	8/9	(51)
29.	Deng L et al	China	March, 2020	33	17	16	8/9	(52)
30.	Dong X et al	China	March, 2020	135	72	63	6/9	(53)
31.	Xiaobo et al	China	March, 2020	52	35	17	8/9	(13)
32.	Zhou F et al	China	March, 2020	191	119	72	6/9	(14)
33.	Wu Y et al	China	March, 2020	297	147	150	8/9	(54)
34.	Gao Q et al	China	January to February ,2020	213	108	105	7/9	(55)
35.	Chen X et al	China	February 2020	291	145	146	8/9	(56)
36.	Zhang G et al	China	December 2019	221	108	113	7/9	(57)
37.	Wu W et al	China	March, 2020	21	10	11	8/9	(58)
38.	Cao M et al	China	February, 2020	128	60	68	7/9	(59)
39.	Chung et al	China	March, 2020	20	13	7	7/9	(60)
40.	Xiao F et al	China	March, 2020	73	41	32	7/9	(61)
41.	Qi D et al	China	January to February ,2020	267	149	118	6/9	(62)
42.	Liang et al	China	China	1590	911	679	7/9	(63)

43.	Wang Y et al	China	February, 2020	55	22	23	6/9	(64)
44.	Nicholas E et al	UK	April 2020	68	32	36	9/9	(65)
45.	Mizumoto K et al	Japan	March, 2020	634	321	313	8/9	(39)
46.	Chen X et al	China	March, 2020	48	37	11	7/9	(66)
47.	Cheng J et al	China	March, 2020	1079	573	505	6/9	(67)
48.	Li J et al	China	March, 2020	47	28	19	9/9	(29)
49.	Tian S et al	China	April 2020	262	127	135	8/9	(68)
50.	Li et al	China	March, 2020	425	240	185	7/9	(69)
51.	Liu Y et al	China	February, 2020	109	59	50	6/9	(1[illegible])
52.	Cao W et al	China	February, 2020	198	101	97	9/9	(70)
53.	Chaolin et al	China	February, 2020	41	30	11	6/9	(71)
54.	Yang X et al	China	February, 2020	52	35	17	8/9	(13)
55.	Liu L et al	China	February, 2020	51	32	19	8/9	(72)
56.	Huang C et al	China	February, 2020	41	30	11	8/9	(1[illegible])
57.	Wang D et al	China	February, 2020	138	75	63	6/9	(73)

Table 2

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

Table 3

Variable	Event	Total	Male	Studies	Male (%)	Female (%)	P value
Smoking	2863	11590	8693	19	75	25	0.002
Comorbidities							
HTN	46546	169694	101410	46	59.7	40.3	0.042
DM	24773	176952	125768	48	71.1	28.9	0.012
Chronic respiratory disease	15883	171707	135902	36	79	21	0.021
Cardio vascular disease	4352	174085	152276	39	81.7	18.3	0.001
Patient condition							
Sever / critical illness	38128	158870	105322	49	66.3	33.7	0.003
Death	699028	158870	125322	46	78.8	21.2	0.001

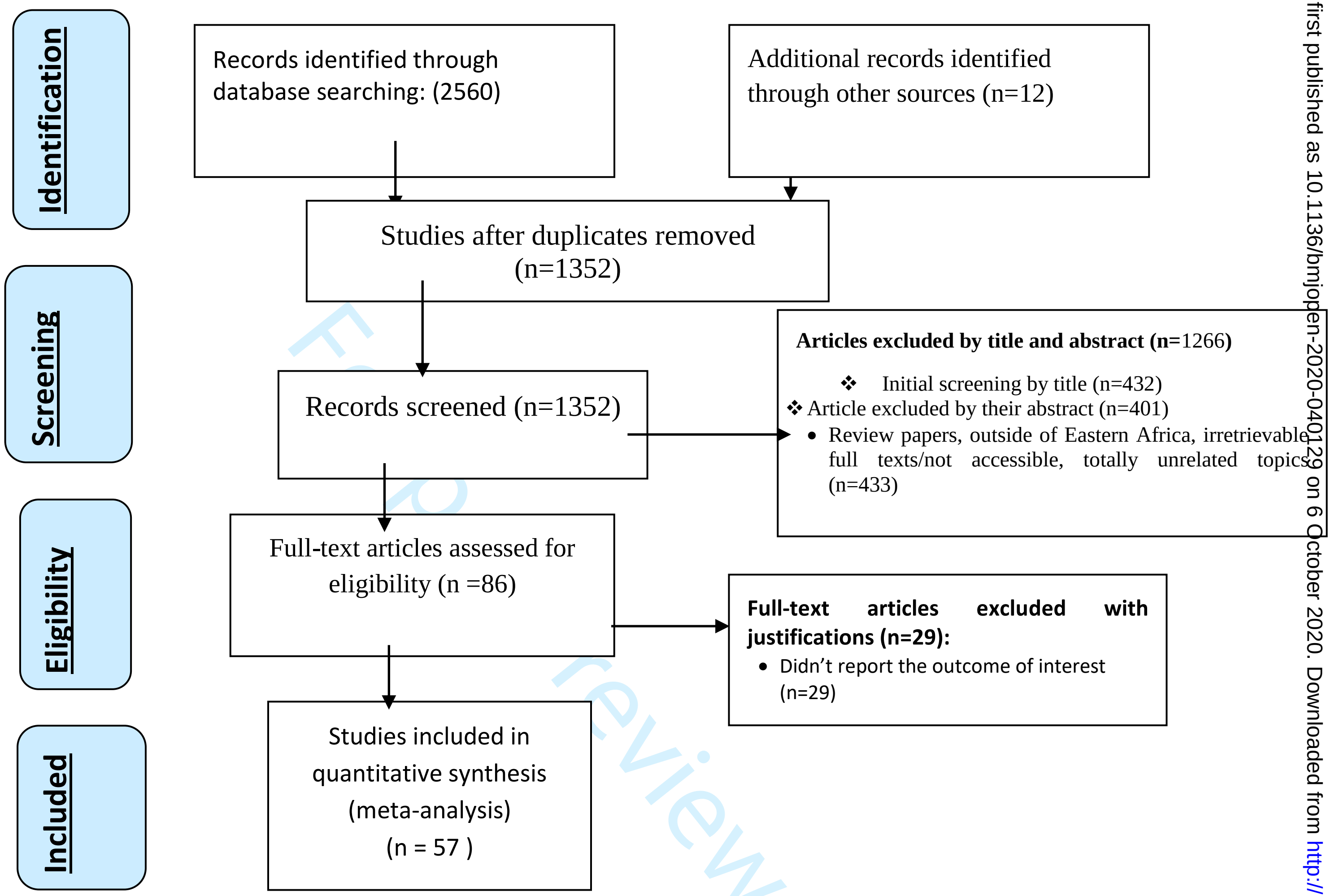


Figure 1: PRISMA flow diagram showed the results of the search and reasons for exclusion

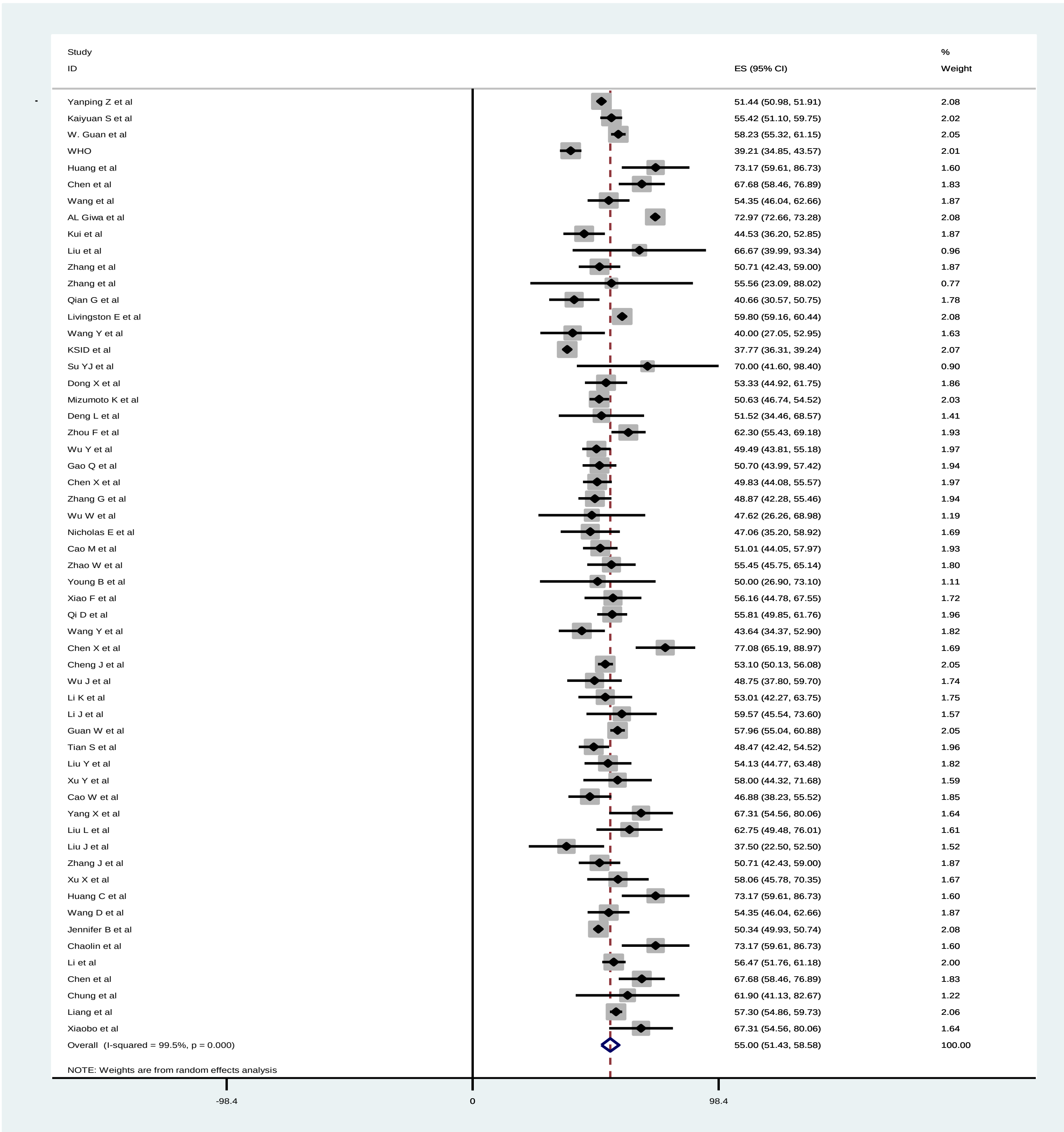
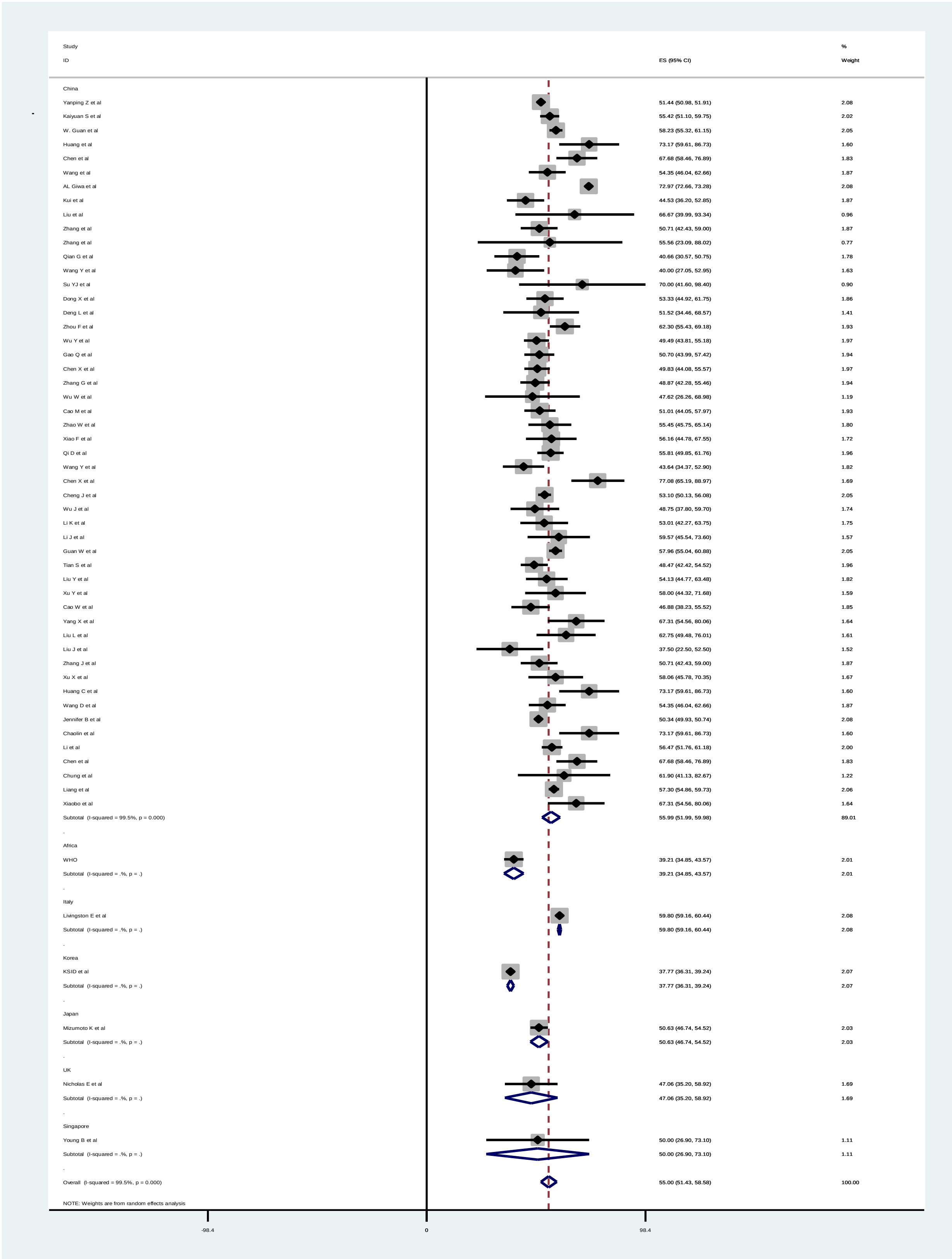


