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

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3 1 **Sex difference in coronavirus disease (COVID-19): A systematic review and meta-analysis**

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25
26 12 **Running title:** Sex difference in coronavirus disease (COVID-19)

27
28 13 **Abstract**

29
30 14 **Objective:** To assess the sex difference in the prevalence of coronavirus disease (COVID-19) confirmed cases

31
32 15 **Design:** Systematic review and meta-analysis.

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34 16 **Setting:** PubMed, Cochrane library, and Google Scholar were searched for related information. The authors developed a data
35 17 extraction form on the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number
36 18 female patients, and the number of male patients. Using STATA 14 for analysis authors pooled the overall prevalence male and/or
37 19 female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I² statistics.
38 20 Subgroup and sensitivity analysis was done Publication bias was also checked.

39
40 21 **Participants:** Studies with COVID-19 confirmed cases were included.

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

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

24 **Result:** A total of 57 studies with 221195 participants were used for analysis. The pooled prevalence of COVID-19 among males was
25 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
26 study. Moreover a funnel plot showed symmetrical distribution. Egger's regression test p-value was not significant, which indicates
27 the absence of publication bias in both outcomes.

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

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

34 **Background**

35 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
36 indicated by the substantial rise in the number of cases and the fast geographical spread of the disease (1-4). The WHO announced that
37 the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19) (5, 6). The virus has now been named Severe Acute
38 Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) (7). COVID-19
39 has now been declared as a Public Health Emergency of International Concern by the WHO on 30th January 2020(8).

40 COVID-19 affects people differently, in terms of infection with the virus SARS-CoV-2 and mortality rates(9,10).

41 Susceptibility to COVID-19 seems to be associated with age, biological sex, and comorbidities (11). Although the COVID-19 causes
42 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:

69 □ Are men more susceptible to getting COVID-19?

70 **Methods**

71 *Search strategy*

72 This systematic review and meta-analysis identified studies that revealed data on the proportion of sex in COVID-19 confirmed case.
73 We retrieved studies from Google Scholar, PubMed, Scopus, Web of Sciences Cochrane library, research gate, and institutional
74 repositories. The search included keywords that are the combinations of population, condition/outcome, and context. A snowball
75 searching for the references of relevant papers for linked articles was also performed. Those search terms or phrases including were:
76 The search terms used were: “Novel coronavirus,” “Novel coronavirus 2019”, “2019 nCoV”, “COVID-19”, “Wuhan coronavirus,”
77 “Wuhan pneumonia,” and “SARS-CoV-2.” Articles published in English language were considered from January 1, 2020. The
78 searches were concluded by March 27, 2020, and four different researchers independently evaluated search results. Using those key
79 terms, the following search map was applied: (prevalence OR proportion OR magnitude) AND (Male OR Female) AND (Novel
80 coronavirus OR Novel coronavirus 2019 OR 2019 nCoV OR COVID-19 OR Wuhan coronavirus OR Wuhan pneumonia OR SARS-
81 CoV-2) AND COVID-19 confirmed patients on PubMed database (Table S1). Thus, the PubMed search combines #1 AND #2 AND
82 #3 AND #4 (Table S1). The searching date was January 2000 to December 2019.

83 **Study selection and screening**

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

89 Inclusion and exclusion criteria

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

95 **Patient and Public Involvement:** Patients or the public WERE NOT involved in the design, or conduct, or reporting, or
96 dissemination plans of our research

97 Quality assessment

98 Using the Joanna Briggs Institute (JBI) quality appraisal checklist the authors appraised the quality of included studies (27). There was
99 a team of four reviewers and the papers were split amongst the team. Each paper was then assessed by two reviewers and any
100 disagreements were discussed with the third and the fourth reviewers. Studies were considered as low risk or good quality when it
101 scored 4 and above (27), whereas the studies scored 3 and below were considered as high risk or poor quality (Table S2).

102 Data extraction

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

109 **Synthesis of results**

110 The authors transformed the data to STATA 14 for analysis after it was extracted in an excel sheet considering prevalence male and
111 female reported. We pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the
112 heterogeneity of effect size using the Q statistic and the I² statistics. In this study, the I² statistic value of zero indicates true
113 homogeneity, whereas the value 25, 50, and 75% represented low, moderate and high heterogeneity, respectively. Subgroup analysis
114 was done by the study country and sample size. Sensitivity analysis was employed to examine the effect of a single study on the
115 overall estimation. Publication bias was checked by the funnel plot and more objectively through Egger's regression test.

116 **Result**

117 **Study selection**

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

121 **Characteristics of included studies**

122 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
123 The studies included participants ranging from 9 (75) to 78771 (45) (Table1).

124 **Meta-analysis**

125 **Prevalence of COVID-19 among male**

126 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
127 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
128 pooled prevalence of severe illness is 55.00(51.43-56.58; I²=99.5%; p<0.001) (Fig.2).

129 **Subgroup analysis of COVID-19 confirmed cases among male**

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3 130 The subgroup analysis was done through stratification by country. Based on this, the prevalence of severe illness was found to be
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5 131 61.34 in china and 29.9 in Italy (Supplementary Fig 1).
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7 132 **Sensitivity analysis**

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10 133 We employed a leave-one-out sensitivity analysis to identify the impact of individual research on the pooled prevalence of severe
11 134 illness among COVID-19 confirmed cases. The results of this sensitivity analysis showed that our findings were not dependent on a
12 135 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)
13 136 Yanping Z ET al after the deletion of a single study (Figure 3).
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17 137 **Publication Bias**

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20 138 We have also checked publication bias and, a funnel plot showed symmetrical distribution. Egger's regression test p-value was 0.599,
21 139 which indicates the absence of publication bias (Figure 4).
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24 140 **Discussion**

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27 141 Recently, following the COVID-19 outbreak, numerous questions have been raised; comprising what is their sex difference in getting
28 142 COVID-19?. This systematic review and meta-analysis were conducted to assess the sex difference in getting COVID -19 disease and
29 143 this review revealed the pooled prevalence of COVID-19 among males and females.
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33 144 Fifty seven studies were included in the final analysis. The pooled prevalence COVID -19 confirmed cases among males and females
34 145 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
35 146 (76, 77).
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3 147 Biological sex variation is said to be one of the reason for the sex discrepancy of COVID-19(78). Women's innate immune response
4 148 affected by sex chromosomes and sex hormones plays a role. As a result, women are in general able to mount a more vigorous
5 149 immune response to infections [and] vaccinations(79).

6
7
8 150 Some previous studies on coronaviruses in mice have suggested that the hormone estrogen may have a protective role. Estrogens
9 151 suppress the escalation phase of the immune response that leads to increased cytokine release(80). The authors showed that female
10 152 mice treated with an estrogen receptor antagonist died at close to the same rate as the male mice(81).

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12
13 153 In addition behavioral factors, like smoking and alcohol consumption, which tend to occur more among men, those behaviors
14 154 predisposes males for cardiac and respiratory diseases. This may also explain the overall higher mortality rate among men (82-84).

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16 155 A systematic review and meta-analysis revealed that comorbid disease, such as respiratory system disease, hypertension, and
17 156 cardiovascular disease as risk a risk factors for death compared with patients without comorbidity(85).

18 19 20 157 **Strength and limitations**

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22 158 This systematic review and meta- analysis has several strengths: we used a pre-specified protocol for search strategy and data
23 159 abstraction and used internationally accepted tools for a critical appraisal system for quality assessment of individual studies. Besides
24 160 we employed subgroup analysis, publication bias and sensitivity analysis Nevertheless, this review had some limitations: because of
25 161 the inclusion of studies which are published in English only, language bias is likely. In addition most included are from China due to
26 162 lack of literatures from other countries in the world which reported the outcome of interest. However, the data in this review permit to
27 163 systematically review and analyze the pooled prevalence of severe illness and mortality among COVID-19 confirmed patients

28 29 30 31 32 33 164 **Conclusions**

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35
36 165 The prevalence of COVID-19 is higher among males than females. This can be explained with the hormonal and chromosomal
37 166 variation between males and females. In addition the high prevalence of smoking and alcohol consumption has contributed for
38 167 increased high prevalence of COVID-19 among males. Although there has been a rapid surge in research in response to the outbreak

168 of COVID-19, additional studies regarding discrepancy in severe illness and mortality due to COVID-19 among males and females
169 and factors which determine the exposure, severity and mortality due to COVID-19 is recommended. Everyone should take actions,
170 such as hand washing with sanitizer, social distancing, avoid crowding (2m apart if coming together is must) avoid smoking and
171 alcohol consumption especially among men to help slow the spread of COVID-19.