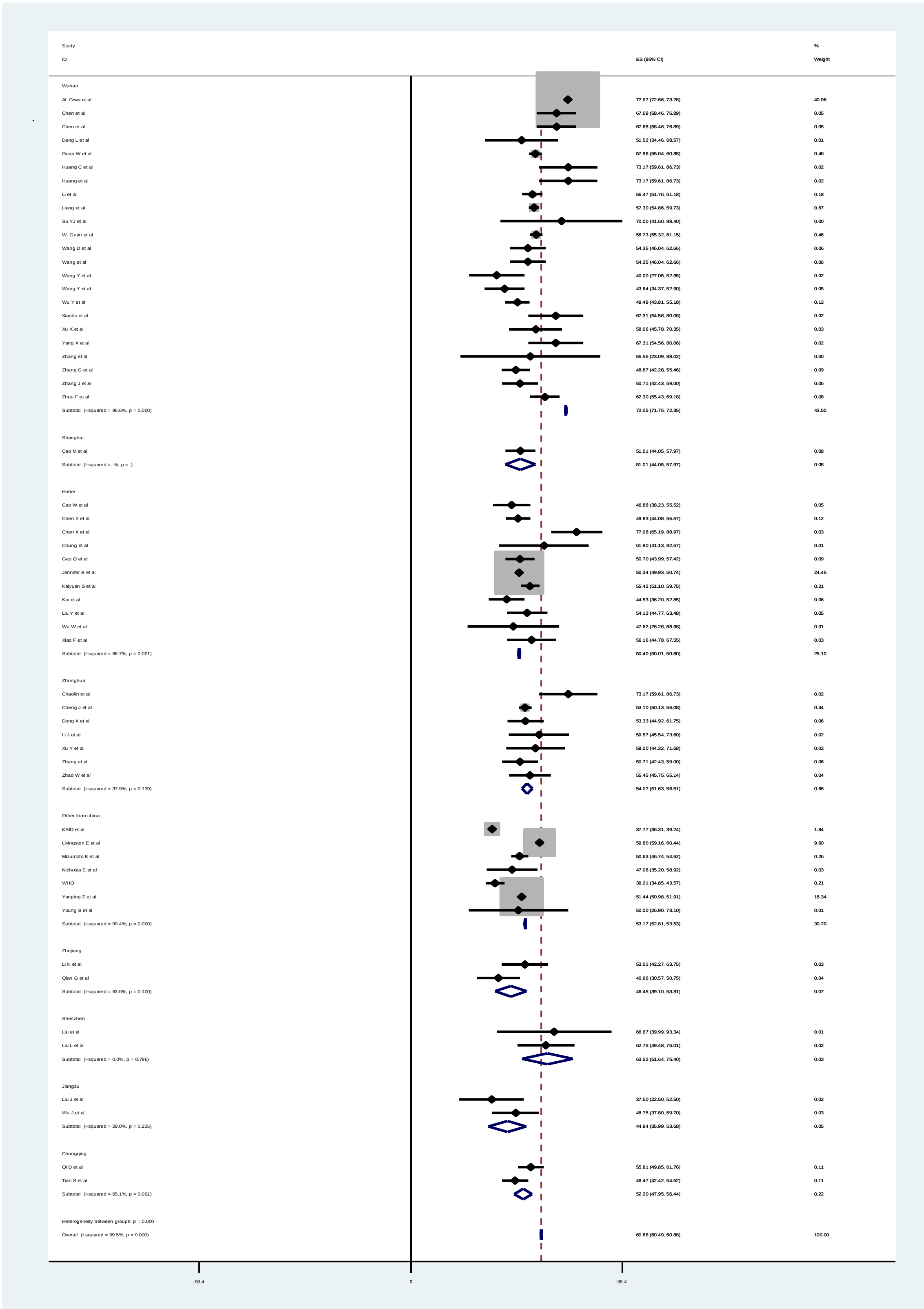
Figure 2: Forest plot showing the pooled prevalence of COVID-19 confirmed cases among male

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

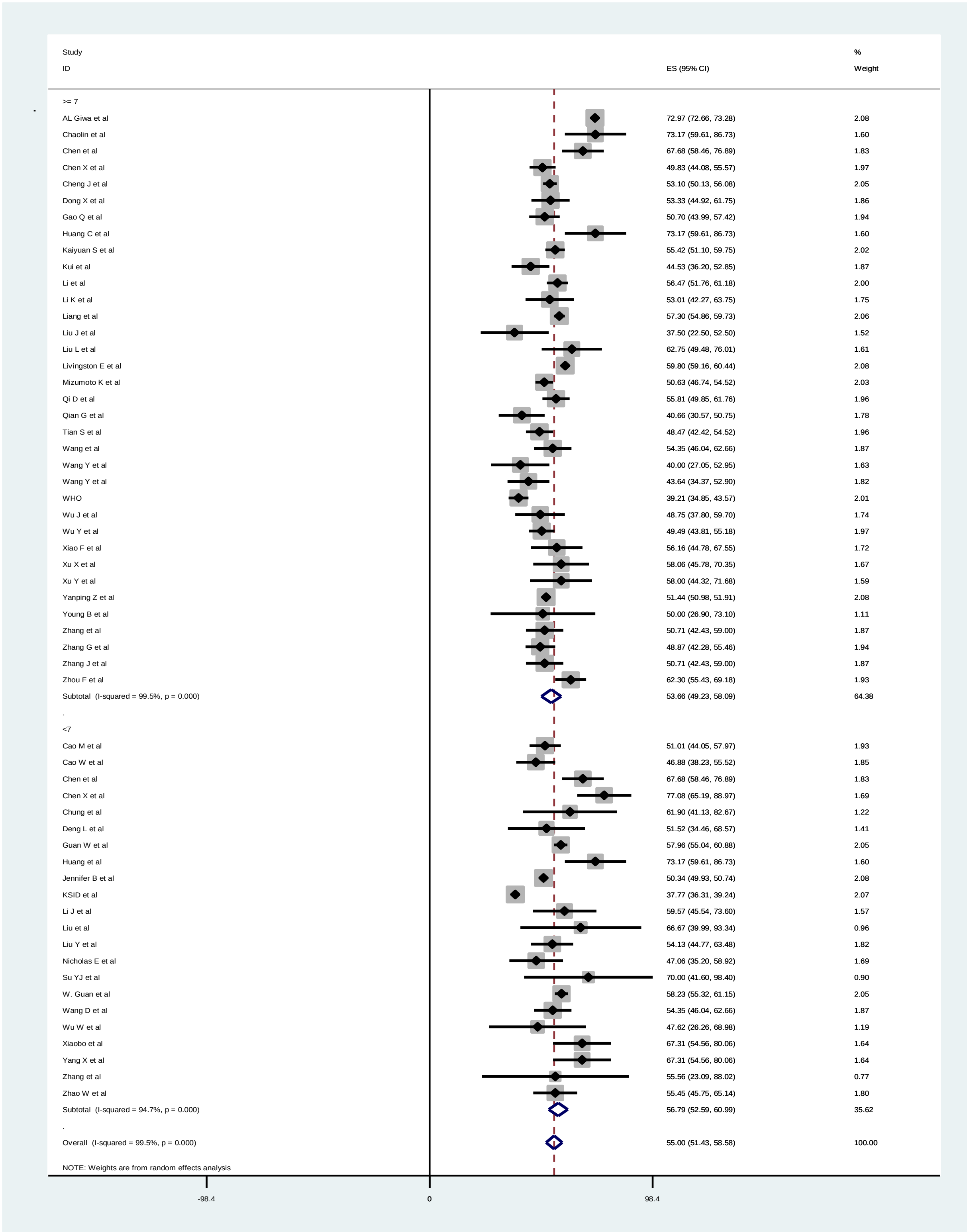
Figure 3: sensitivity analysis for pooled prevalence of COVID-19 confirmed cases among males



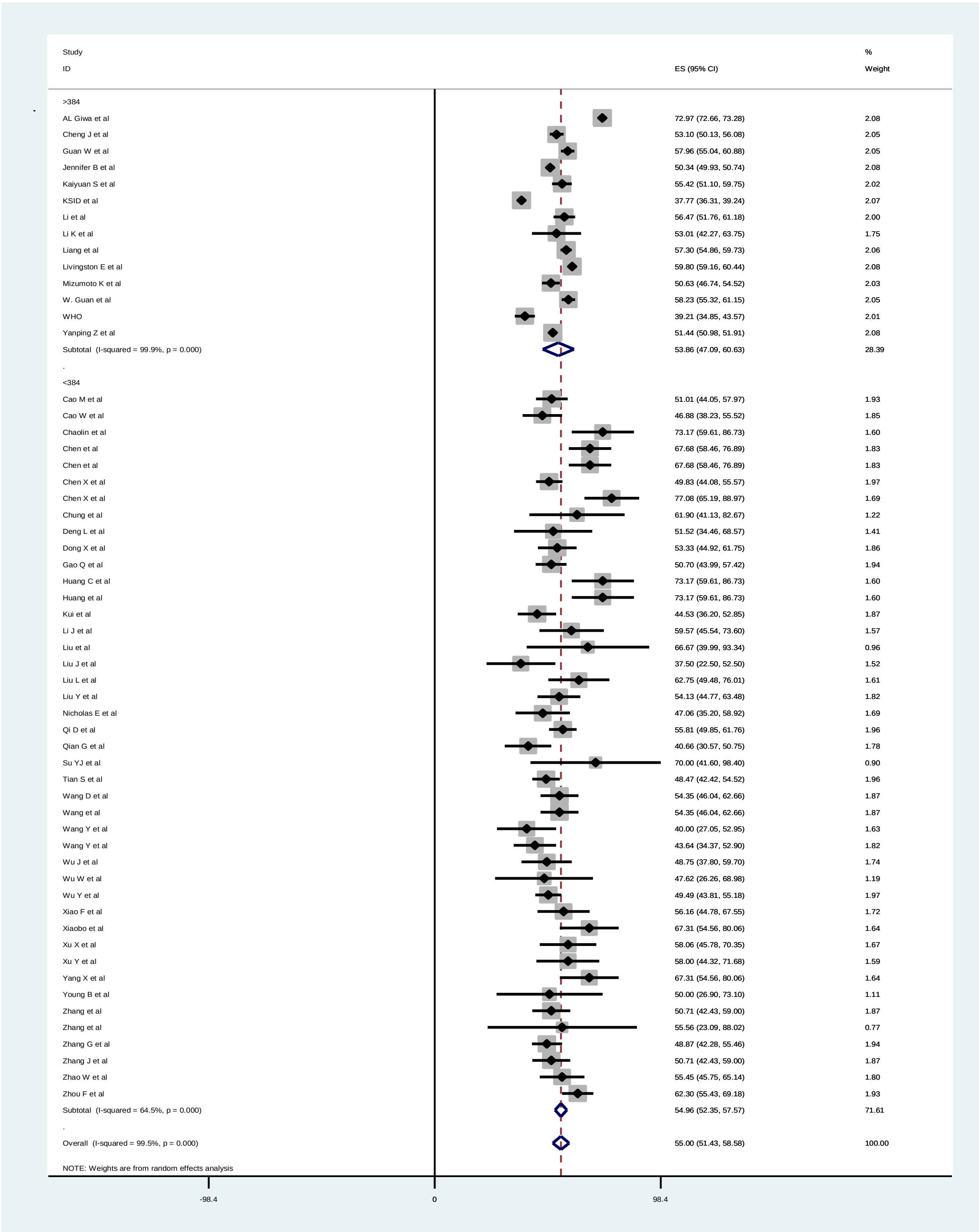
Supplementary Figure 1: Sub group analysis for prevalence of COVID-19 among males by countries



Supplementary Figure 2: Subgroup analysis of the prevalence of COVID-19 by province in china



Supplementary Figure 3: Subgroup analysis of the prevalence of COVID-19 by quality score



Supplementary Figure 4: Subgroup analysis of the prevalence of COVID-19 by sample size

Table S1. Search strategy used for one of the databases

Medline/PubMed			
	Search terms		
Group	***Non-MeSH terms***	**MeSH (sub-terms in MeSH)**	**Citations**
#1	Magnitude Epidemiology proportion	Prevalence	
#2	Female	Male	
#3	Novel coronavirus Novel coronavirus 2019 2019 nCoV Wuhan coronavirus Wuhan pneumonia SARS-CoV-2	COVID-19	
#4		COVID-19 confirmed patients	
#1 AND #2 AND #3 AND #4			

(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 (MeSH term) on PubMed database (Table S1). Thus, the PubMed search combines #1 AND #2 AND #3 AND #4

Table S2: Quality appraisal result of included studies in East Africa, from 2002- 2019. Using Joanna Briggs Institute (JBI) quality appraisal checklist

Author	Quality assessment questions													
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Yes Total	Quality status	Overall appraisal
Cross-sectional studies														
1. Li K et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
2. Liu Y et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
3. Liu Y et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
4. Liu J et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
5. Wu J et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
6. Xu X et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
7. Xu Y et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
8. Yao et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
9. Young et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
10. Zhang J et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
11. Zhang M et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
12. Zhao et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
13. Zhu et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
14. Yanping Z et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
15. W. Guan et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
16. WHO ,2020	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
17. Huang et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
18. Chen et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
19. Wang et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included
20. Kaiyuan S et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
21. AL Giwa et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
22. Qian G et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
23. Livingston E et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
24. Wang Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
25. KSID,2020	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
26. Su YJ et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
27. Jennifer B et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
28. Kui et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
29. Deng L et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
30. Dong X et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
31. Xiaobo et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
32. Zhou F et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
33. Wu Y et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
34. Gao Q et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
35. Chen X et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
36. Zhang G et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
37. Wu W et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
38. Cao M et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
39. Chung et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included

40. Xiao F et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
41. Qi D et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
42. Liang et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included
43. Wang Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
44. Nicholas E et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
45. Mizumoto K et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
46. Chen X et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
47. Cheng J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
48. Li J et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
49. Tian S et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
50. Li et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
51. Liu Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
52. Cao W et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
53. Chaolin et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
54. Yang X et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
55. Liu L et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
56. Huang C et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
57. Wang D et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
58. Cheng J et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
59. Wu J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
60. Li K et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
61. Li J et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
62. Guan W et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
63. Tian S et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
64. Liu Y et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
65. Xu Y et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
66. Cao W et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
67. Yang X et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
68. Liu L et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
69. Zhang J et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included

Key: Y=yes, N=no, UC=unclear, Q=Question

JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data

Criteria	Yes	No	Un clear	Not applicable
1. Was the sample frame appropriate to address the target population?				
2. Were study participants sampled in an appropriate way?				
3. Was the sample size adequate?				
4. Were the study subjects and the setting described in detail?				
5. Was the data analysis conducted with sufficient coverage of the identified sample?				
6. Were valid methods used for the identification of the condition?				
7. Was the condition measured in a standard, reliable way for all participants?				
8. Was there appropriate statistical analysis?				
9. Was the response rate adequate, and if not, was the low response rate managed appropriately?				

BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-040129.R2
Article Type:	Original research
Date Submitted by the Author:	28-Jul-2020
Complete List of Authors:	Abate, Biruk; Woldia University, Nursing; Woldia University, Nursing Kassie, Ayelign; Woldia University, Nursing; Wudu, Mesfin; Woldia University, Nursing; Woldia University, Nursing Aragie, Teshome ; Nursing
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Epidemiology, Global health, Infectious diseases, Nursing
Keywords:	INFECTIOUS DISEASES, Epidemiology < INFECTIOUS DISEASES, IMMUNOLOGY, Epidemiology < TROPICAL MEDICINE, EPIDEMIOLOGY

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

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***Running title*:** Sex difference in coronavirus disease (COVID-19)

Abstract

Objective: To assess the sex difference in the prevalence of coronavirus disease (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 the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number female patients, and the number of male patients. Using STATA 14 for analysis authors pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I^2 statistics. Subgroup and sensitivity analysis was done Publication bias was also checked.

Participants: Studies with COVID-19 confirmed cases were included.

Intervention: sex (male/female) of COVID-19 confirmed cases were considered

Primary and secondary outcome measures: Primary outcomes were prevalence of COVID-19 among males and females.

Result: A total of 57 studies with 221195 participants were used for analysis. The pooled prevalence of COVID-19 among males was found to be 55.00(51.43-56.58; I2=99.5%; p<0.001). The 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 the absence of publication bias in both outcomes.

Conclusions: The prevalence of symptomatic COVID-19 found to be higher among males than females. The high prevalence of smoking and alcohol consumption has contributed for high prevalence of COVID-19 among males. Additional studies regarding discrepancy severity and mortality rate due to COVID-19 among males and females and associated factors is recommended.

Keywords: COVID-19; sex difference; Systematic review; Meta-analysis

Article summary

- A total of 57 studies with 221195 participants were used for the systematic review and meta-analysis.
- The pooled prevalence of COVID-19 among males was found to be 55.00(51.43-56.58; I2=99.5%; p<0.001). The 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 the absence of publication bias in both outcomes.
- The prevalence of symptomatic COVID-19 found to be higher among males than females.
- The high prevalence of smoking and alcohol consumption has contributed for high prevalence of COVID-19 among males.
- Additional studies regarding discrepancy severity and mortality rate due to COVID-19 among males and females and associated factors is recommended.

Strength and limitations

This systematic review and meta- analysis has several strengths: we used a pre-specified protocol for search strategy and data abstraction and used internationally accepted tools for a critical appraisal system for quality assessment of individual studies. Besides we employed subgroup analysis, publication bias and sensitivity analysis. Nevertheless, this review had some limitations: because of the inclusion of studies which are published in English only, language bias is likely. In addition most included are from China due to lack of literatures from other countries in the world which reported the outcome of interest. However, the data in this review permit to systematically review and analyze the pooled prevalence of COVID-19 among males.

Background

A COVID-19, first identified in Wuhan, China in late 2019, has rapidly evolved 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 now been named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) (7). COVID-19 has now been declared as a Public Health Emergency of International Concern by the WHO on 30th January 2020(8). COVID-19 affects people differently, in terms of infection with the virus SARS-CoV-2 and mortality rates(9, 10).

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

The report in the lancet and Global Health 5050 summarize, sex-disaggregated data are essential for understanding the distributions of risk, infection, and disease in the population, and the extent to which sex and gender affect clinical outcomes(18). Besides, knowing the degree to which outbreaks upsets women and men in different way is an important step for generating effective, equitable policies and interventions. Since the occurrence of COVID-19 infection in Wuhan, China, in December 2019 (19), it has quickly spread across China and numerous other countries(20-24). So far, 2019-nCoV has affected more than 193 countries with 2,733,591 confirmed cases, including 191185 deaths and 751,404 recovery (25). Even though, some previously published papers haven showed the sex variation, those findings are not conclusive due to inconsistency in prevalence of COVID-19 among males and females. Moreover, there is lack of systematic review and meta-analysis which indicated the worldwide clear picture of sex variation on the risk of COVID-19. Hence, this systematic review and meta-analysis was conducted to assess the pooled prevalence of COVID-19 among males and females.

Review question

The review questions of this systematic review and meta-analysis were:

- Are men more susceptible to getting symptomatic COVID-19?

Methods

Search strategy

This systematic review and meta-analysis identified studies that revealed data on the proportion of sex in COVID-19 confirmed case. We retrieved studies from Google Scholar, PubMed, Scopus, Web of Sciences Cochrane library, research gate, and institutional repositories. The search included keywords that are the combinations of population, condition/outcome, and context. A snowball searching for the references of relevant papers for linked articles was also performed. Those search terms or phrases including were: The search terms used were: “Novel coronavirus,” “Novel coronavirus 2019”, “2019 nCoV”, “COVID-19”, “Wuhan coronavirus,” “Wuhan pneumonia,” and “SARS-CoV-2.” Articles published in English language were considered from January 1, 2020. The

83 searches were concluded by March 27, 2020, and four different researchers independently evaluated search results. Using those 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 (Table S1). Thus, the PubMed search combines #1 AND #2 AND #3 AND #4 (Table S1). The searching date was January 2000 to December 2019.

Study selection and screening

The retrieved studies were exported to Endnote version 8 reference managers to remove duplicate studies. Two investigators (BB and AM) independently screened the selected studies using article's title and abstracts before retrieval of full-text papers. We used pre-specified inclusion criteria to further screen the full-text articles. Disagreements were discussed during a consensus meeting or, if necessary, by including the third and fourth researchers (MW and TG) to make the final decision for the selection of studies to be included in the systematic review and meta-analysis.

Inclusion and exclusion criteria

Those studies had reported the proportion of male and/or female among COVID-19 confirmed patients and published in the English language. Studies which didn't report the prevalence of male and/or female among COVID-19 confirmed patients were excluded. Citations without abstract and/or full-text, anonymous reports, editorials, and qualitative studies were excluded from the analysis. The Prevalence of male and female as the proportion of male and/or female among COVID-19 confirmed cases within a specific population and multiply by 100 to be prevalence report in both case.

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 (26). There was a team of four reviewers and the papers were split amongst the team. Each paper was then assessed by two reviewers and any disagreements were discussed with the third and the fourth reviewers. Studies were considered as low risk or good quality when it scored 4 and above (26), whereas the studies scored 3 and below were considered as high risk or poor quality (Table S2).

Data extraction

The authors developed a data extraction form on the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number female patients, and the number of male patients. The data extraction sheet was piloted using 4 papers randomly, and it was adjusted after piloted the template. Two of the authors extracted the data using the extraction form in collaboration. The third and fourth authors checked the correctness of the data independently. Any disagreements between reviewers were resolved through discussions with third and fourth reviewers when required. The mistyping of data was resolved through crosschecking with the included papers. The case definition considered was as follows: confirmed case: detection of SARS-CoV-2 nucleic acid in a clinical specimen; possible case: any person with at least one of the following symptoms: cough, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia; probable case: any person with at least one of the following symptoms : cough, fever, shortness of breath, 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

The authors transformed the data to STATA 14 for analysis after it was extracted in an excel sheet considering prevalence male and female reported. We pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I^2 statistics. In this study, the I^2statistic value of zero indicates true homogeneity, whereas the value 25, 50, and 75% represented low, moderate and high heterogeneity, respectively. Subgroup analysis was done by the 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 the funnel plot and more objectively through Egger's regression test.

Result

Study selection

A total of 2574 studies were identified using electronic searches (through Database searching (n = 2560)) and other sources (n =12)). After duplication removal, a total of 1352 articles remained (1222 duplicated). Finally, 86 studies were screened for full-text review and, 57 articles (n=221195 patients) were selected for the analysis (Fig.1). This citation manager automatically identifies duplicates creates a separate group among imported references, which can be deleted. For those different citation for the same paper we screened and de-duplicated the citations by hand, which were recorded on a Microsoft Excel spreadsheet after assessing if they have the same author, title, publication date, volume, issue, sample size, etc we removed the duplicated one.

Characteristics of included studies

A total of 57 studies included in the systematic review and meta-analysis (1, 10, 13, 14, 24, 27-73). All studies published in 2020 G.C The studies included participants ranging from 9 (74)to 78771 (44) (Table1).

Meta-analysis

Prevalence of COVID-19 among male

All studies (n=57) with a total of 2,21195 patients had reported the sex proportion of COVID-19 (1, 10, 13, 14, 24, 27-73).The prevalence of COVID-19 among male ranges from 37.5 Liu J et al (30) to 77.08 Chen X et al (56) random-effects model analysis from those studies revealed that, the pooled prevalence of COVID-19 confirmed cases is 55.00(51.43-56.58; I^2=99.5%; p<0.001) (Fig.2).

Subgroup analysis of COVID-19 confirmed cases among male

The subgroup analysis was done through stratification by country, providences, 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), 50.00(26.90-73.10) in China, Africa, Italy, Korea, and Singapore respectively (Table 2 and Supplementary Fig 1).

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

Regarding quality score the pooled prevalence of COVID-19 among male in studies which scored greater than or equal to seven was 53.66(95% CI:49.23-58.09) ;I^2 =99.5, P= 0.00, and 56.79(95% CI:52.79-60.990) ;I^2 =94.7, P= 0.00 among studies scored less than seven from JBI quality appraisal checklist(Table 2 and Supplementary Fig 3).

Regarding sample size the pooled prevalence of COVID-19 among male in studies which have sample size greater than or equal to 384 was 53.86(95% CI:47.09-60.63) ;I^2 =99.9, P= 0.00, and 54.96(95% CI:52.35-57.57) ;I^2 =64.5, P= 0.00 among studies scored less than seven from JBI quality appraisal checklist(Table 2 and Supplementary 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-19confirmed cases. The results of 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) Li J ET al and 25.0 (19.87-30.13) Yanping Z ET al after the deletion of a single study (Figure 3).

Publication Bias

We have also checked 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) indicates the absence of publication bias.

Meta-regression

Univariate meta-regression analyses revealed that the prevalence of smoking was found to be high in males .This contributed for high prevalence of COVID-19 among males (P=0.002). Comorbidities like hypertension (0.042), diabetic mellitus (0.012, chronic respiratory disease (0.021), and cardio vascular disease (0.001) were also found to be higher in males and these significantly increases the prevalence of COVID-19. Besides, higher proportion of sever/critical illness (0.003) and death (0.001) were also observed among males (Table 3).

Discussion

This systematic review and meta-analysis were conducted to assess the sex difference in getting COVID -19 diseases. Fifty seven studies were included in the final analysis. The result of this systematic review and meta-analysis revealed that the pooled prevalence of COVID -19 confirmed cases among males and females was found to be 55.00(51.43-56.58; I2=99.5%; p<0.001) and 45.00(41.42-48.57) respectively. This indicates COVID -19 is prevalent in males than females.

This finding was also reported by other studies (75, 76). A study in Ontario, Canada showed that men were more likely to test positive(77, 78). In Pakistan 72% of COVID-19 cases were male(79). According to Global Health 5050 data gathering, the number of COVID-19 confirmed cases and the death rate due to COVID-19 is high among males in different countries (15-17).

This might be due to behavioral factors and roles which increase the risk of acquiring COVID-19 tend to occur more among men. Male are more involved in different risky behaviors like alcohol consumption (80-82), key activities in burial rites; as employees in basic sectors and occupations that continue being active and require them to work outside the home and interact with other people during the containment phase (e.g., food or pharmacy manufacturing and sales, agriculture or food production and distribution, transportation, and security). Because of such behaviors males mostly don't stay at home, sit together, and remove their mask while they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease. In China 50% of men in smoke, but because it is not considered acceptable for women to smoke, only 2% of them do so. Smoking is associated with adverse 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 (83). Besides, smoking is related to higher expression of ACE2 (the receptor for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), which might be the reason for the higher prevalence of COVID-19 in this subgroup of patients than in women (84).

Men tended to develop more symptomatic and serious cases than women, according to the clinical classification of severity. Similar occasions occurred during previous coronavirus epidemics: men had worse outcomes of illness from severe acute respiratory syndrome (SARS), (85)and a higher risk of dying from Middle East respiratory syndrome (MERS)(86). Biological sex variation is said to be one of the reason for the sex discrepancy of COVID-19 cases, severity and mortality(87). Women are in general able to mount a more vigorous immune response to infections and vaccinations(88). Some previous studies on coronaviruses in mice have suggested that the hormone estrogen may have a protective role. Estrogens suppress the escalation phase of the immune response that leads to increased cytokine release(89). The authors showed that female mice treated with an estrogen receptor antagonist died at close to the same rate as the male mice(90).

The X chromosome is known to contain the largest number of immune-related genes in the whole genome(86)._With their XX chromosome, women have a double copy of key immune genes compared to the single copy in XY men. This boost extends to both the general reaction to infection (the innate response) and also to the more specific response to microbes including antibody formation (adaptive immunity)(86). 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.

Besides, the above listed behavioral factors like smoking and alcohol consumption tend to occur more among men, those behaviors predisposes males for cardiac and respiratory diseases. This may also explain the overall higher mortality rates among men (84, 91, 92). A systematic review and meta-analysis revealed that comorbid disease, such as respiratory system disease, hypertension, and cardiovascular disease as risk a risk factors for death compared with patients without comorbidity(93).

Conclusions

The prevalence of symptomatic COVID-19 is higher among males than females. This can be explained with prevalent behaviors which increase the risk of acquiring COVID-19 are among males. Males are more involved in different risky behaviors like alcohol consumption (3-5), and occupational exposures because of which males mostly don't stay at home, sit together, remove their mask while they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease; that is why it is more prevalent in male. Smoking and drinking alcohol reduce your overall health and therefore make you more susceptible to symptomatic COVID-19 infection. Although there has been a rapid surge in research in response to the outbreak of COVID-19, additional studies regarding discrepancy in severe illness and mortality due to COVID-19 among males and females and factors which determine the exposure, severity and mortality due to COVID-19 is recommended.

Abbreviations

COVID-19: coronavirus disease 2019; WHO: World Health Organization; ICTV: International Committee of Taxonomy of Viruses; SARS-CoV-2: Sever Acute Respiratory Syndrome Coronavirus 2; CI: Confidence Interval; AOR: Adjusted odds ratio; ARTI: Acute Respiratory Tract Infections

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and material

227 The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

228 **Competing interests**

229 We have confirmed that we have no competing interests.

230 **Funding**

231 No funding was obtained for this study

232

233

234 **Authors' contributions**

235 BB, AM, MW, and TG: developed the study design and protocol, literature review, selection of studies, quality assessment, data
236 extraction, statistical analysis, interpretation of the data and developing the initial drafts of the manuscript and prepared the final draft
237 of the manuscript. All authors read and approved the final manuscript.