172 **Abbreviations**

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

176 **Declarations**

177 **Ethics approval and consent to participate**

178 Not applicable

179 **Consent for publication**

180 Not applicable

181 **Availability of data and material**

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

183 **Competing interests**

184 We have confirmed that we have no competing interests.

185 **Funding**

186 No funding was obtained for this study

187 **Authors' contributions**

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

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345 **Figure and Table Legend**

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

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

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

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

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

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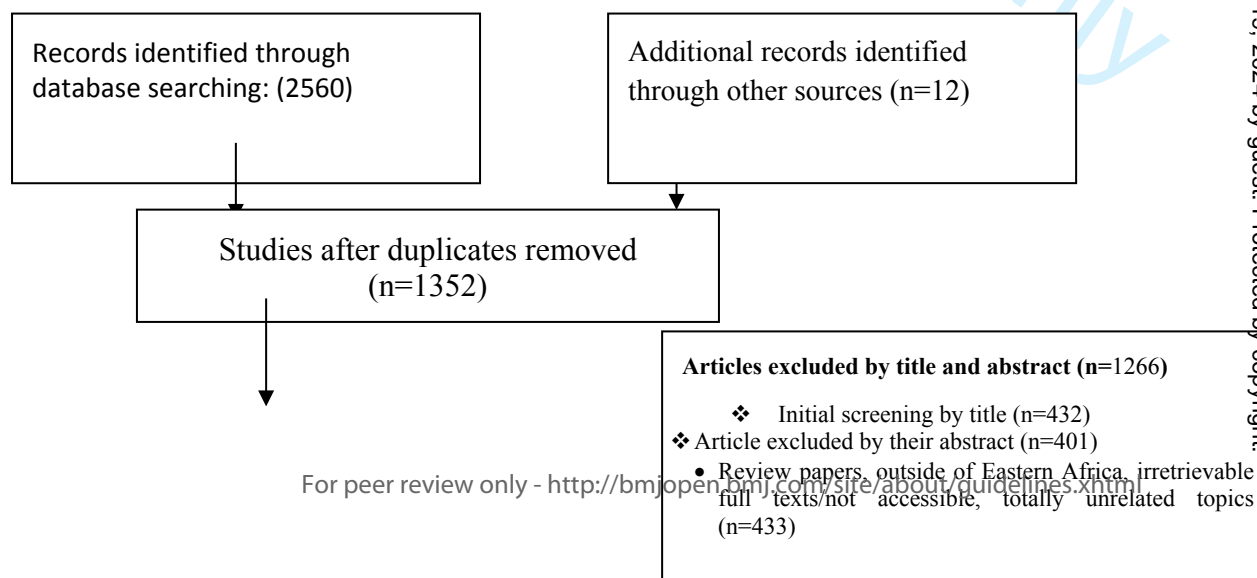
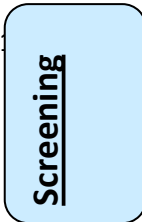
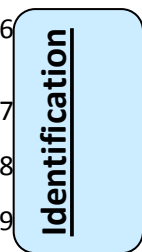
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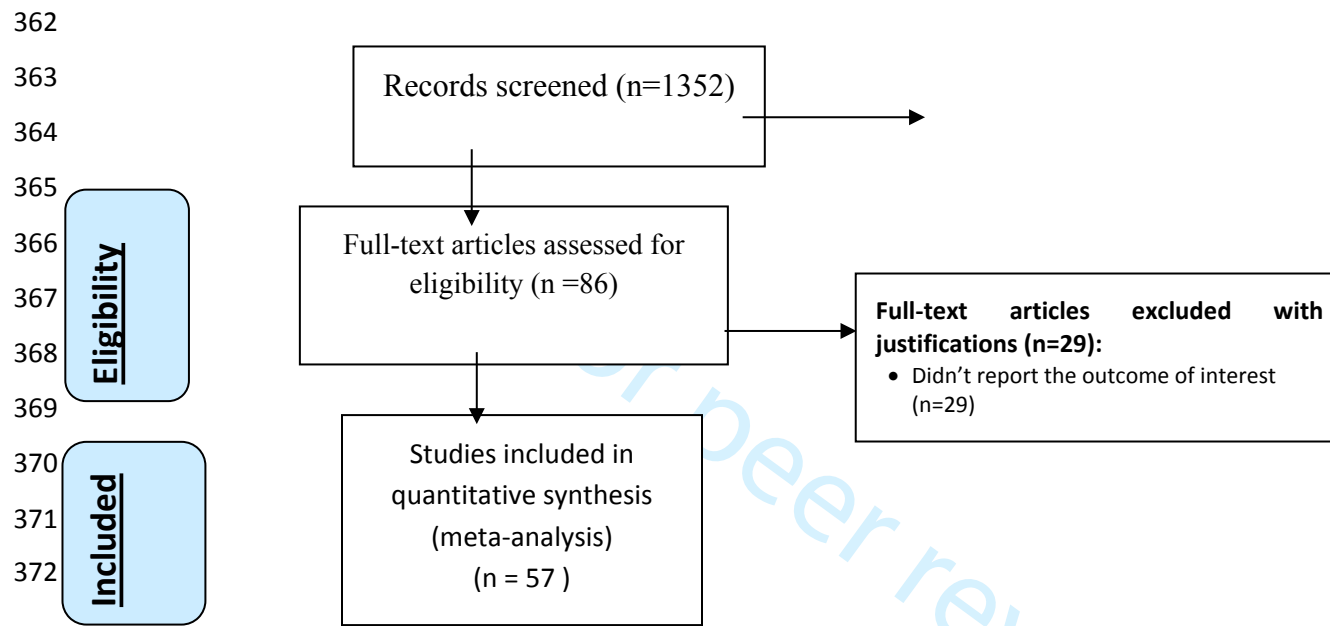


Figure 1

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)

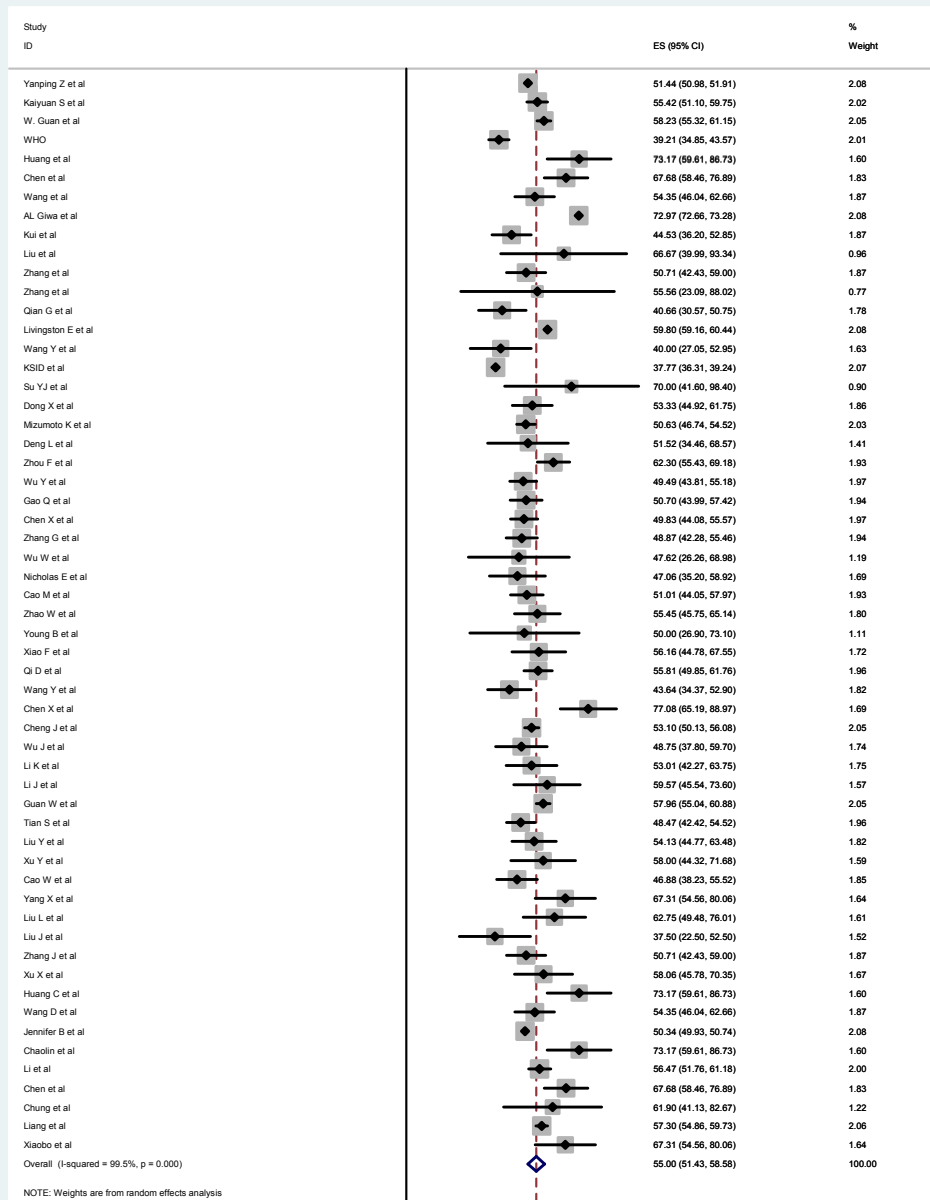
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49.	Tian S et al	China	April 2020	262	127	135	(69)
50.	Li et al	China	March, 2020	425	240	185	(70)
51.	Liu Y et al	China	February, 2020	109	59	50	(1)
52.	Cao W et al	China	February, 2020	198	101	97	(71)
53.	Chaolin et al	China	February, 2020	41	30	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)