238 **Acknowledgments**

239 We would like to thank the authors of the included primary studies.

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Table Legend

Table 1: Characteristics of included studies for male/female among COVID-19 confirmed cases

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

Table 3: **a meta-regression analysis showing factors which have effect on the sex difference of COVID-19**

Table 1

Sr no	Author	Country	Study Period	Sample Size	Male	Female	Quality score	Reference
1.	Li K et al	China	Jan-Feb	83	44	39	6/9	(27)
2.	Liu Y et al	China	Jan11-Jan20	12	8	4	9/9	(28)
3.	Liu Y et al	China	Jan23-Feb8	109	59	50	6/9	(29)
4.	Liu J et al	China	Jan-Feb	40	15	25	8/9	(30)
5.	Wu J et al	China	Jan22-Feb14	80	39	41	8/9	(31)
6.	Xu X et al	China	Jan10-Jan26	62	36	26	8/9	(1[illegible])
7.	Xu Y et al	China	Jan-Feb	50	29	21	6/9	(32)
8.	Yao et al	China	Jan01-Feb07	195	115	80	8/9	(33)
9.	Young et al	China	Jan22-Jan31	18	9	9	6/9	(34)
10.	Zhang J et al	China	Jan16-Feb03	140	71	69	8/9	(35)
11.	Zhang M et al	China	Jan18-Feb03	9	5	4	7/9	(36)
12.	Zhao et al	China	Jan16-Feb03	101	56	45	8/9	(37)
13.	Zhu et al	China	Dec01-Feb15	12	8	4	7/9	(38)
14.	Yanping Z et al	China	February 2020	44672	22981	21691	8/9	(39)
15.	W. Guan et al	China	February 2020	1099	640	459	7/9	(40)
16.	WHO ,2020	Africa	March 2020	482	189	177	7/9	(41)
17.	Huang et al	China	Jan, 2020	41	30	11	7/9	(1)
18.	Chen et al	China	December 2020	99	67	32	6/9	(42)
19.	Wang et al	China	March 2020	138	75	63	7/9	(2[illegible])

20.	Kaiyuan S et al	China	February, 2020	507	281	201	6/9	(43)
21.	AL Giwa et al	China	March, 2020	78771	57482	21289	9/9	(44)
22.	Qian G et al	China	March, 2020	91	37	54	8/9	(45)
23.	Livingston E et al	Italy	March, 2020	22512	13462	9050	7/9	(46)
24.	Wang Y et al	China	March, 2020	110	48	62	6/9	(47)
25.	KSID,2020	Korea	February, 2020	4212	1591	2621	9/9	(48)
26.	Su YJ et al	China	March, 2020	10	7	3	6/9	(49)
27.	Jennifer B et al	China	March, 2020	59600	30000	29600	8/9	(50)
28.	Kui et al	China	March, 2020	137	61	76	8/9	(51)
29.	Deng L et al	China	March, 2020	33	17	16	8/9	(52)
30.	Dong X et al	China	March, 2020	135	72	63	6/9	(53)
31.	Xiaobo et al	China	March, 2020	52	35	17	8/9	(12)
32.	Zhou F et al	China	March, 2020	191	119	72	6/9	(14)
33.	Wu Y et al	China	March, 2020	297	147	150	8/9	(54)
34.	Gao Q et al	China	January to February ,2020	213	108	105	7/9	(55)
35.	Chen X et al	China	February 2020	291	145	146	8/9	(56)
36.	Zhang G et al	China	December 2019	221	108	113	7/9	(57)
37.	Wu W et al	China	March, 2020	21	10	11	8/9	(58)
38.	Cao M et al	China	February, 2020	128	60	68	7/9	(59)
39.	Chung et al	China	March, 2020	20	13	7	7/9	(60)
40.	Xiao F et al	China	March, 2020	73	41	32	7/9	(61)
41.	Qi D et al	China	January to February ,2020	267	149	118	6/9	(62)
42.	Liang et al	China	China	1590	911	679	7/9	(63)
43.	Wang Y et al	China	February, 2020	55	22	23	6/9	(64)
44.	Nicholas E et al	UK	April 2020	68	32	36	9/9	(65)
45.	Mizumoto K et al	Japan	March, 2020	634	321	313	8/9	(39)
46.	Chen X et al	China	March, 2020	48	37	11	7/9	(66)
47.	Cheng J et al	China	March, 2020	1079	573	505	6/9	(67)
48.	Li J et al	China	March, 2020	47	28	19	9/9	(29)
49.	Tian S et al	China	April 2020	262	127	135	8/9	(68)
50.	Li et al	China	March, 2020	425	240	185	7/9	(69)
51.	Liu Y et al	China	February, 2020	109	59	50	6/9	(1)
52.	Cao W et al	China	February, 2020	198	101	97	9/9	(70)
53.	Chaolin et al	China	February, 2020	41	30	11	6/9	(71)
54.	Yang X et al	China	February, 2020	52	35	17	8/9	(13)
55.	Liu L et al	China	February, 2020	51	32	19	8/9	(72)
56.	Huang C et al	China	February, 2020	41	30	11	8/9	(1)
57.	Wang D et al	China	February, 2020	138	75	63	6/9	(73)

Table 2

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

Table 3

Variable	**Event**	**Total**	**Male**	**Studies**	**Male (%)**	**Female (%)**	**P value**
Smoking	2863	11590	8693	19	75	25	0.002
Comorbidities							
HTN	46546	169694	101410	46	59.7	40.3	0.042
DM	24773	176952	125768	48	71.1	28.9	0.012
Chronic respiratory disease	15883	171707	135902	36	79	21	0.021
Cardio vascular disease	4352	174085	152276	39	81.7	18.3	0.001
Patient condition							
Sever / critical illness	38128	158870	105322	49	66.3	33.7	0.003
Death	699028	158870	125322	46	78.8	21.2	0.001

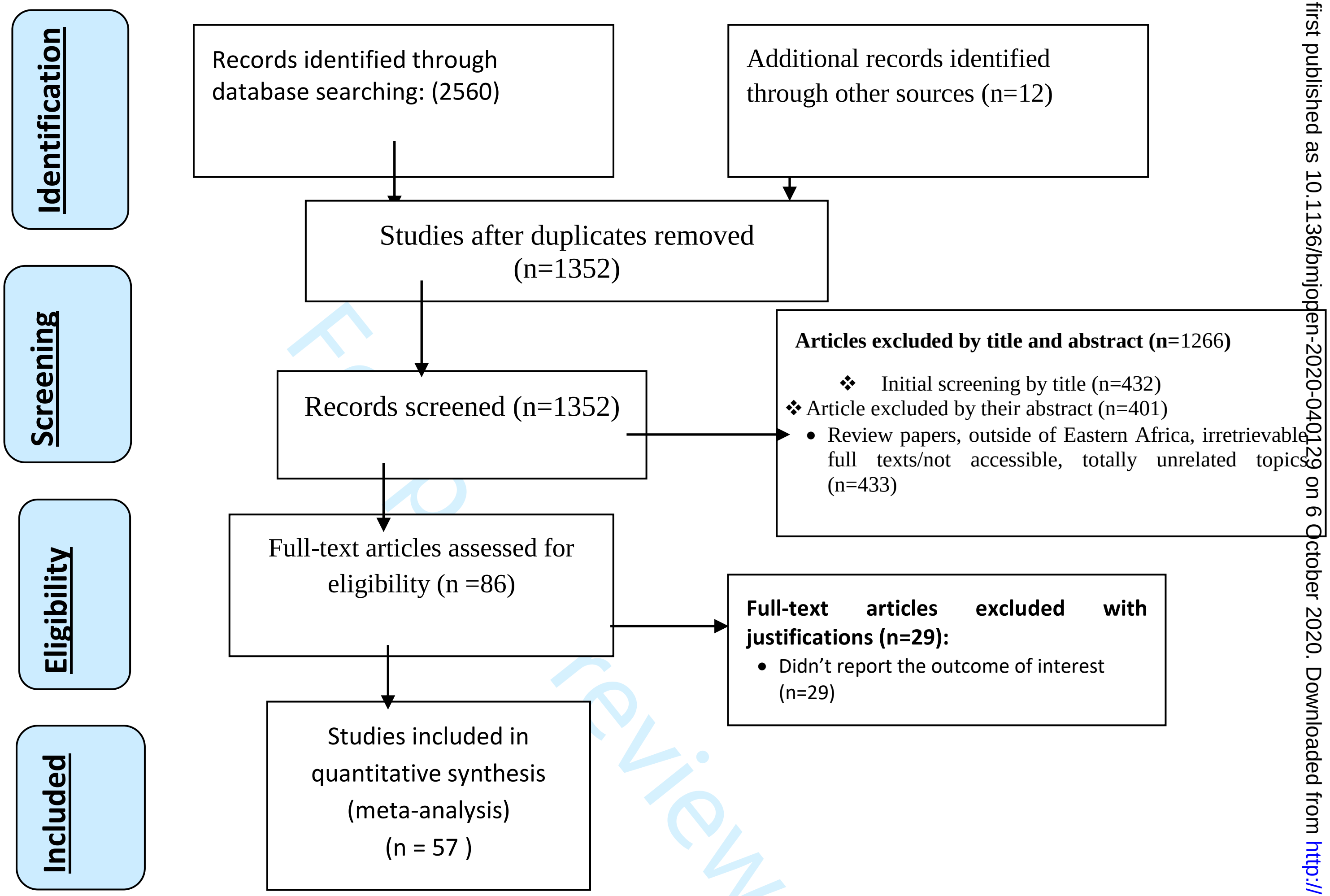


Figure 1: PRISMA flow diagram showed the results of the search and reasons for exclusion

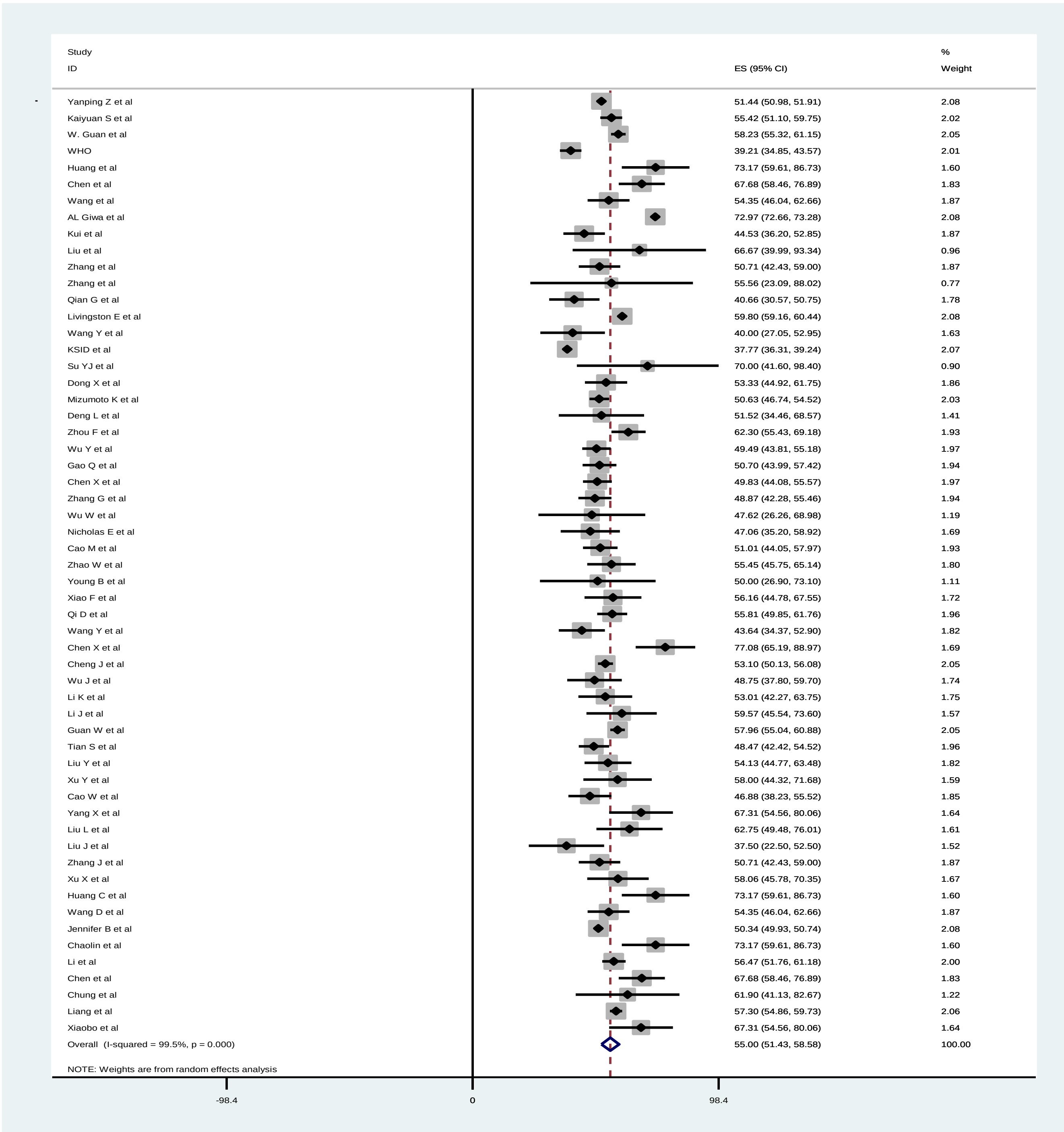
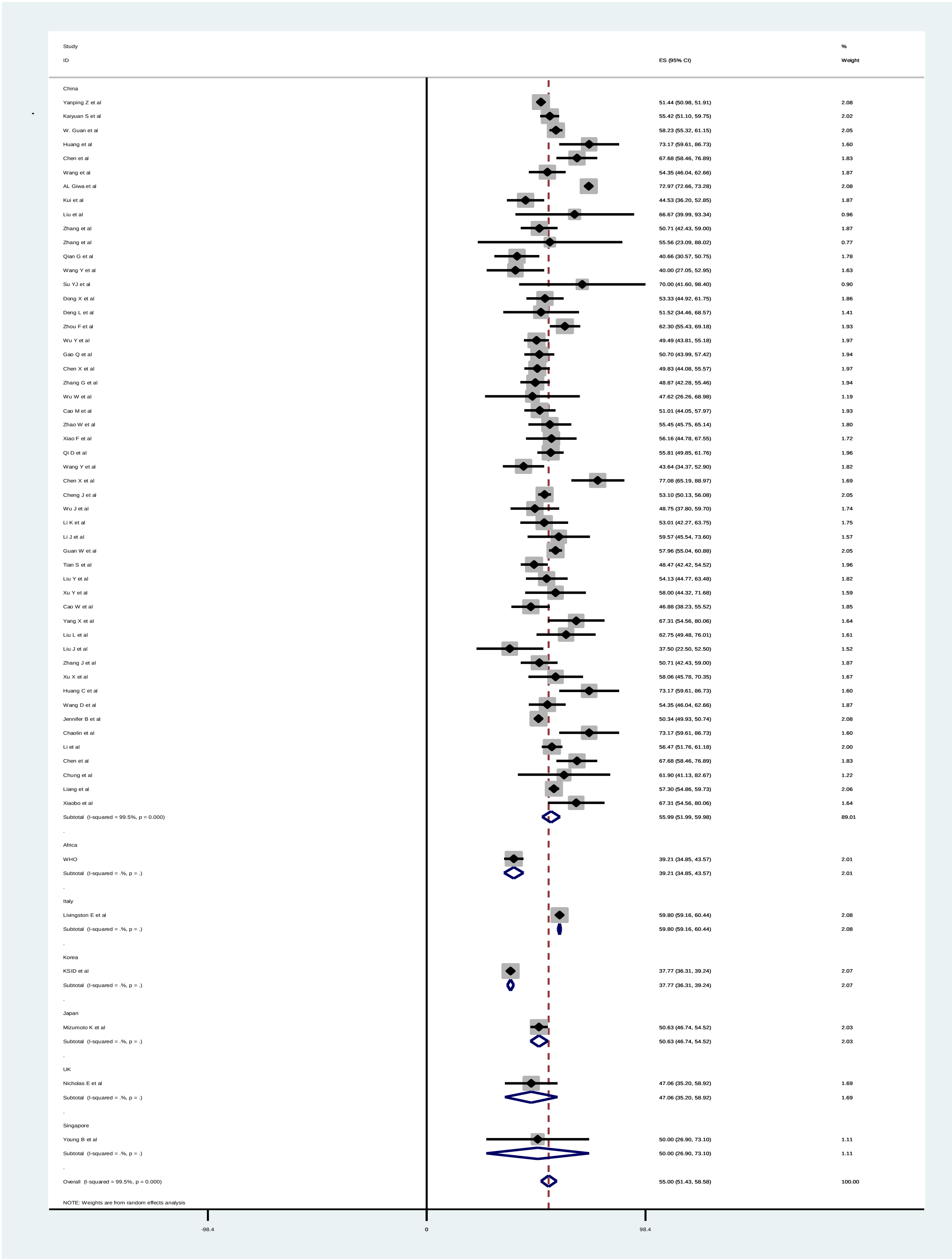


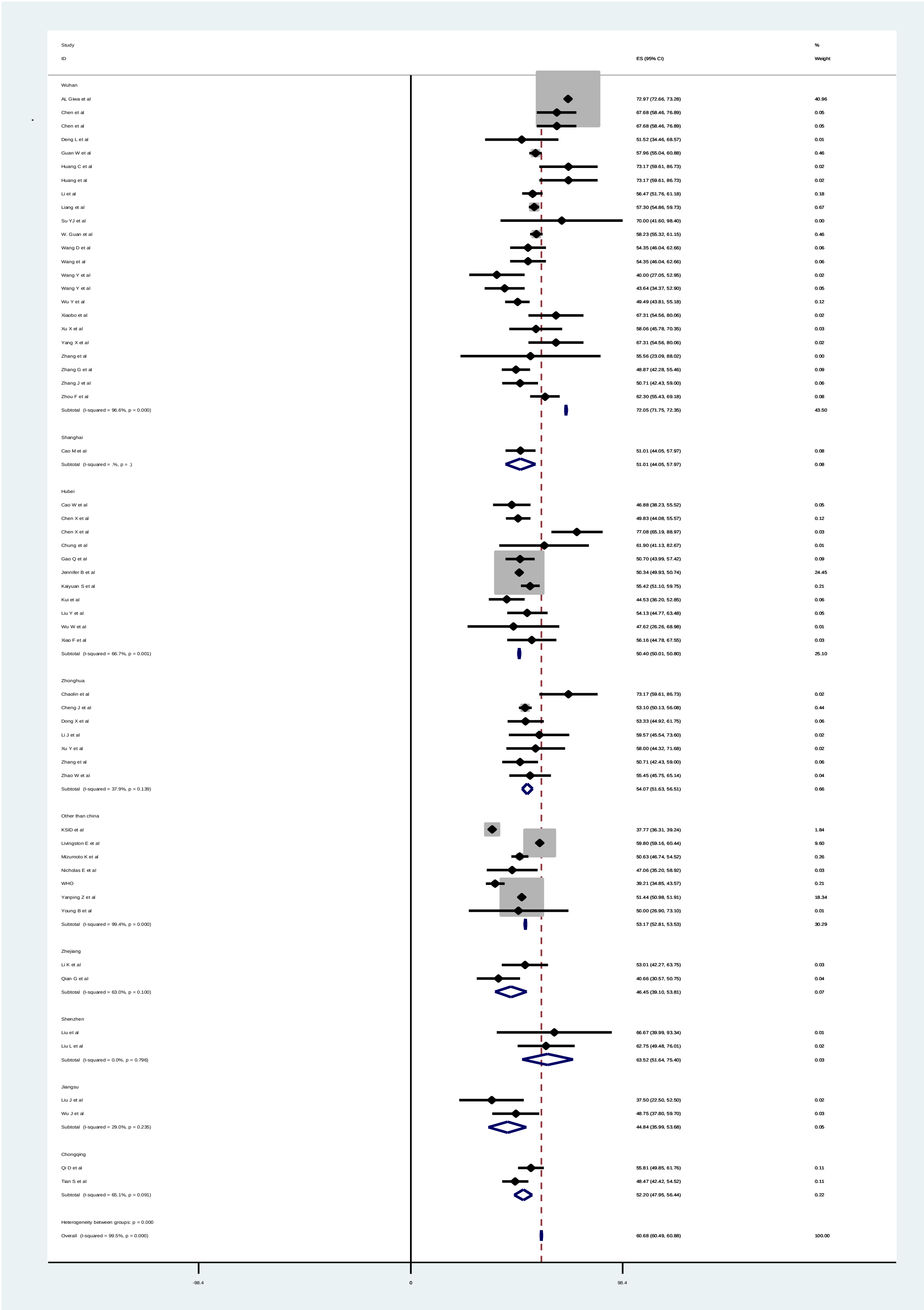
Figure 2: Forest plot showing the pooled prevalence of COVID-19 confirmed cases among male

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

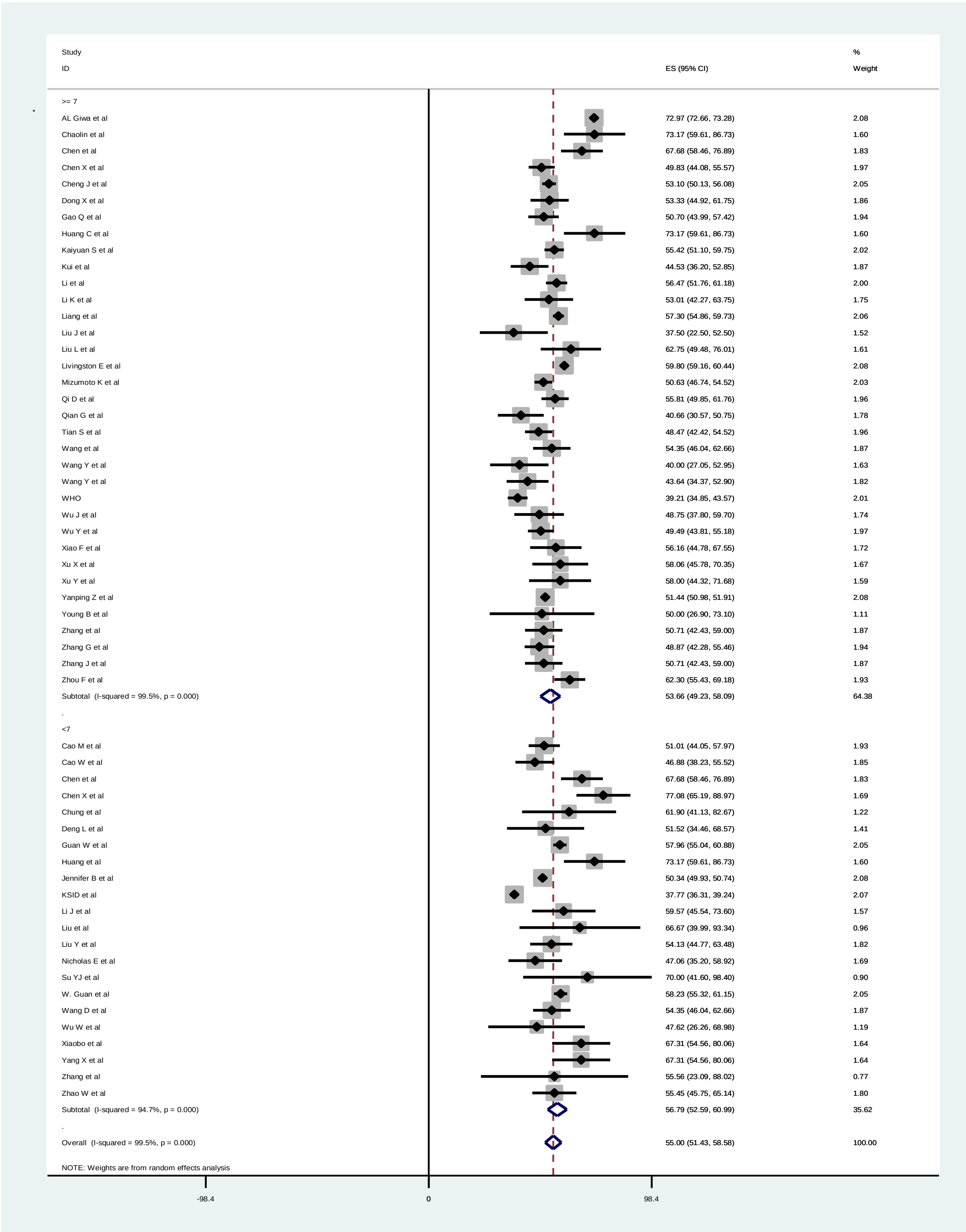
Figure 3: sensitivity analysis for pooled prevalence of COVID-19 confirmed cases among males



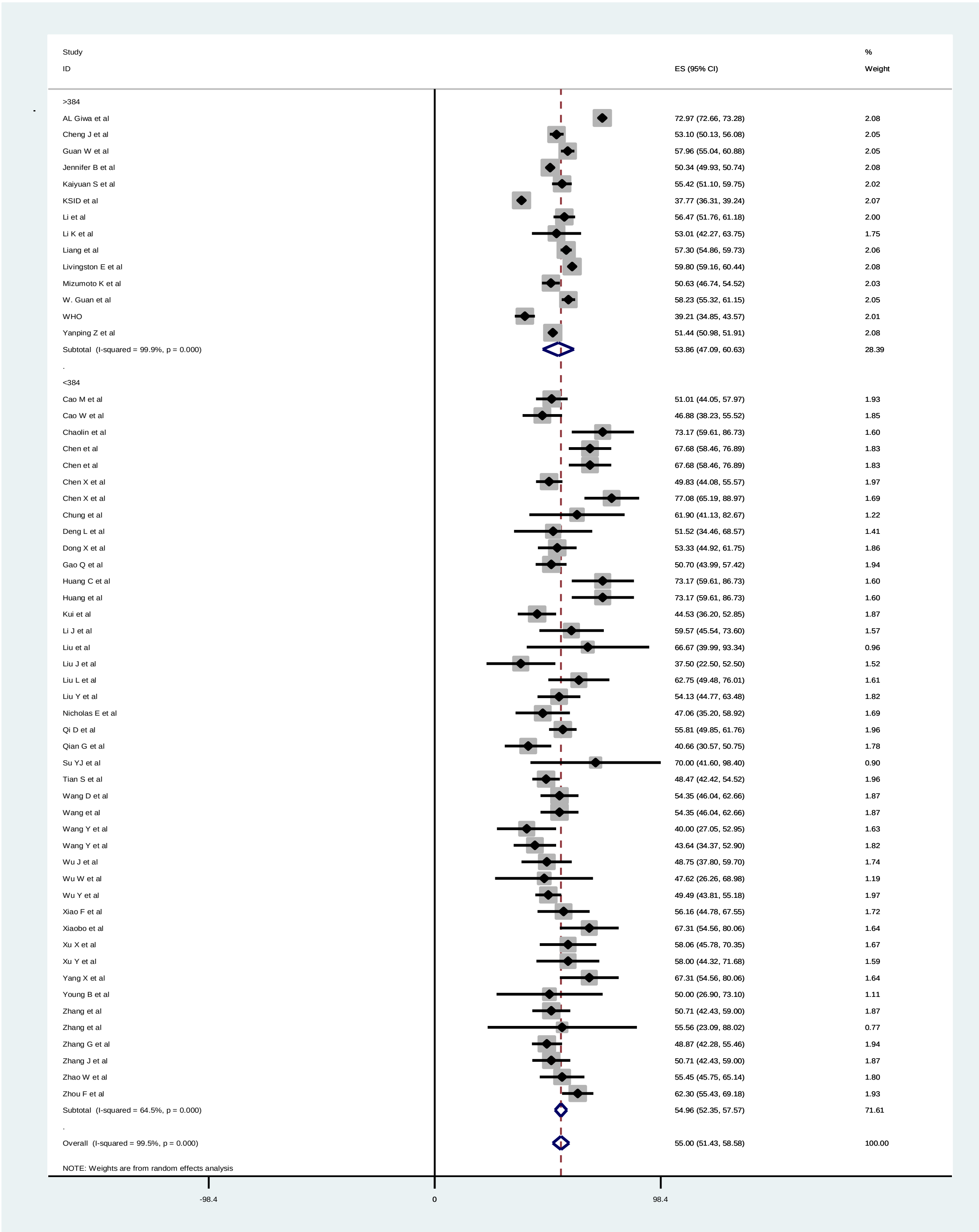
Supplementary Figure 1: Subgroup analysis for prevalence of COVID-19 among males by countries



Supplementary Figure 2: Subgroup analysis of the prevalence of COVID-19 by province in china



Supplementary Figure 3: Subgroup analysis of the prevalence of COVID-19 by quality score



Supplementary Figure 4: Subgroup analysis of the prevalence of COVID-19 by sample size

Table S1. Search strategy used for one of the databases

Medline/PubMed	Search terms		
Group	***Non-MeSH terms***	**MeSH (sub-terms in MeSH)**	**Citations**
#1	Magnitude Epidemiology proportion	Prevalence	
#2	Female	Male	
#3	Novel coronavirus Novel coronavirus 2019 2019 nCoV Wuhan coronavirus Wuhan pneumonia SARS-CoV-2	COVID-19	
#4		COVID-19 confirmed patients	
#1 AND #2 AND #3 AND #4			

(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 (MeSH term) on PubMed database (Table S1). Thus, the PubMed search combines #1 AND #2 AND #3 AND #4

Table S2: Quality appraisal result of included studies in East Africa, from 2002- 2019. Using Joanna Briggs Institute (JBI) quality appraisal checklist

Author	Quality assessment questions										Yes Total	Quality status	Overall appraisal
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11			
Cross-sectional studies													
1. Li K et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
2. Liu Y et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
3. Liu Y et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
4. Liu J et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
5. Wu J et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
6. Xu X et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
7. Xu Y et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
8. Yao et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
9. Young et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
10. Zhang J et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
11. Zhang M et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
12. Zhao et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
13. Zhu et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
14. Yanping Z et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
15. W. Guan et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
16. WHO ,2020	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
17. Huang et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
18. Chen et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
19. Wang et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included
20. Kaiyuan S et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
21. AL Giwa et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
22. Qian G et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
23. Livingston E et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
24. Wang Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
25. KSID,2020	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
26. Su YJ et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
27. Jennifer B et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
28. Kui et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
29. Deng L et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
30. Dong X et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
31. Xiaobo et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
32. Zhou F et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
33. Wu Y et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
34. Gao Q et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
35. Chen X et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
36. Zhang G et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
37. Wu W et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
38. Cao M et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
39. Chung et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included

40. Xiao F et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
41. Qi D et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
42. Liang et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included
43. Wang Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
44. Nicholas E et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
45. Mizumoto K et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
46. Chen X et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
47. Cheng J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
48. Li J et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
49. Tian S et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
50. Li et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
51. Liu Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
52. Cao W et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
53. Chaolin et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
54. Yang X et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
55. Liu L et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
56. Huang C et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
57. Wang D et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
58. Cheng J et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
59. Wu J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
60. Li K et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
61. Li J et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
62. Guan W et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
63. Tian S et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
64. Liu Y et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
65. Xu Y et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
66. Cao W et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
67. Yang X et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
68. Liu L et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
69. Zhang J et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included

Key: Y=yes, N=no, UC=unclear, Q=Question

JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data

Criteria	Yes	No	Un clear	Not applicable
1. Was the sample frame appropriate to address the target population?				
2. Were study participants sampled in an appropriate way?				
3. Was the sample size adequate?				
4. Were the study subjects and the setting described in detail?				
5. Was the data analysis conducted with sufficient coverage of the identified sample?				
6. Were valid methods used for the identification of the condition?				
7. Was the condition measured in a standard, reliable way for all participants?				
8. Was there appropriate statistical analysis?				
9. Was the response rate adequate, and if not, was the low response rate managed appropriately?				