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381 Figure 2

Study omitted	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

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383 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

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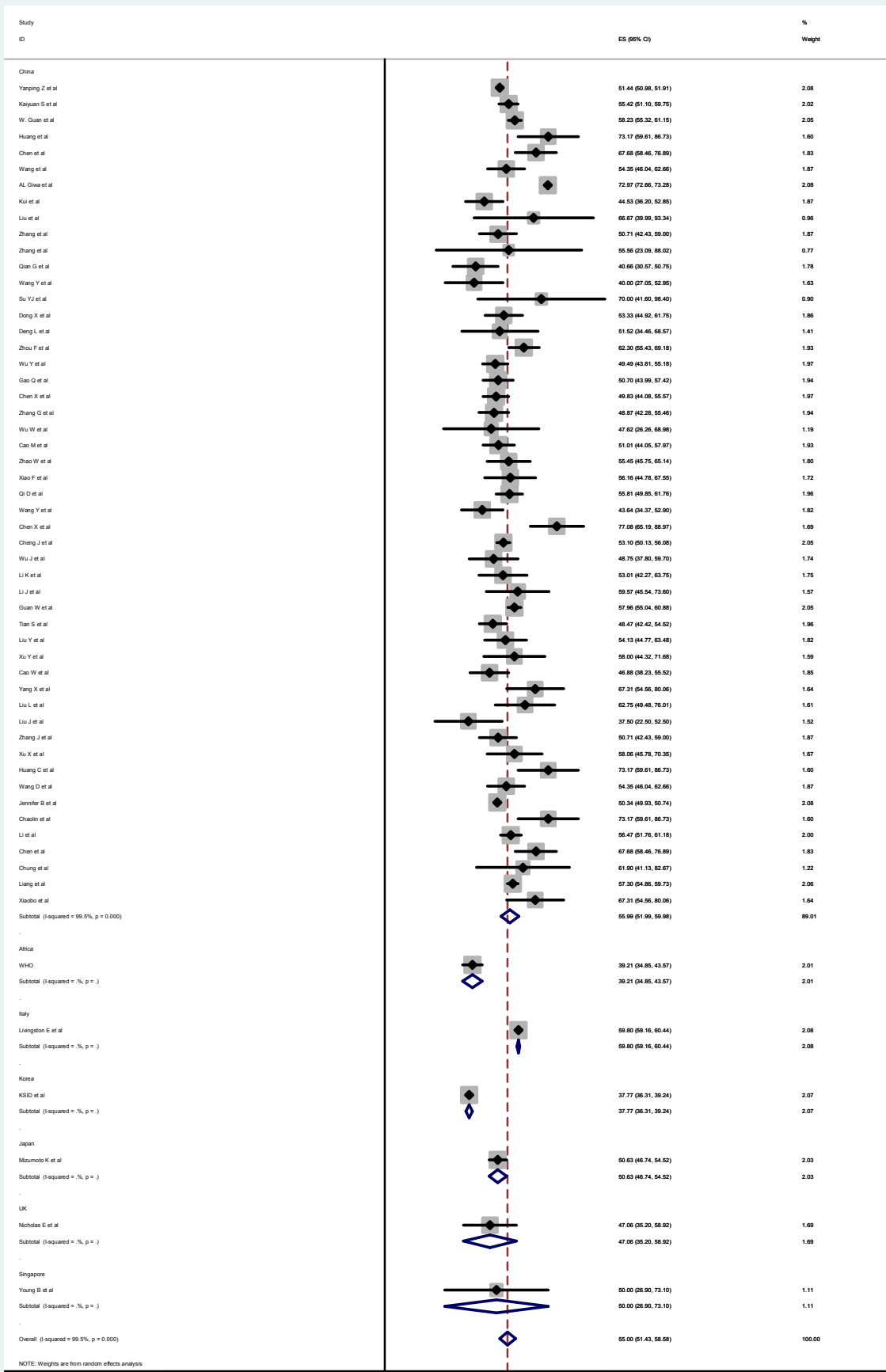
385 Figure 4

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3 Supplementary Figure 1: Sub group analysis for prevalence of COVID-19 among males
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Table S1. Search strategy used for one of the databases

Medline/PubMed			
Group	Search terms		Citations
	<i>Non-MeSH terms</i>	MeSH (sub-terms in MeSH)	
#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

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3	40. Xiao F et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
4	41. Qi D et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
5	42. Liang et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included
6	43. Wang Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
7	44. Nicholas E et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
8	45. Mizumoto K et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
9	46. Chen X et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
10	47. Cheng J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
11	48. Li J et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
12	49. Tian S et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
13	50. Li et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
14	51. Liu Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
15	52. Cao W et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
16	53. Chaolin et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
17	54. Yang X et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
18	55. Liu L et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
19	56. Huang C et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
20	57. Wang D et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
21	58. Cheng J et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
22	59. Wu J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
23	60. Li K et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
24	61. Li J et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
25	62. Guan W et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
26	63. Tian S et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
27	64. Liu Y et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
28	65. Xu Y et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
29	66. Cao W et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
30	67. Yang X et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
31	68. Liu L et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
32	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

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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

Page 1 of 2

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 at each 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	

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

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

13 **Abstract**

14 **Objective:** To assess the sex difference in the prevalence of coronavirus disease (COVID-19) confirmed cases

15 **Design:** Systematic review and meta-analysis.

16 **Setting:** PubMed, Cochrane library, and Google Scholar were searched for related information. The authors developed a data
17 extraction form on the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number
18 female patients, and the number of male patients. Using STATA 14 for analysis authors pooled the overall prevalence male and/or
19 female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I² statistics.
20 Subgroup and sensitivity analysis was done Publication bias was also checked.

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3 21 **Participants:** Studies with COVID-19 confirmed cases were included.
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6 22 **Intervention:** sex (male/female) of COVID-19 confirmed cases were considered
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8 23 **Primary and secondary outcome measures:** Primary outcomes were prevalence of COVID-19 among males and females.
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10 24 **Result:** A total of 57 studies with 221195 participants were used for analysis. The pooled prevalence of COVID-19 among males was
11 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
12 study. Moreover a funnel plot showed symmetrical distribution. Egger's regression test p-value was not significant, which indicates
13 the absence of publication bias in both outcomes.
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16 28 **Conclusions:** The prevalence of symptomatic COVID-19 is higher among males than females. The high prevalence of smoking and
17 alcohol consumption has contributed for increased high prevalence of COVID-19 among males. Additional studies regarding
18 discrepancy in severe illness and mortality due to COVID-19 among males and females and factors which determine the exposure,
19 severity and mortality due to COVID-19 is recommended.
20 30

21 31
22 32 **Keywords:** COVID-19; sex difference; Systematic review; Meta-analysis
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24 33 **Strength and limitations**

25 34 This systematic review and meta- analysis has several strengths: we used a pre-specified protocol for search strategy and data
26 35 abstraction and used internationally accepted tools for a critical appraisal system for quality assessment of individual studies. Besides
27 36 we employed subgroup analysis, publication bias and sensitivity analysis. Nevertheless, this review had some limitations: because of
28 37 the inclusion of studies which are published in English only, language bias is likely. In addition most included are from China due to
29 38 lack of literatures from other countries in the world which reported the outcome of interest. However, the data in this review permit to
30 39 systematically review and analyze the pooled prevalence of COVID-19 among males.
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41 Background

42 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
43 indicated by the substantial rise in the number of cases and the fast geographical spread of the disease (1-4). The WHO announced that
44 the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19) (5, 6). The virus has now been named Severe
45 Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) (7).
46 COVID-19 has now been declared as a Public Health Emergency of International Concern by the WHO on 30th January 2020(8).
47 COVID-19 affects people differently, in terms of infection with the virus SARS-CoV-2 and mortality rates(9,10).
48 Susceptibility to symptomatic COVID-19 seems to be associated with age, biological sex, and comorbidities (11). Although the
49 COVID-19 causes a mild illness in a majority of cases, severe illness requiring hospital admission is not uncommon (12). Besides, it
50 has the potential to precipitate a life-threatening critical illness, characterized by respiratory failure, circulatory shock, sepsis or other
51 organ failure, requiring intensive care(13, 14). According to Global Health 5050 data gathering, the number of COVID-19 confirmed
52 cases and the death rate due to COVID-19 is high among males in different countries (15-17).

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

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

63 **Review question**

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

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

66 **Methods**

67 *Search strategy*

68 This systematic review and meta-analysis identified studies that revealed data on the proportion of sex in COVID-19 confirmed case.
69 We retrieved studies from Google Scholar, PubMed, Scopus, Web of Sciences Cochrane library, research gate, and institutional
70 repositories. The search included keywords that are the combinations of population, condition/outcome, and context. A snowball
71 searching for the references of relevant papers for linked articles was also performed. Those search terms or phrases including were:
72 The search terms used were: “Novel coronavirus,” “Novel coronavirus 2019”, “2019 nCoV”, “COVID-19”, “Wuhan coronavirus,”
73 “Wuhan pneumonia,” and “SARS-CoV-2.” Articles published in English language were considered from January 1, 2020. The
74 searches were concluded by March 27, 2020, and four different researchers independently evaluated search results. Using those key
75 terms, the following search map was applied: (prevalence OR proportion OR magnitude) AND (Male OR Female) AND (Novel
76 coronavirus OR Novel coronavirus 2019 OR 2019 nCoV OR COVID-19 OR Wuhan coronavirus OR Wuhan pneumonia OR SARS-
77 CoV-2) AND COVID-19 confirmed patients on PubMed database (Table S1). Thus, the PubMed search combines #1 AND #2 AND
78 #3 AND #4 (Table S1). The searching date was January 2000 to December 2019.

79 **Study selection and screening**

80 The retrieved studies were exported to Endnote version 8 reference managers to remove duplicate studies. Two investigators (BB and
81 AM) independently screened the selected studies using article's title and abstracts before retrieval of full-text papers. We used pre-

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3 82 specified inclusion criteria to further screen the full-text articles. Disagreements were discussed during a consensus meeting or, if
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5 83 necessary, by including the third and fourth researchers (MW and TG) to make the final decision for the selection of studies to be
6
7 84 included in the systematic review and meta-analysis.

85 **Inclusion and exclusion criteria**

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

91 **Patient and Public Involvement:** Patients or the public WERE NOT involved in the design, or conduct, or reporting, or
92 dissemination plans of our research

93 **Quality assessment**

94 Using the Joanna Briggs Institute (JBI) quality appraisal checklist the authors appraised the quality of included studies (26). There was
95 a team of four reviewers and the papers were split amongst the team. Each paper was then assessed by two reviewers and any
96 disagreements were discussed with the third and the fourth reviewers. Studies were considered as low risk or good quality when it
97 scored 4 and above (26), whereas the studies scored 3 and below were considered as high risk or poor quality (Table S2).

98 **Data extraction**

99 The authors developed a data extraction form on the excel sheet and the following data were extracted for eligible studies: author,
100 country, sample size, number female patients, and the number of male patients. The data extraction sheet was piloted using 4 papers
101 randomly, and it was adjusted after piloted the template. Two of the authors extracted the data using the extraction form in

102 collaboration. The third and fourth authors checked the correctness of the data independently. Any disagreements between reviewers
103 were resolved through discussions with third and fourth reviewers when required. The mistyping of data was resolved through
104 crosschecking with the included papers. The case definition considered was as follows: confirmed case: detection of SARS-CoV-2
105 nucleic acid in a clinical specimen; possible case: any person with at least one of the following symptoms: cough, fever, shortness
106 of breath, sudden onset of anosmia, ageusia or dysgeusia; probable case: any person with at least one of the following symptoms :
107 cough, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia, with close contact with a confirmed COVID-19
108 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,
109 in a residential institution for vulnerable people where ongoing COVID-19 transmission has been confirmed.

110 **Synthesis of results**

111 The authors transformed the data to STATA 14 for analysis after it was extracted in an excel sheet considering prevalence male and
112 female reported. We pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the
113 heterogeneity of effect size using the Q statistic and the I² statistics. In this study, the I² statistic value of zero indicates true
114 homogeneity, whereas the value 25, 50, and 75% represented low, moderate and high heterogeneity, respectively. Subgroup analysis
115 was done by the study country and sample size. Sensitivity analysis was employed to examine the effect of a single study on the
116 overall estimation. Publication bias was checked by the funnel plot and more objectively through Egger's regression test.

117 **Result**

118 **Study selection**

119 A total of 2574 studies were identified using electronic searches (through Database searching (n = 2560)) and other sources (n =12)).
120 After duplication removal, a total of 1352 articles remained (1222 duplicated). Finally, 86 studies were screened for full-text review
121 and, 57 articles (n=221195 patients) were selected for the analysis (Fig.1). This citation manager automatically identifies duplicates
122 creates a separate group among imported references, which can be deleted. For those different citation for the same paper we screened

123 and de-duplicated the citations by hand, which were recorded on a Microsoft Excel spreadsheet after assessing if they have the same
124 author, title, publication date, volume, issue, sample size, etc we removed the duplicated one.

125 **Characteristics of included studies**

126 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
127 The studies included participants ranging from 9 (74) to 78771 (44) (Table 1).

128 **Meta-analysis**

129 **Prevalence of COVID-19 among male**

130 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
131 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
132 from those studies revealed that, the pooled prevalence of COVID-19 confirmed cases is 55.00(51.43-58.58; $I^2=99.5\%$; $p<0.001$)
133 (Fig.2).

134 **Subgroup analysis of COVID-19 confirmed cases among male**

135 The subgroup analysis was done through stratification by country, providences, sample size and quality score. Based on this, the
136 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),
137 50.00(26.90-73.10) in China, Africa, Italy, Korea, and Singapore respectively (Table 2 and Supplementary Fig 1).

138 The pooled prevalence of COVID-19 among male in Wuhan, Shanghai, Hubei, Zhonghua, outside china, Zhejiang, Shenzhen, Jiangsu,
139 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) ; $I^2=66.7$;
140 $P=0.001$, 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-
141 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
142 52.20(95% CI:47.95-56.44) ; $I^2=65.1$, $P=0.09$ respectively (Table 2 and Supplementary Fig 2).

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3 143 Regarding quality score the pooled prevalence of COVID-19 among male in studies which scored greater than or equal to seven was
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5 144 53.66(95% CI:49.23-58.09) ;I² =99.5, P= 0.00, and 56.79(95% CI:52.79-60.990) ;I² =94.7, P= 0.00 among studies scored less than
6
7 145 seven from JBI quality appraisal checklist(Table 2 and Supplementary Fig 3).

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9 146 Regarding sample size the pooled prevalence of COVID-19 among male in studies which have sample size greater than or equal to
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11 147 384 was 53.86(95% CI:47.09-60.63) ;I² =99.9, P= 0.00, and 54.96(95% CI:52.35-57.57) ;I² =64.5, P= 0.00 among studies scored less
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13 148 than seven from JBI quality appraisal checklist(Table 2 and Supplementary figure 4).

15 149 **Sensitivity analysis**

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18 150 We employed a leave-one-out sensitivity analysis to identify the impact of individual research on the pooled prevalence of severe
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20 151 illness among COVID-19confirmed cases. The results of this sensitivity analysis showed that our findings were not dependent on a
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22 152 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)
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24 153 Yanping Z ET al after the deletion of a single study (Figure 3).

25 154 **Publication Bias**

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28 155 We have also checked publication bias and, a funnel plot showed symmetrical distribution. Egger's regression test p-value was 0.599.
29
30 156 Both the symmetric funnel plot and the insignificant p-value (<0.05) indicates the absence of publication bias.

31 32 157 **Meta-regression**

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34 158 Univariate meta-regression analyses revealed that the prevalence of smoking was found to be high in males. This contributed for high
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36 159 prevalence of COVID-19 among males (P=0.002). Comorbidities like hypertension (0.042), diabetic mellitus (0.012, chronic
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38 160 respiratory disease (0.021), and cardio vascular disease (0.001) were also found to be higher in males and these significantly increases
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40 161 the prevalence of COVID-19. Besides, higher proportion of sever/critical illness (0.003) and death (0.001) were also observed among
41
42 162 males (Table 3).

163 Discussion

164 This systematic review and meta-analysis were conducted to assess the sex difference in getting COVID -19 diseases. Fifty seven
165 studies were included in the final analysis. The result of this systematic review and meta-analysis revealed that the pooled prevalence
166 of COVID -19 confirmed cases among males and females was found to be 55.00(51.43-56.58; I²=99.5%; p<.001) and 45.00(41.42-
167 48.57) respectively. This indicates COVID -19 is prevalent in males than females.

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

171 This might be due to behavioral factors and roles which increase the risk of acquiring COVID-19 tend to occur more among men.
172 Male are more involved in different risky behaviors like alcohol consumption (80-82), key activities in burial rites; as employees in
173 basic sectors and occupations that continue being active and require them to work outside the home and interact with other people
174 during the containment phase (e.g., food or pharmacy manufacturing and sales, agriculture or food production and distribution,
175 transportation, and security). Because of such behaviors males mostly don't stay at home, sit together, and remove their mask while
176 they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease. In China 50% of
177 men in smoke, but because it is not considered acceptable for women to smoke, only 2% of them do so. Smoking is associated with
178 adverse outcomes of COVID-19: for instance, the combined results of five studies showed that smokers were 1.4 times more likely
179 than non-smokers to have severe symptoms of COVID-19 (83). Besides, smoking is related to higher expression of ACE2 (the
180 receptor for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), which might be the reason for the higher prevalence of
181 COVID-19 in this subgroup of patients than in women (84).