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

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-040129.R3
Article Type:	Original research
Date Submitted by the Author:	10-Aug-2020
Complete List of Authors:	Abate, Biruk; Woldia University, Nursing; Woldia University, Nursing Kassie, Ayelign; Woldia University, Nursing; Wudu, Mesfin; Woldia University, Nursing; Woldia University, Nursing Aragie, Teshome ; Nursing Masresha, Setamlak Adane ; Woldia University, College of Health Sciences, Department of Public Health
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Epidemiology, Global health, Infectious diseases, Nursing
Keywords:	INFECTIOUS DISEASES, Epidemiology < INFECTIOUS DISEASES, IMMUNOLOGY, Epidemiology < TROPICAL MEDICINE, EPIDEMIOLOGY

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

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***Running title*:** Sex difference in coronavirus disease (COVID-19)

Abstract

Objective: To assess the sex difference in the prevalence of coronavirus disease (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 the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number female patients, and the number of male patients. Using STATA 14 for analysis authors pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I^2 statistics. Subgroup and sensitivity analysis was done Publication bias was also checked.

Participants: Studies with COVID-19 confirmed cases were included.

Intervention: sex (male/female) of COVID-19 confirmed cases were considered

Primary and secondary outcome measures: Primary outcomes were prevalence of COVID-19 among males and females.

Result: A total of 57 studies with 221195 participants were used for analysis. The pooled prevalence of COVID-19 among males was found to be 55.00(51.43-56.58; I2=99.5%; p<0.001). The 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 the absence of publication bias in both outcomes.

Conclusions: The prevalence of symptomatic COVID-19 found to be higher among males than females. The high prevalence of smoking and alcohol consumption has contributed for high prevalence of COVID-19 among males. Additional studies regarding discrepancy severity and mortality rate due to COVID-19 among males and females and associated factors is recommended.

Keywords: COVID-19; sex difference; Systematic review; Meta-analysis

Article summary

Strength and limitations

- We used a pre-specified protocol for search strategy and data abstraction and
- We used internationally accepted tools for a critical appraisal system for quality assessment of individual studies.

- Because of the inclusion of studies which are published in English only, language bias is likely.
- In addition most included are from China due to lack of literatures from other countries in the world which reported the outcome of interest.

Background

A COVID-19, first identified in Wuhan, China in late 2019, has rapidly evolved 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 now been named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) (7). COVID-19 has now been declared as a Public Health Emergency of International Concern by the WHO on 30th January 2020(8). COVID-19 affects people differently, in terms of infection with the virus SARS-CoV-2 and mortality rates(9, 10).

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

The report in the lancet and Global Health 5050 summarize, sex-disaggregated data are essential for understanding the distributions of risk, infection, and disease in the population, and the extent to which sex and gender affect clinical outcomes (18). Besides, knowing the degree to which outbreaks upsets women and men in different way is an important step for generating effective, equitable policies and interventions. Since the occurrence of COVID-19 infection in Wuhan, China, in December 2019 (19), it has quickly spread across China and numerous other countries(20-24). So far, 2019-nCoV has affected more than 193 countries with 2,733,591 confirmed cases, including 191185 deaths and 751,404 recovery (25). Even though, some previously published papers haven showed the sex variation, those findings are not conclusive due to inconsistency in prevalence of COVID-19 among males and females. Moreover, there is lack of systematic review and meta-analysis which indicated the worldwide clear picture of sex variation on the risk of COVID-19. Hence, this systematic review and meta-analysis was conducted to assess the pooled prevalence of COVID-19 among males and females.

Review question

The review questions of this systematic review and meta-analysis were:

- Are men more susceptible to getting symptomatic COVID-19?

Methods

Search strategy

This systematic review and meta-analysis identified studies that revealed data on the proportion of sex in COVID-19 confirmed case. We used the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines to search electronic databases it presents as a supplementary file ("PRISMA checklist COVID with SEX.pdf (v1.0). We retrieved studies from Google Scholar, PubMed, Scopus, Web of Sciences Cochrane library, research gate, and institutional repositories as described in detail previously (26, 27). The search included keywords that are the combinations of population, condition/outcome, and context. A snowball searching for the references of relevant papers for linked articles was also performed. Those search terms or phrases including were: The search terms used were: "Novel coronavirus," "Novel coronavirus 2019", "2019 nCoV", "COVID-19", "Wuhan coronavirus," "Wuhan pneumonia," and "SARS-CoV-2." Articles published in English language were considered from January 1, 2020. The searches were concluded by March 27, 2020, and four different researchers independently evaluated search results. Using those 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 (Table S1). Thus, the PubMed search combines #1 AND #2 AND #3 AND #4 (Table S1). The searching date was January 2000 to December 2019.

Study selection and screening

The retrieved studies were exported to Endnote version 8 reference managers to remove duplicate studies as described in detail previously (26, 27). Two investigators (BB and AM) independently screened the selected studies using article's title and abstracts before retrieval of full-text papers. We used pre-specified inclusion criteria to further screen the full-text articles. Disagreements were discussed during a consensus meeting or, if necessary, by including the third and fourth researchers (MW and TG) to make the final decision for the selection of studies to be included in the systematic review and meta-analysis.

Inclusion and exclusion criteria

Those studies had reported the proportion of male and/or female among COVID-19 confirmed patients and published in the English language. Studies which didn't report the prevalence of male and/or female among COVID-19 confirmed patients were excluded. Citations without abstract and/or full-text, anonymous reports, editorials, and qualitative studies were excluded from the analysis. The Prevalence of male and female as the proportion of male and/or female among COVID-19 confirmed cases within a specific population and multiply by 100 to be prevalence report in both case.

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). There was a team of four reviewers and the papers were split amongst the team. Each paper was then assessed by two reviewers and any disagreements were discussed with the third and the fourth reviewers. Studies were considered as low risk or good quality when it scored 4 and above (28), whereas the studies scored 3 and below were considered as high risk or poor quality as described in detail previously (26, 27) (Table S2).

Data extraction

The authors developed a data extraction form on the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number female patients, and the number of male patients as described in detail previously (26, 27). The data extraction sheet was piloted using 4 papers randomly, and it was adjusted after piloted the template as described in detail previously (26, 27). Two of the authors extracted the data using the extraction form in collaboration. The third and fourth authors checked the correctness of the data independently. Any disagreements between reviewers were resolved through discussions with third and fourth reviewers when required as described in detail previously (26, 27). The mistyping of data was resolved through crosschecking with the included papers. The case definition considered was as follows: confirmed case: detection of SARS-CoV-2 nucleic acid in a clinical specimen; possible case: any person with at least one of the following symptoms: cough, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia; probable case: any person with at least one of the following symptoms : cough, fever, shortness of breath, 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

The authors transformed the data to STATA 14 for analysis after it was extracted in an excel sheet considering prevalence male and female reported. We pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I^2 statistics. In this study, the I^2statistic value of zero indicates true homogeneity, whereas the value 25, 50, and 75% represented low, moderate and high heterogeneity, respectively. Subgroup analysis was done by the 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 the funnel plot and more objectively through Egger's regression test.

Result

Study selection

A total of 2574 studies were identified using electronic searches (through Database searching (n = 2560)) and other sources (n =12)). After duplication removal, a total of 1352 articles remained (1222 duplicated). Finally, 86 studies were screened for full-text review and, 57 articles (n=221195 patients) were selected for the analysis (Figure1). This citation manager automatically identifies duplicates creates a separate group among imported references, which can be deleted. For those different citation for the same paper we screened and de-duplicated the citations by hand, which were recorded on a Microsoft Excel spreadsheet after assessing if they have the same author, title, publication date, volume, issue, sample size, etc we removed the duplicated one.

Characteristics of included studies

A total of 57 studies included in the systematic review and meta-analysis (1, 10, 13, 14, 24, 29-75). All studies published in 2020 G.C The studies included participants ranging from 9 (76)to 78771 (46) (Table1).

Meta-analysis

Prevalence of COVID-19 among male

All studies (n=57) with a total of 2,21195 patients had reported the sex proportion of COVID-19 (1, 10, 13, 14, 24, 29-75).The prevalence of COVID-19 among male ranges from 37.5 Liu J et al (32) to 77.08 Chen X et al (58) random-effects model analysis from those studies revealed that, the pooled prevalence of COVID-19 confirmed cases is 55.00(51.43-58.58; I^2=99.5%; p<0.001) (Figure 2).

Subgroup analysis of COVID-19 confirmed cases among male

The subgroup analysis was done through stratification by country, providences, 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), 50.00(26.90-73.10) in China, Africa, Italy, Korea, and Singapore respectively (Table 2 and Supplementary Fig 1).

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

Regarding quality score the pooled prevalence of COVID-19 among male in studies which scored greater than or equal to seven was 53.66(95% CI:49.23-58.09) ;I^2 =99.5, P= 0.00, and 56.79(95% CI:52.79-60.990) ;I^2 =94.7, P= 0.00 among studies scored less than seven from JBI quality appraisal checklist(Table 2 and Supplementary Fig 3).

Regarding sample size the pooled prevalence of COVID-19 among male in studies which have sample size greater than or equal to 384 was 53.86(95% CI:47.09-60.63) ;I^2 =99.9, P= 0.00, and 54.96(95% CI:52.35-57.57) ;I^2 =64.5, P= 0.00 among studies scored less than seven from JBI quality appraisal checklist(Table 2 and Supplementary 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-19confirmed cases. The results of 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) Li J ET al and 25.0 (19.87-30.13) Yanping Z ET al after the deletion of a single study (Figure 3).

Publication Bias

We have also checked 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) indicates the absence of publication bias.

Meta-regression

Univariate meta-regression analyses revealed that the prevalence of smoking was found to be high in males . This contributed for high prevalence of COVID-19 among males (P=0.002). Comorbidities like hypertension (0.042), diabetic mellitus (0.012, chronic respiratory disease (0.021), and cardio vascular disease (0.001) were also found to be higher in males and these significantly increases the prevalence of COVID-19. Besides, higher proportion of sever/critical illness (0.003) and death (0.001) were also observed among males (Table 3).

Discussion

This systematic review and meta-analysis were conducted to assess the sex difference in getting COVID -19 diseases. Fifty seven studies were included in the final analysis. The result of this systematic review and meta-analysis revealed that the pooled prevalence of COVID -19 confirmed cases among males and females was found to be 55.00(51.43-56.58; I2=99.5%; p<0.001) and 45.00(41.42-48.57) respectively. This indicates COVID -19 is prevalent in males than females.

This finding was also reported by 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 gathering, the number of COVID-19 confirmed cases and the death rate due to COVID-19 is high among males in different countries (15-17).

This might be due to behavioral factors and roles which increase the risk of acquiring COVID-19 tend to occur more among men. Male are more involved in different risky behaviors like alcohol consumption (82-84), key activities in burial rites; as employees in basic sectors and occupations that continue being active and require them to work outside the home and interact with other people during the containment phase (e.g., food or pharmacy manufacturing and sales, agriculture or food production and distribution, transportation, and security). Because of such behaviors males mostly don’t stay at home, sit together, and remove their mask while they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease. In China 50% of men in smoke, but because it is not considered acceptable for women to smoke, only 2% of them do so. Smoking is associated with adverse 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). Besides, smoking is related to higher expression of ACE2 (the receptor for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), which might be the reason for the higher prevalence of COVID-19 in this subgroup of patients than in women (86).

Men tended to develop more symptomatic and serious cases than women, according to the clinical classification of severity. Similar occasions occurred during previous coronavirus epidemics: men had worse outcomes of illness from severe acute respiratory syndrome (SARS), (87)and a higher risk of dying from Middle East respiratory syndrome (MERS)(88). Biological sex variation is said to be one of the reason for the sex discrepancy of 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 the hormone estrogen may have a protective role. Estrogens suppress the escalation phase of the immune response that leads to increased cytokine release(91). The authors showed that female mice treated with an estrogen receptor antagonist died at close to the same rate as the 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 to the single copy in XY men. This boost extends to both the general reaction to infection (the innate response) and also 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.

Besides, the above listed behavioral factors like smoking and alcohol consumption tend to occur more among men, those behaviors predisposes males for cardiac and respiratory diseases. This may also explain the overall higher mortality rates among men (86, 93, 94). A systematic review and meta-analysis revealed that comorbid disease, such as respiratory system disease, hypertension, and cardiovascular disease as risk a risk factors for death compared with patients without comorbidity(95).

Conclusions

The prevalence of symptomatic COVID-19 found to be higher among males than females. The high prevalence of smoking and alcohol consumption has contributed for high prevalence of COVID-19 among males (3-5), and occupational exposures because of which males mostly don't stay at home, sit together, remove their mask while they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease; that is why it is more prevalent in male. Smoking and drinking alcohol reduce your overall health and therefore make you more susceptible to symptomatic COVID-19 infection. Although there has been a rapid surge in research in response to the outbreak of COVID-19, additional studies regarding discrepancy in severe illness and mortality due to COVID-19 among males and females and factors which determine the exposure, severity and mortality due to COVID-19 is recommended.

Abbreviations

COVID-19: coronavirus disease 2019; WHO: World Health Organization; ICTV: International Committee of Taxonomy of Viruses; SARS-CoV-2: Sever Acute Respiratory Syndrome Coronavirus 2; CI: Confidence Interval; AOR: Adjusted odds ratio; ARTI: Acute Respiratory Tract Infections

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and material

The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

We have confirmed that we have no competing interests.

Funding

No funding was obtained for this study

Authors' contributions

BB, AM, MW, TG and SA: developed the study design and protocol, literature review, selection of studies, quality assessment, data extraction, statistical analysis, interpretation of the data and developing the initial drafts of the manuscript and prepared the final draft of the manuscript. All authors read and approved the final manuscript.

Acknowledgments

We would like to thank the authors of the included primary studies.

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Figure Legends

Figure1: PRISMA flow diagram showed the results of the search and reasons for exclusion

Figure 2: Forest plot showing the pooled prevalence of COVID-19 confirmed cases among male

Figure 3: Sensitivity analysis for pooled prevalence of COVID-19 confirmed cases among males

Table Legends

Table 1: Characteristics of included studies for male/female among COVID-19 confirmed cases

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

Table 3: **a meta-regression analysis showing factors which have effect on the sex difference of COVID-19**

Table 1

Sr no	Author	Country	Study Period	Sample Size	Male	Female	Quality score	Reference
1.	Li K et al	China	Jan-Feb	83	44	39	6/9	(29)
2.	Liu Y et al	China	Jan11-Jan20	12	8	4	9/9	(30)
3.	Liu Y et al	China	Jan23-Feb8	109	59	50	6/9	(31)
4.	Liu J et al	China	Jan-Feb	40	15	25	8/9	(32)
5.	Wu J et al	China	Jan22-Feb14	80	39	41	8/9	(33)
6.	Xu X et al	China	Jan10-Jan26	62	36	26	8/9	(1[illegible])
7.	Xu Y et al	China	Jan-Feb	50	29	21	6/9	(34)
8.	Yao et al	China	Jan01-Feb07	195	115	80	8/9	(35)
9.	Young et al	China	Jan22-Jan31	18	9	9	6/9	(36)
10.	Zhang J et al	China	Jan16-Feb03	140	71	69	8/9	(37)
11.	Zhang M et al	China	Jan18-Feb03	9	5	4	7/9	(38)
12.	Zhao et al	China	Jan16-Feb03	101	56	45	8/9	(39)
13.	Zhu et al	China	Dec01-Feb15	12	8	4	7/9	(40)
14.	Yanping Z et al	China	February 2020	44672	22981	21691	8/9	(41)
15.	W. Guan et al	China	February 2020	1099	640	459	7/9	(42)
16.	WHO ,2020	Africa	March 2020	482	189	177	7/9	(43)
17.	Huang et al	China	Jan, 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 S et al	China	February, 2020	507	281	201	6/9	(45)
21.	AL Giwa et al	China	March, 2020	78771	57482	21289	9/9	(46)
22.	Qian G et al	China	March, 2020	91	37	54	8/9	(47)
23.	Livingston E et al	Italy	March, 2020	22512	13462	9050	7/9	(48)
24.	Wang Y et al	China	March, 2020	110	48	62	6/9	(49)
25.	KSID,2020	Korea	February, 2020	4212	1591	2621	9/9	(50)
26.	Su YJ et al	China	March, 2020	10	7	3	6/9	(51)
27.	Jennifer B et al	China	March, 2020	59600	30000	29600	8/9	(52)
28.	Kui et al	China	March, 2020	137	61	76	8/9	(53)
29.	Deng L et al	China	March, 2020	33	17	16	8/9	(54)
30.	Dong X 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 F et al	China	March, 2020	191	119	72	6/9	(14)
33.	Wu Y et al	China	March, 2020	297	147	150	8/9	(56)
34.	Gao Q et al	China	January to February ,2020	213	108	105	7/9	(57)
35.	Chen X et al	China	February 2020	291	145	146	8/9	(58)
36.	Zhang G et al	China	December 2019	221	108	113	7/9	(59)
37.	Wu W et al	China	March, 2020	21	10	11	8/9	(60)
38.	Cao M 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 F et al	China	March, 2020	73	41	32	7/9	(63)
41.	Qi D et al	China	January to February ,2020	267	149	118	6/9	(64)
42.	Liang et al	China	China	1590	911	679	7/9	(65)
43.	Wang Y et al	China	February, 2020	55	22	23	6/9	(66)
44.	Nicholas E et al	UK	April 2020	68	32	36	9/9	(67)
45.	Mizumoto K et al	Japan	March, 2020	634	321	313	8/9	(4
46.	Chen X et al	China	March, 2020	48	37	11	7/9	(68)
47.	Cheng J et al	China	March, 2020	1079	573	505	6/9	(69)
48.	Li J et al	China	March, 2020	47	28	19	9/9	(3
49.	Tian S 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 Y et al	China	February, 2020	109	59	50	6/9	(1)
52.	Cao W et al	China	February, 2020	198	101	97	9/9	(72)
53.	Chaolin et al	China	February, 2020	41	30	11	6/9	(73)
54.	Yang X et al	China	February, 2020	52	35	17	8/9	(1
55.	Liu L et al	China	February, 2020	51	32	19	8/9	(74)
56.	Huang C et al	China	February, 2020	41	30	11	8/9	(1)
57.	Wang D et al	China	February, 2020	138	75	63	6/9	(75)

Table 2

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

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Variable	Event	Total	Male	Studies	Male (%)	Female (%)	P value
Smoking	2863	11590	8693	19	75	25	0.002
Comorbidities							
HTN	46546	169694	101410	46	59.7	40.3	0.042
DM	24773	176952	125768	48	71.1	28.9	0.012
Chronic respiratory disease	15883	171707	135902	36	79	21	0.021
Cardio vascular disease	4352	174085	152276	39	81.7	18.3	0.001
Patient condition							
Sever / critical illness	38128	158870	105322	49	66.3	33.7	0.003
Death	699028	158870	125322	46	78.8	21.2	0.001

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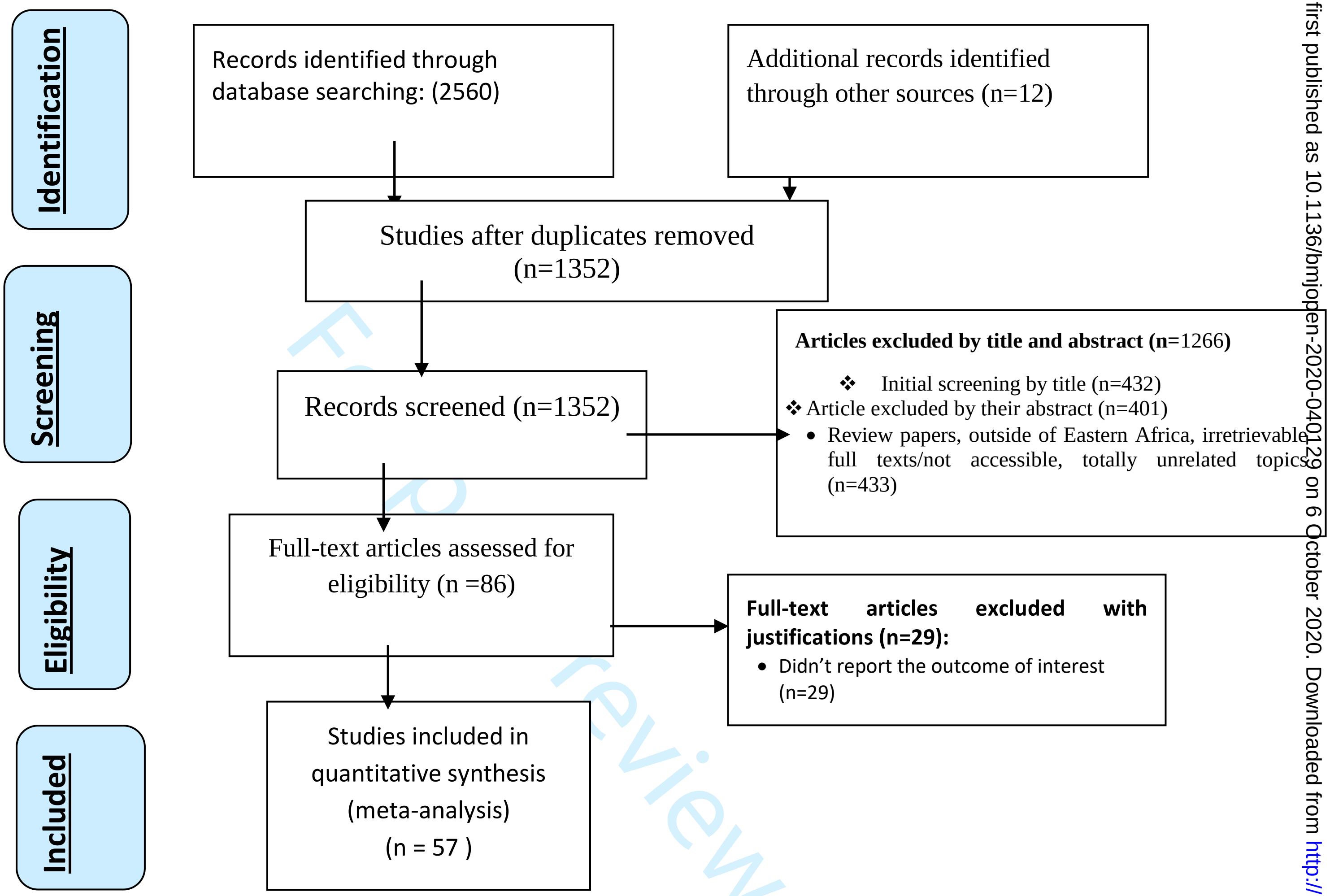


Figure 1: PRISMA flow diagram showed the results of the search and reasons for exclusion

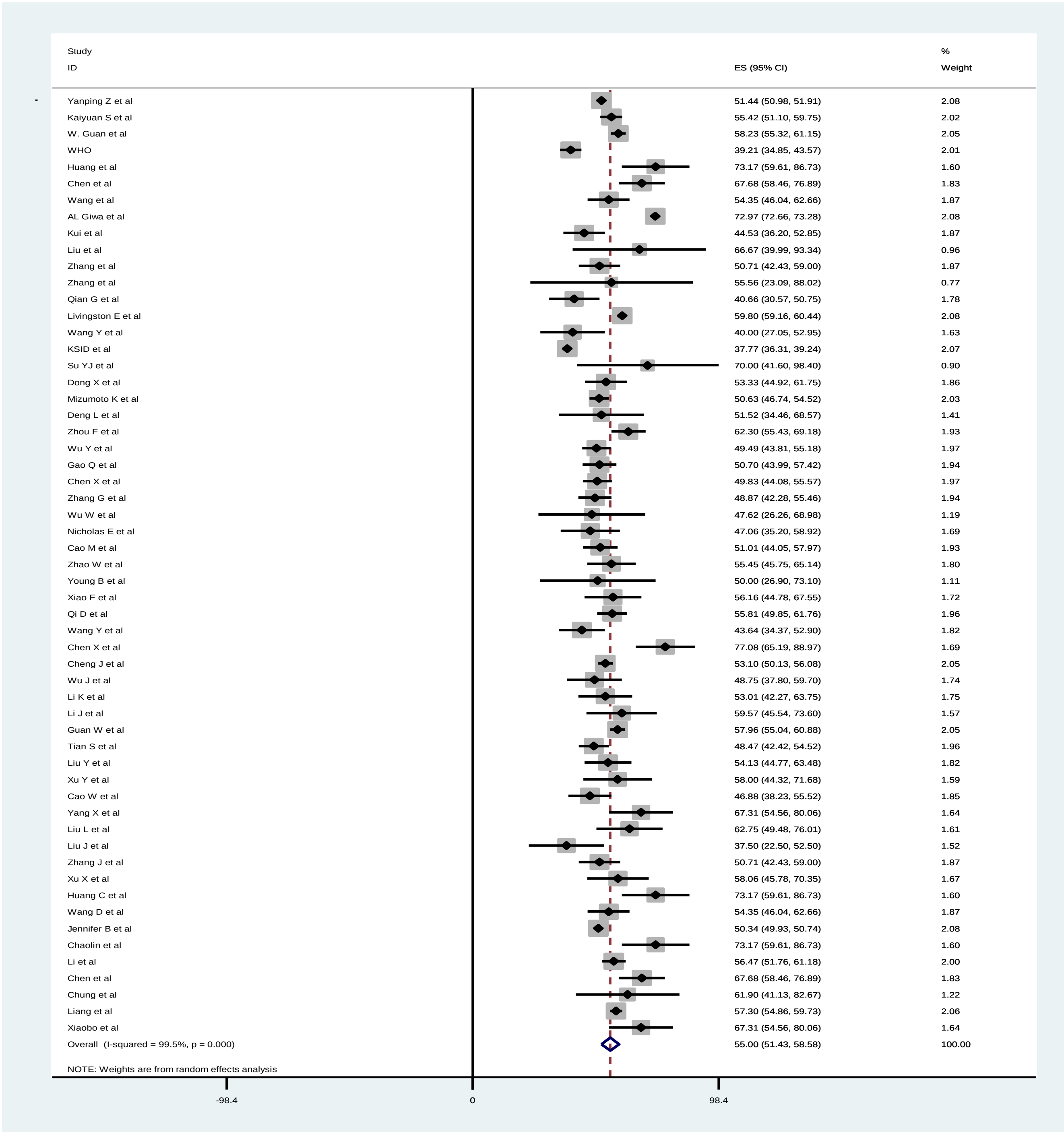
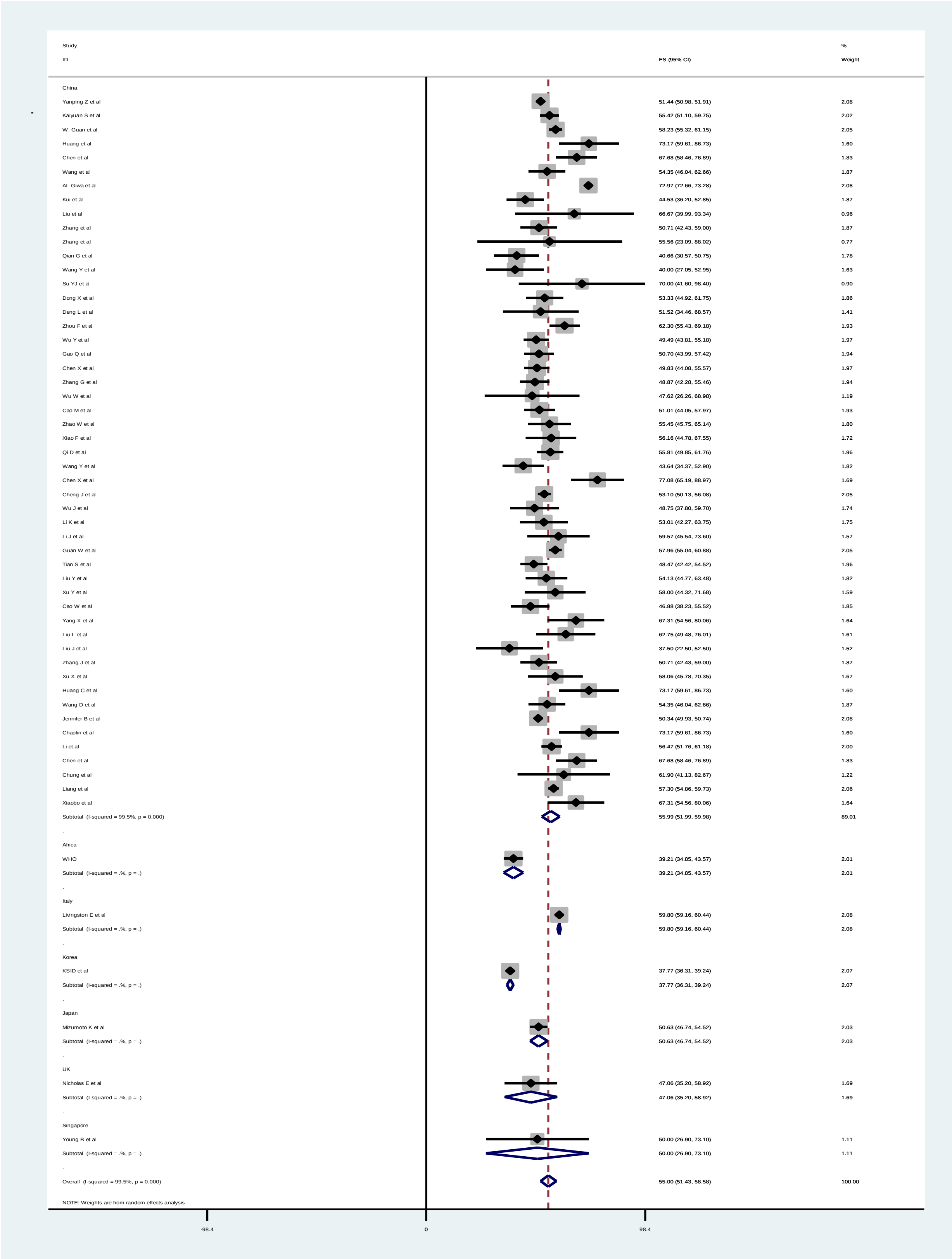