182 Men tended to develop more symptomatic and serious cases than women, according to the clinical classification of severity. Similar
183 occasions occurred during previous coronavirus epidemics: men had worse outcomes of illness from severe acute respiratory
184 syndrome (SARS), (85)and a higher risk of dying from Middle East respiratory syndrome (MERS)(86). Biological sex variation is said
185 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
186 more vigorous immune response to infections and vaccinations(88). Some previous studies on coronaviruses in mice have suggested
187 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(85). 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**

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3 209 COVID-19: coronavirus disease 2019; WHO: World Health Organization; ICTV: International Committee of Taxonomy of Viruses;
4
5 210 SARS-CoV-2: Sever Acute Respiratory Syndrome Coronavirus 2; CI: Confidence Interval; AOR: Adjusted Odds ratio; ARTI: Acute
6
7 211 Respiratory Tract Infections

8
9 212 **Declarations**

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11 213 **Ethics approval and consent to participate**

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14 214 Not applicable

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16 215 **Consent for publication**

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19 216 Not applicable

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21 217 **Availability of data and material**

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24 218 The datasets analyzed during the current study are available from the corresponding author upon reasonable request.

25
26 219 **Competing interests**

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29 220 We have confirmed that we have no competing interests.

30
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225 Authors' contributions

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

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17 398 **Table Legend**

19 399 Table 1: Characteristics of included studies for male/female among COVID-19 confirmed cases

21 400 Table 2: Subgroup analysis of the pooled prevalence of COVID-19 by country, province, quality score, and sample size

23 401 Table 3: **a meta-regression analysis showing factors which have effect on the sex difference of COVID-19**

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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	(2)
2.	Liu Y et al	China	Jan11-Jan20	12	8	4	9/9	(2)
3.	Liu Y et al	China	Jan23-Feb8	109	59	50	6/9	(2)
4.	Liu J et al	China	Jan-Feb	40	15	25	8/9	(3)
5.	Wu J et al	China	Jan22-Feb14	80	39	41	8/9	(3)
6.	Xu X et al	China	Jan10-Jan26	62	36	26	8/9	(1)
7.	Xu Y et al	China	Jan-Feb	50	29	21	6/9	(3)
8.	Yao et al	China	Jan01-Feb07	195	115	80	8/9	(3)
9.	Young et al	China	Jan22-Jan31	18	9	9	6/9	(3)
10.	Zhang J et al	China	Jan16-Feb03	140	71	69	8/9	(3)
11.	Zhang M et al	China	Jan18-Feb03	9	5	4	7/9	(3)
12.	Zhao et al	China	Jan16-Feb03	101	56	45	8/9	(3)
13.	Zhu et al	China	Dec01-Feb15	12	8	4	7/9	(3)
14.	Yanping Z et al	China	February 2020	44672	22981	21691	8/9	(3)
15.	W. Guan et al	China	February 2020	1099	640	459	7/9	(4)
16.	WHO ,2020	Africa	March 2020	482	189	177	7/9	(4)
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	(4)
19.	Wang et al	China	March 2020	138	75	63	7/9	(2)
20.	Kaiyuan S et al	China	February, 2020	507	281	201	6/9	(4)
21.	AL Giwa et al	China	March, 2020	78771	57482	21289	9/9	(4)
22.	Qian G et al	China	March, 2020	91	37	54	8/9	(4)
23.	Livingston E et al	Italy	March, 2020	22512	13462	9050	7/9	(4)
24.	Wang Y et al	China	March, 2020	110	48	62	6/9	(4)
25.	KSID,2020	Korea	February, 2020	4212	1591	2621	9/9	(4)
26.	Su YJ et al	China	March, 2020	10	7	3	6/9	(4)
27.	Jennifer B et al	China	March, 2020	59600	30000	29600	8/9	(5)
28.	Kui et al	China	March, 2020	137	61	76	8/9	(5)
29.	Deng L et al	China	March, 2020	33	17	16	8/9	(5)
30.	Dong X et al	China	March, 2020	135	72	63	6/9	(5)
31.	Xiaobo et al	China	March, 2020	52	35	17	8/9	(1)
32.	Zhou F et al	China	March, 2020	191	119	72	6/9	(1)
33.	Wu Y et al	China	March, 2020	297	147	150	8/9	(5)
34.	Gao Q et al	China	January to February ,2020	213	108	105	7/9	(5)
35.	Chen X et al	China	February 2020	291	145	146	8/9	(5)
36.	Zhang G et al	China	December 2019	221	108	113	7/9	(5)
37.	Wu W et al	China	March, 2020	21	10	11	8/9	(5)
38.	Cao M et al	China	February, 2020	128	60	68	7/9	(5)
39.	Chung et al	China	March, 2020	20	13	7	7/9	(6)
40.	Xiao F et al	China	March, 2020	73	41	32	7/9	(6)
41.	Qi D et al	China	January to February ,2020	267	149	118	6/9	(6)
42.	Liang et al	China	China	1590	911	679	7/9	(6)

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411	43.	Wang Y et al	China	February, 2020	55	22	23	6/9
	44.	Nicholas E et al	UK	April 2020	68	32	36	9/9
412	45.	Mizumoto K et al	Japan	March, 2020	634	321	313	8/9
	46.	Chen X et al	China	March, 2020	48	37	11	7/9
	47.	Cheng J et al	China	March, 2020	1079	573	505	6/9
413	48.	Li J et al	China	March, 2020	47	28	19	9/9
	49.	Tian S et al	China	April 2020	262	127	135	8/9
	50.	Li et al	China	March, 2020	425	240	185	7/9
414	51.	Liu Y et al	China	February, 2020	109	59	50	6/9
	52.	Cao W et al	China	February, 2020	198	101	97	9/9
	53.	Chaolin et al	China	February, 2020	41	30	11	6/9
415	54.	Yang X et al	China	February, 2020	52	35	17	8/9
	55.	Liu L et al	China	February, 2020	51	32	19	8/9
	56.	Huang C et al	China	February, 2020	41	30	11	8/9
416	57.	Wang D et al	China	February, 2020	138	75	63	6/9

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429 Table 2

430	Variables	Characteristics	Pooled prevalence (95% CI)	I²(P-value)
431	By province in china	Wuhan	72.05 (71.71-72.35)	96.6 (0.00)
432		Shanghai	51.01 (44.05-57.97)	-
433		Hubei	50.40 (50.1-50.80)	66.7 (0.001)
434		Zhonghua	54.07 (95% CI:51.63-56.51)	37.9 (0.139)
435		Zhejiang	46.45 (39.10-53.81)	99.4 (0.00)
436		Shenzhen	63.52 (51.64-75.40)	0.0 (0.796)
437		Jiangsu	44.84 (35.99-53.68)	29 (0.235)
438		Chongqing	52.20 (47.95-56.44)	65.1 (0.09)
439		outside china	53.17 (52.81-53.53)	99.4 (0.00)
440		By country	China	55.99(51.99-59.99)
441	Africa		39.21(34.85-43.84)	-
442	Italy		59.80(59.16-60.44)	-
443	Korea		37.77(36.31-39.24)	-
444	Singapore		50.00(26.90-73.10)	-
445	By JBI quality score	≥7	53.66 (95% CI:49.23-58.09)	99.5 (0.00)
446		<7	56.79 (95% CI:52.79-60.990)	94.7 (0.00)
447	By sample size	≥384	53.86 (47.09-60.63)	99.9 (0.00)
448		<384	54.96 (52.35-57.57)	64.5(0.00)

447 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

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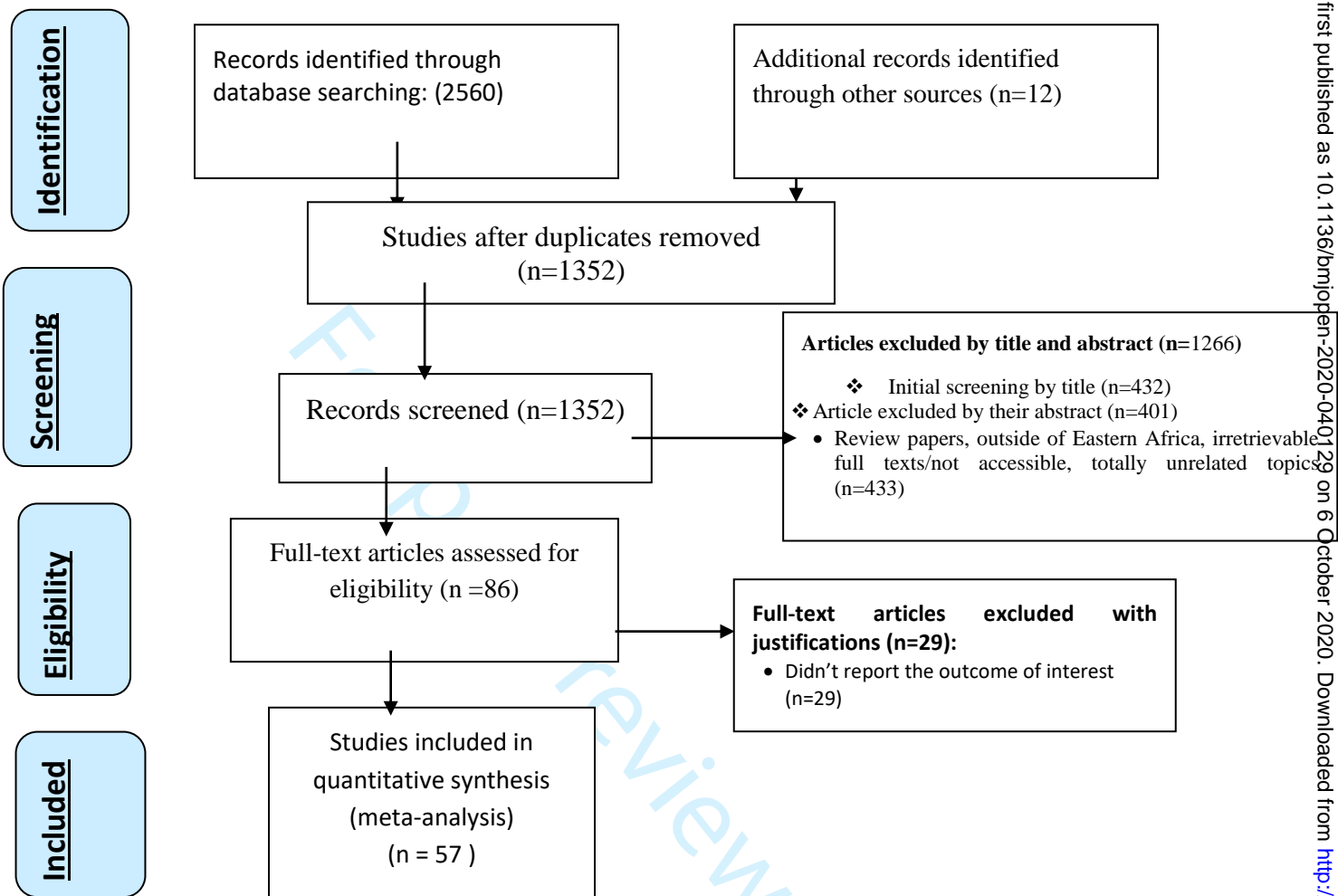


Figure 1: PRISMA flow diagram showed the results of the search and reasons for exclusion

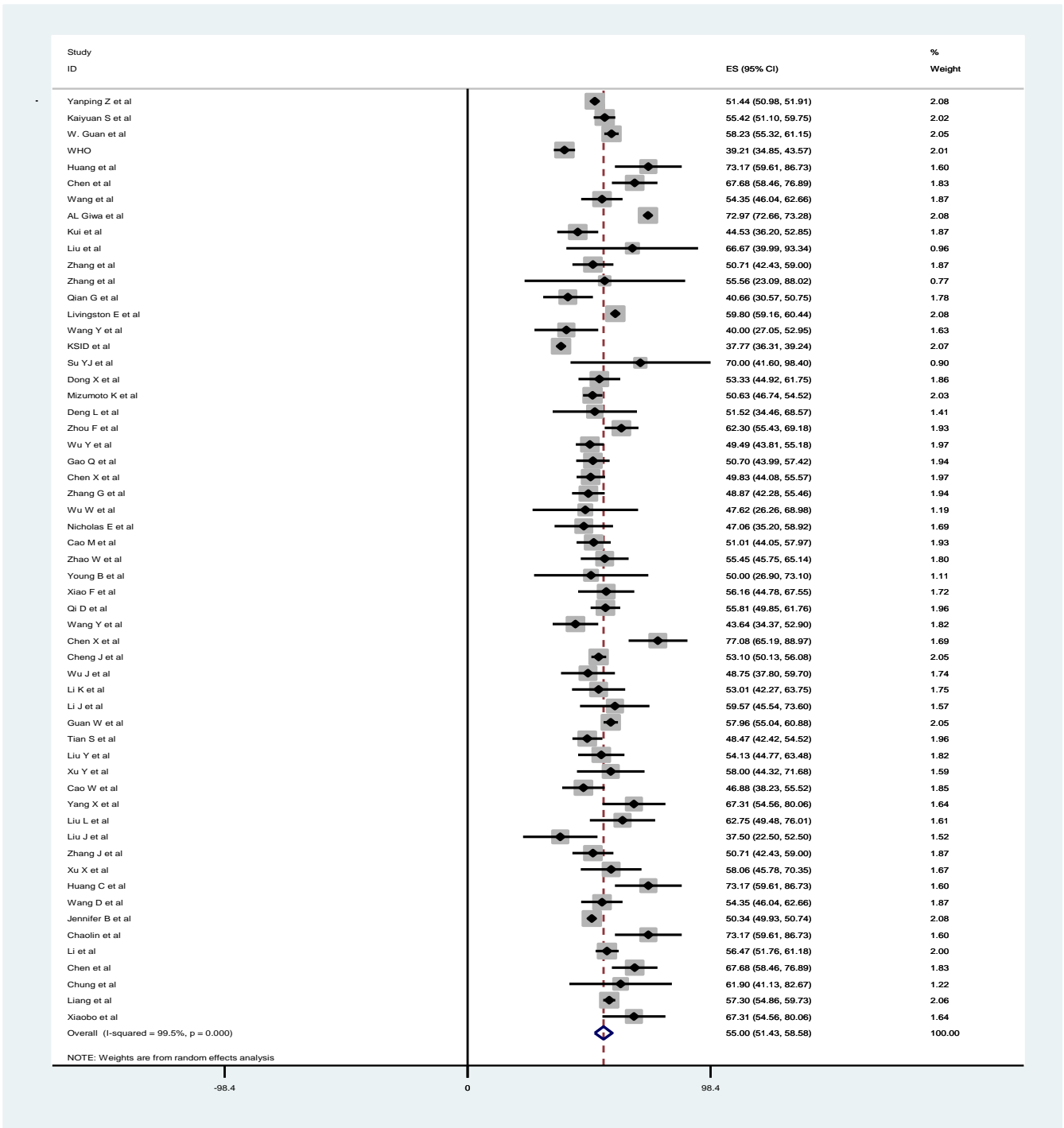
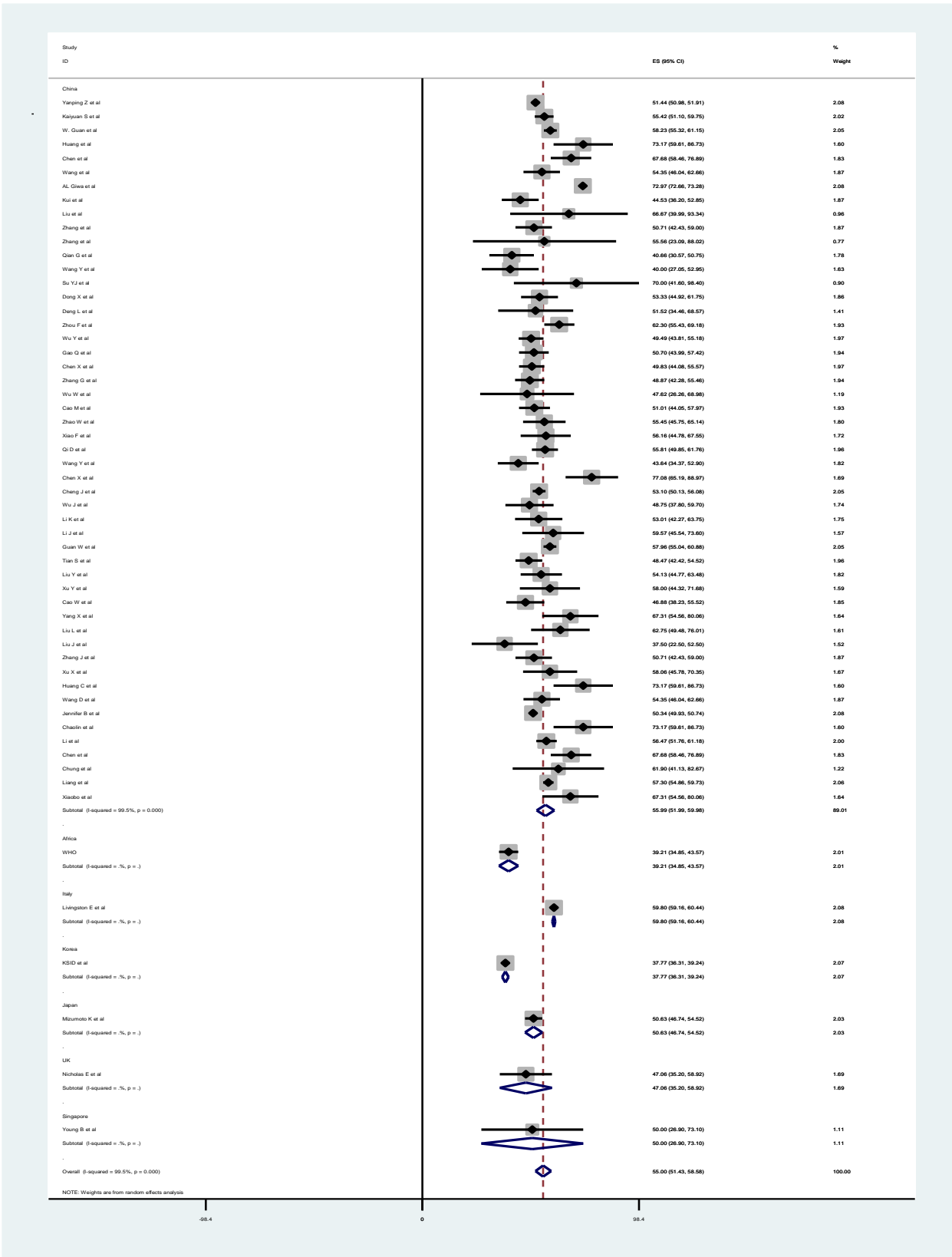