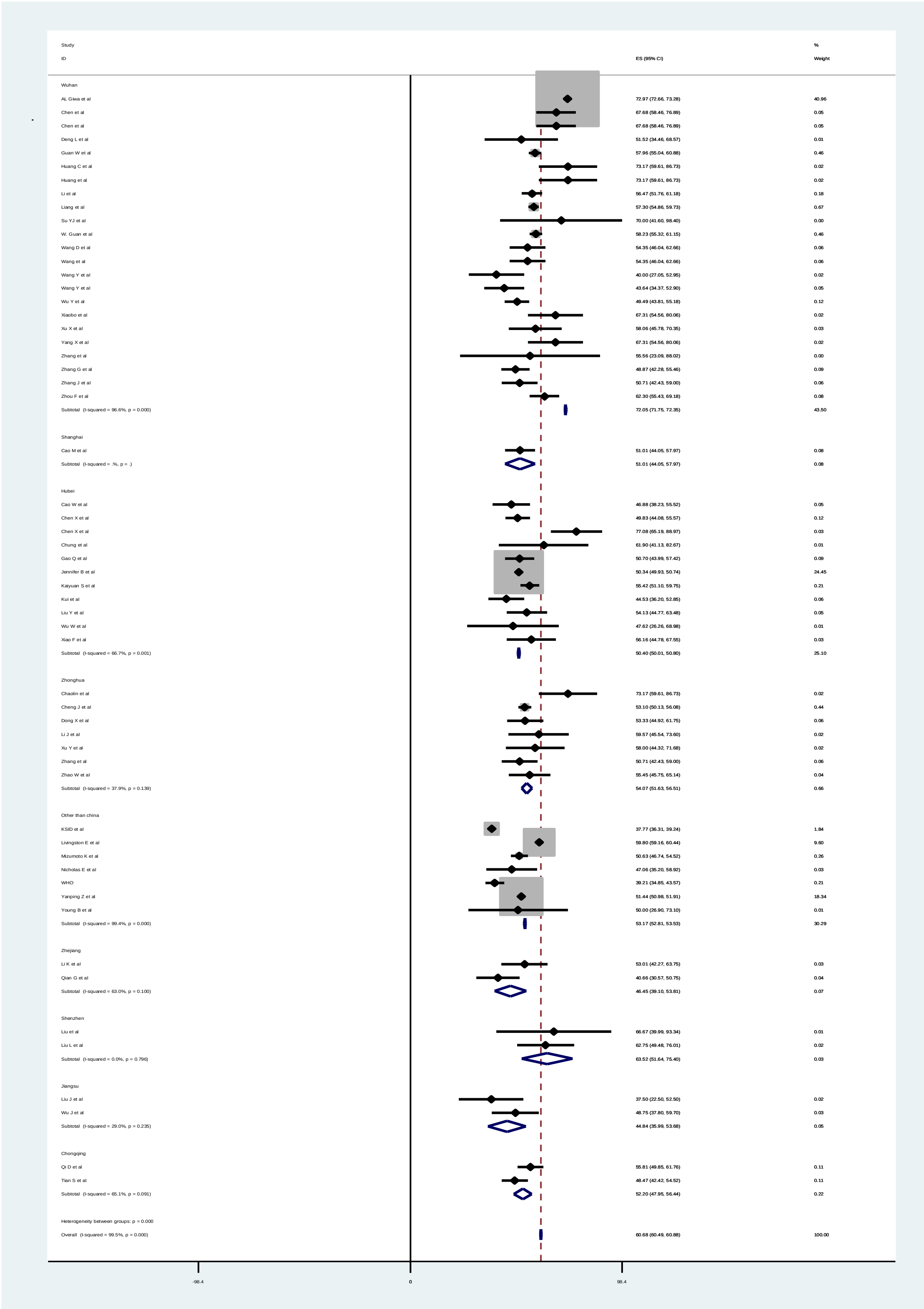
Figure 2: Forest plot showing the pooled prevalence of COVID-19 confirmed cases among male

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

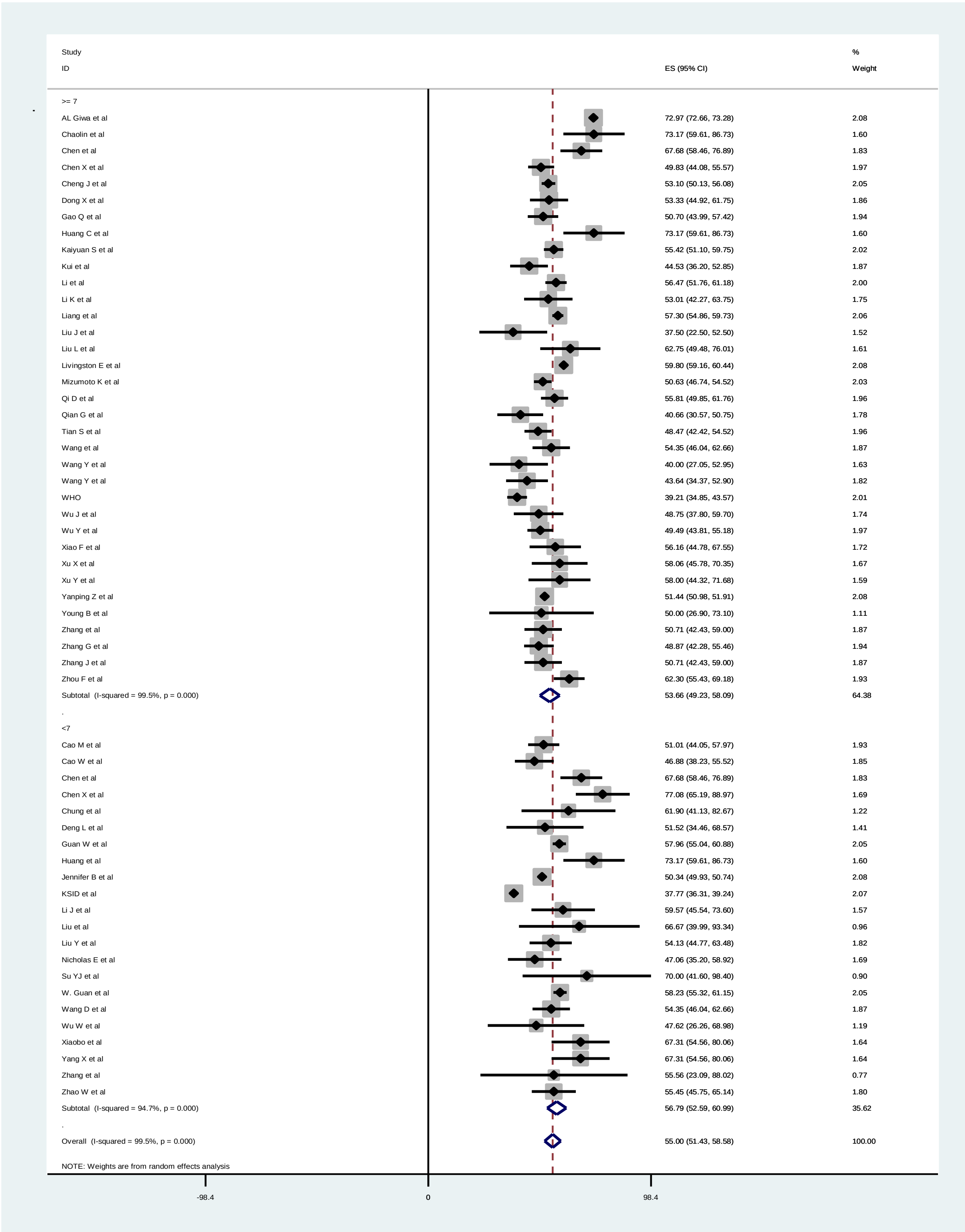
Figure 3: sensitivity analysis for pooled prevalence of COVID-19 confirmed cases among males



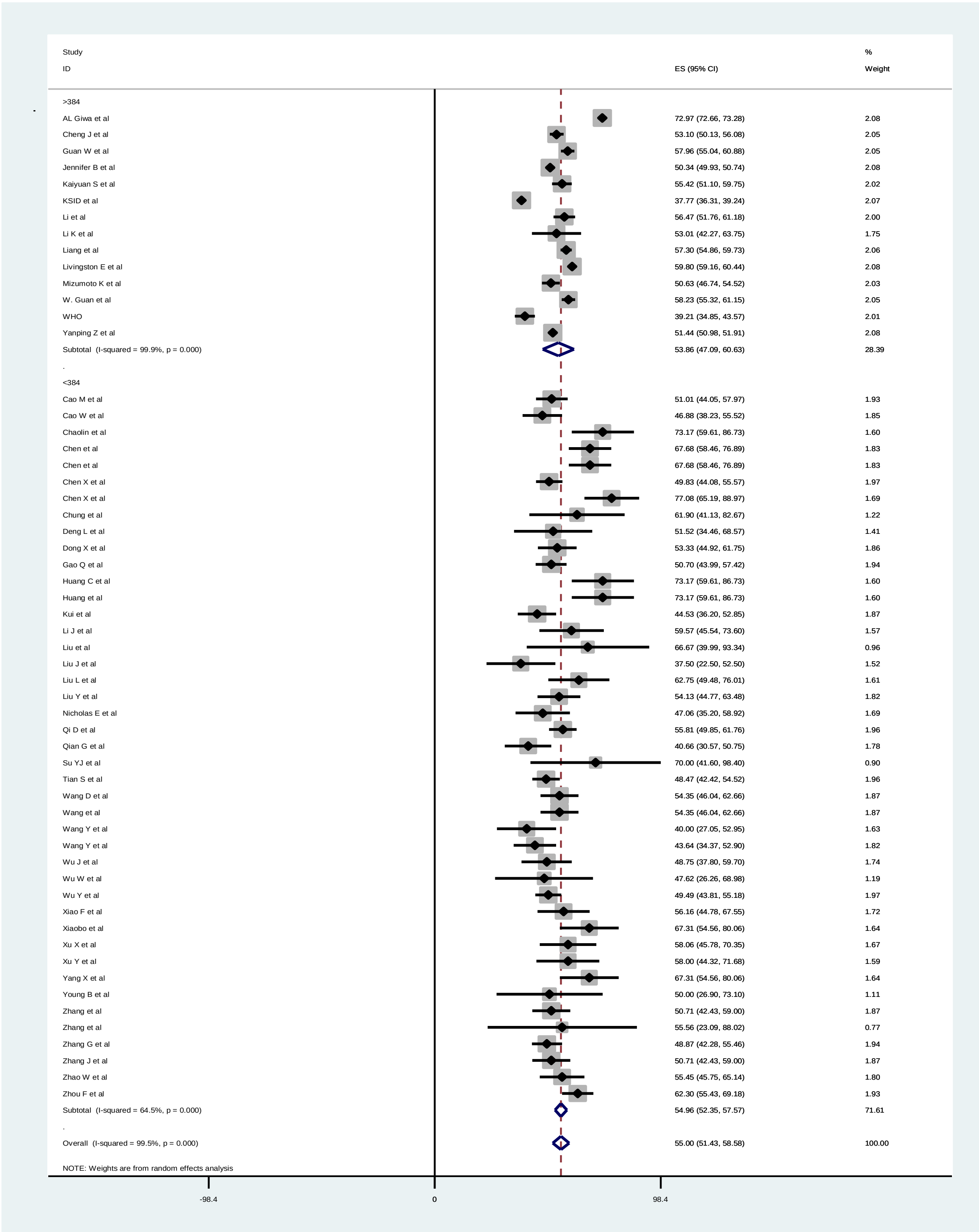
Supplementary Figure 1: Subgroup analysis for prevalence of COVID-19 among males by countries



Supplementary Figure 2: Subgroup analysis of the prevalence of COVID-19 by province in china



Supplementary Figure 3: Subgroup analysis of the prevalence of COVID-19 by quality score



Supplementary Figure 4: Subgroup analysis of the prevalence of COVID-19 by sample size

Table S1. Search strategy used for one of the databases

Medline/PubMed			
	Search terms		
Group	***Non-MeSH terms***	**MeSH (sub-terms in MeSH)**	**Citations**
#1	Magnitude Epidemiology proportion	Prevalence	
#2	Female	Male	
#3	Novel coronavirus Novel coronavirus 2019 2019 nCoV Wuhan coronavirus Wuhan pneumonia SARS-CoV-2	COVID-19	
#4		COVID-19 confirmed patients	
#1 AND #2 AND #3 AND #4			

(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 (MeSH term) on PubMed database (Table S1). Thus, the PubMed search combines #1 AND #2 AND #3 AND #4

Table S2: Quality appraisal result of included studies in East Africa, from 2002- 2019. Using Joanna Briggs Institute (JBI) quality appraisal checklist

Author	Quality assessment questions										Yes Total	Quality status	Overall appraisal
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11			
Cross-sectional studies														
1. Li K et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
2. Liu Y et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
3. Liu Y et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
4. Liu J et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
5. Wu J et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
6. Xu X et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
7. Xu Y et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
8. Yao et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
9. Young et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
10. Zhang J et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
11. Zhang M et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
12. Zhao et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
13. Zhu et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
14. Yanping Z et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
15. W. Guan et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
16. WHO ,2020	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
17. Huang et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
18. Chen et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
19. Wang et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included
20. Kaiyuan S et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
21. AL Giwa et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
22. Qian G et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
23. Livingston E et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
24. Wang Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
25. KSID,2020	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
26. Su YJ et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
27. Jennifer B et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
28. Kui et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
29. Deng L et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
30. Dong X et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
31. Xiaobo et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
32. Zhou F et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
33. Wu Y et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
34. Gao Q et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
35. Chen X et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
36. Zhang G et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
37. Wu W et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
38. Cao M et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
39. Chung et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included

40. Xiao F et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
41. Qi D et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
42. Liang et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included
43. Wang Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
44. Nicholas E et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
45. Mizumoto K et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
46. Chen X et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
47. Cheng J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
48. Li J et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
49. Tian S et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
50. Li et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
51. Liu Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
52. Cao W et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
53. Chaolin et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
54. Yang X et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
55. Liu L et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
56. Huang C et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
57. Wang D et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
58. Cheng J et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
59. Wu J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
60. Li K et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
61. Li J et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
62. Guan W et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
63. Tian S et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
64. Liu Y et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
65. Xu Y et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
66. Cao W et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
67. Yang X et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
68. Liu L et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
69. Zhang J et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included

Key: Y=yes, N=no, UC=unclear, Q=Question

JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data

Criteria	Yes	No	Un clear	Not applicable
1. Was the sample frame appropriate to address the target population?				
2. Were study participants sampled in an appropriate way?				
3. Was the sample size adequate?				
4. Were the study subjects and the setting described in detail?				
5. Was the data analysis conducted with sufficient coverage of the identified sample?				
6. Were valid methods used for the identification of the condition?				
7. Was the condition measured in a standard, reliable way for all participants?				
8. Was there appropriate statistical analysis?				
9. Was the response rate adequate, and if not, was the low response rate managed appropriately?				