Figure 2: Forest plot showing the pooled prevalence of COVID-19 confirmed cases among male

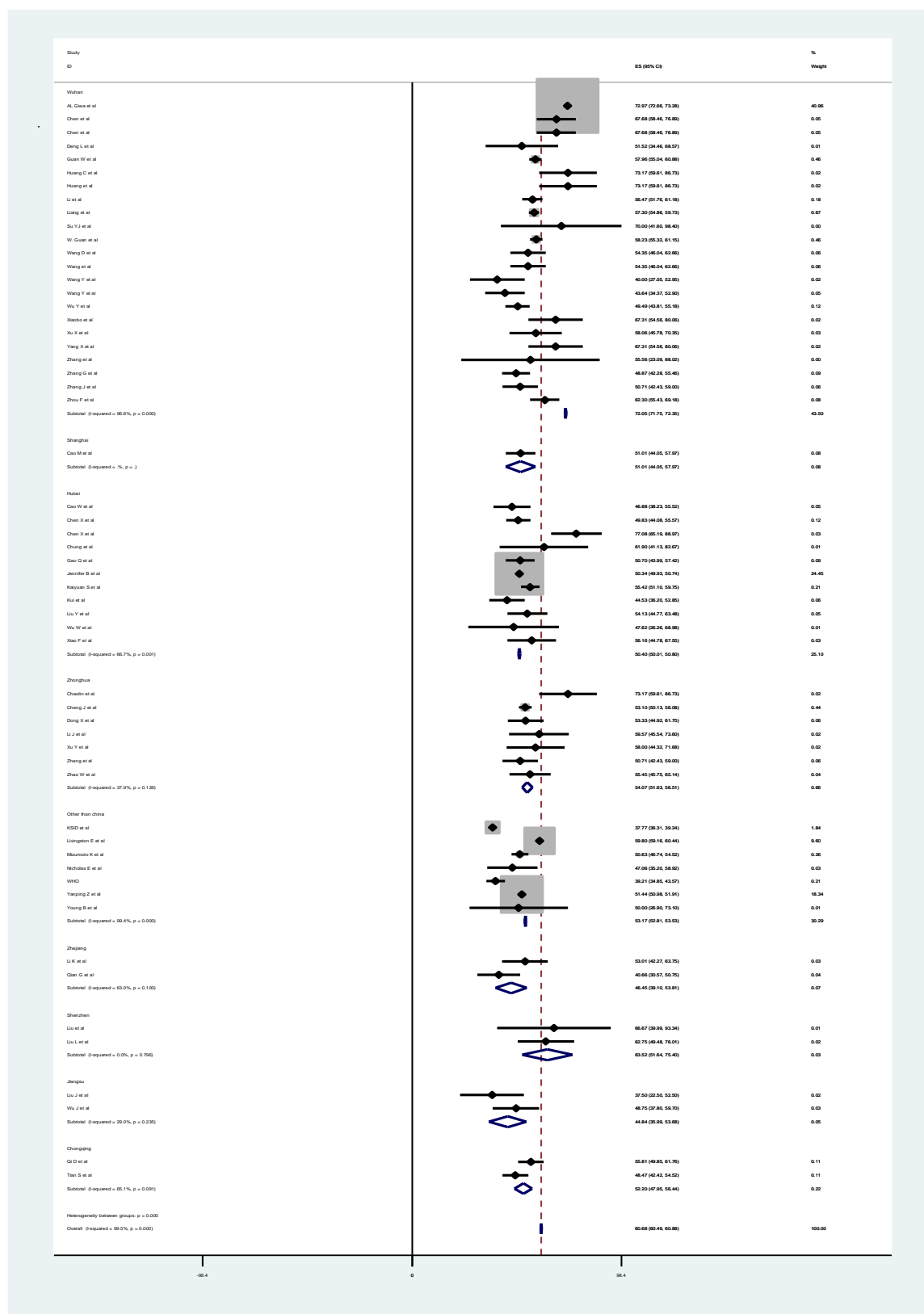
Study omitted	Coef.	[95% Conf. Interval]
Cheng J et al	20.732838	20.445127 21.020546
Xu X et al	17.418531	17.156216 17.680845
Liu L et al	17.381458	17.119438 17.643478
Yao et al	17.516275	17.25304 17.77951
wang Yet al	17.346966	17.085199 17.608732
Wu J et al	17.362354	17.100435 17.624273
Xia W et al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

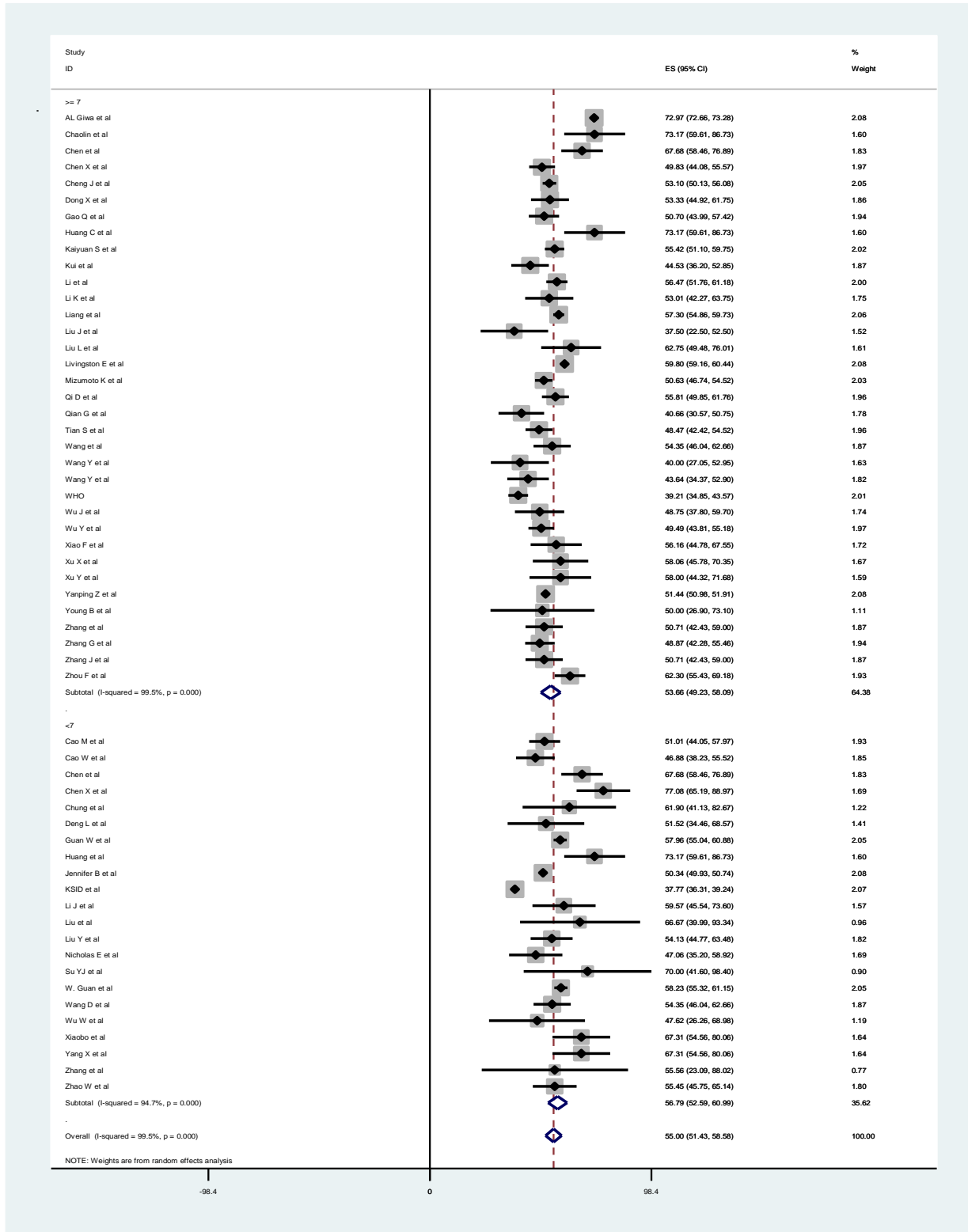


Supplementary Figure 1: Sub group analysis for prevalence of COVID-19 among males by countries

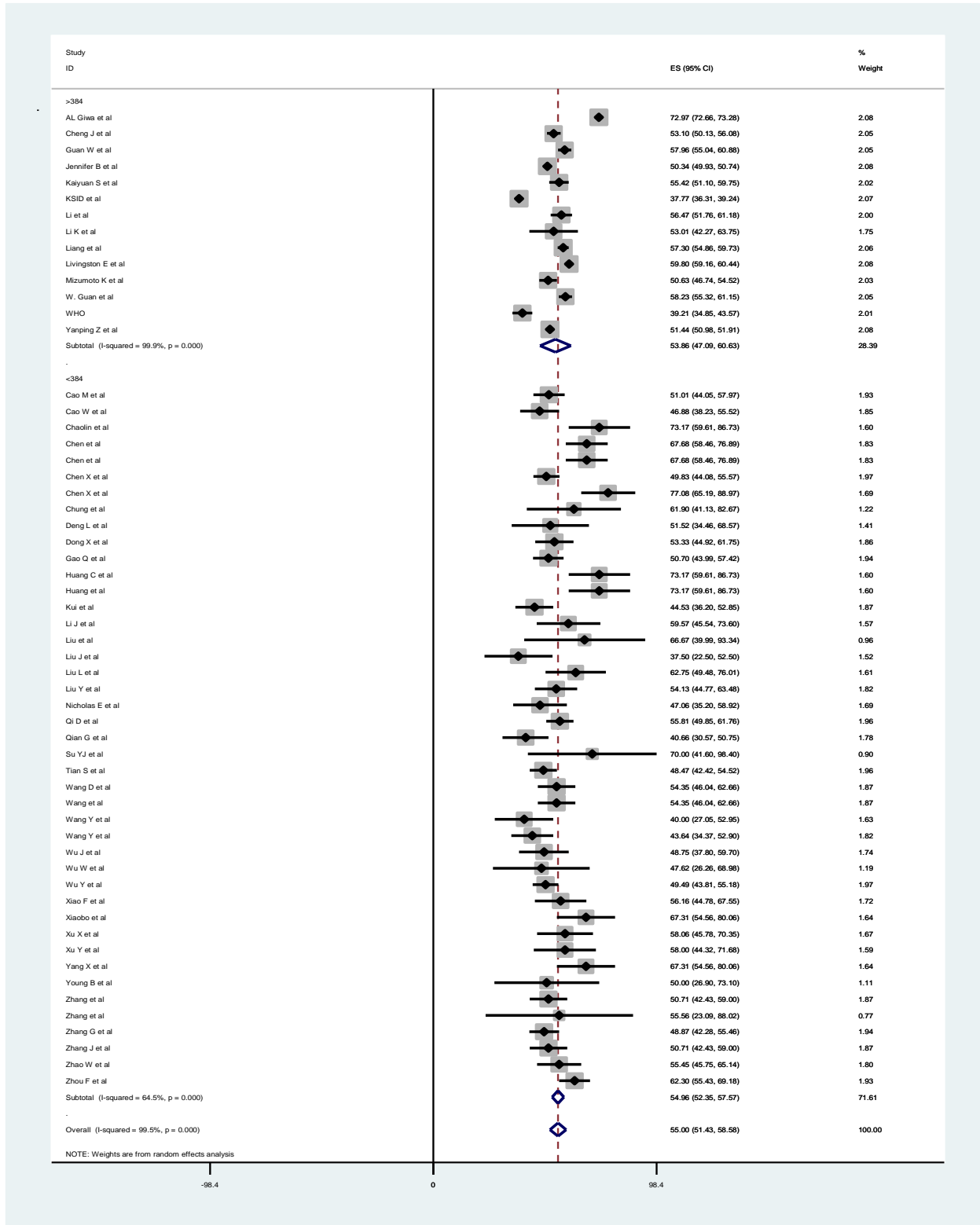
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Supplementary Figure 2: Subgroup analysis of the prevalence of COVID-19 by province in china



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

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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

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60

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?				

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BMJ Open

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

Journal:	<i>BMJ Open</i>
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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1 **Sex difference in coronavirus disease (COVID-19): A systematic review and meta-analysis**

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

13 **Abstract**

14 **Objective:** To assess the sex difference in the prevalence of coronavirus disease (COVID-19) confirmed cases

15 **Design:** Systematic review and meta-analysis.

16 **Setting:** PubMed, Cochrane library, and Google Scholar were searched for related information. The authors developed a data
17 extraction form on the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number
18 female patients, and the number of male patients. Using STATA 14 for analysis authors pooled the overall prevalence male and/or
19 female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I² statistics.
20 Subgroup and sensitivity analysis was done Publication bias was also checked.

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

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

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

24 **Result:** A total of 57 studies with 221195 participants were used for analysis. The pooled prevalence of COVID-19 among males was
25 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
26 study. Moreover a funnel plot showed symmetrical distribution. Egger's regression test p-value was not significant, which indicates
27 the absence of publication bias in both outcomes.

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

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

32 **Article summary**

- 33 • A total of 57 studies with 221195 participants were used for the systematic review and meta-analysis.
- 34 • 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
35 analysis showed the findings were not dependent on a single study. Moreover a funnel plot showed symmetrical distribution.
36 Egger's regression test p-value was not significant, which indicates the absence of publication bias in both outcomes.
- 37 • The prevalence of symptomatic COVID-19 found to be higher among males than females.
- 38 • The high prevalence of smoking and alcohol consumption has contributed for high prevalence of COVID-19 among males.
- 39 • Additional studies regarding discrepancy severity and mortality rate due to COVID-19 among males and females and
40 associated factors is recommended.

42 **Strength and limitations**

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3 43 This systematic review and meta- analysis has several strengths: we used a pre-specified protocol for search strategy and data
4 44 abstraction and used internationally accepted tools for a critical appraisal system for quality assessment of individual studies. Besides
5 45 we employed subgroup analysis, publication bias and sensitivity analysis. Nevertheless, this review had some limitations: because of
6 46 the inclusion of studies which are published in English only, language bias is likely. In addition most included are from China due to
7 47 lack of literatures from other countries in the world which reported the outcome of interest. However, the data in this review permit to
8 48 systematically review and analyze the pooled prevalence of COVID-19 among males.
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17 50 **Background**

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19 51 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
20 52 indicated by the substantial rise in the number of cases and the fast geographical spread of the disease (1-4). The WHO announced that
21 53 the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19) (5, 6). The virus has now been named Severe
22 54 Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) (7).
23 55 COVID-19 has now been declared as a Public Health Emergency of International Concern by the WHO on 30th January 2020(8).
24 56 COVID-19 affects people differently, in terms of infection with the virus SARS-CoV-2 and mortality rates(9-10).
25 57 Susceptibility to symptomatic COVID-19 seems to be associated with age, biological sex, and comorbidities (11). Although the
26 58 COVID-19 causes a mild illness in a majority of cases, severe illness requiring hospital admission is not uncommon (12). Besides, it
27 59 has the potential to precipitate a life-threatening critical illness, characterized by respiratory failure, circulatory shock, sepsis or other
28 60 organ failure, requiring intensive care(13, 14). According to Global Health 5050 data gathering, the number of COVID-19 confirmed
29 61 cases and the death rate due to COVID-19 is high among males in different countries (15-17).
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62 The report in the lancet and Global Health 5050 summarize, sex-disaggregated data are essential for understanding the distributions of
63 risk, infection, and disease in the population, and the extent to which sex and gender affect clinical outcomes (8). Besides, knowing
64 the degree to which outbreaks upsets women and men in different way is an important step for generating effective, equitable policies
65 and interventions. Since the occurrence of COVID-19 infection in Wuhan, China, in December 2019 (19), it has quickly spread across
66 China and numerous other countries(20-24). So far, 2019-nCoV has affected more than 193 countries with 2,733,591 confirmed
67 cases, including 191185 deaths and 751,404 recovery (25). Even though, some previously published papers have showed the sex
68 variation, those findings are not conclusive due to inconsistency in prevalence of COVID-19 among males and females. Moreover,
69 there is lack of systematic review and meta-analysis which indicated the worldwide clear picture of sex variation on the risk of
70 COVID-19. Hence, this systematic review and meta-analysis was conducted to assess the pooled prevalence of COVID-19 among
71 males and females.

72 **Review question**

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

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

75 **Methods**

76 *Search strategy*

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

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3 83 searches were concluded by March 27, 2020, and four different researchers independently evaluated search results. Using those key
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5 84 terms, the following search map was applied: (prevalence OR proportion OR magnitude) AND (Male OR Female) AND (Novel
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7 85 coronavirus OR Novel coronavirus 2019 OR 2019 nCoV OR COVID-19 OR Wuhan coronavirus OR Wuhan pneumonia OR SARS-
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9 86 CoV-2) AND COVID-19 confirmed patients on PubMed database (Table S1). Thus, the PubMed search combines #1 AND #2 AND
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11 87 #3 AND #4 (Table S1). The searching date was January 2000 to December 2019.

12 13 88 **Study selection and screening**

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15 89 The retrieved studies were exported to Endnote version 8 reference managers to remove duplicate studies. Two investigators (BB and
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17 90 AM) independently screened the selected studies using article's title and abstracts before retrieval of full-text papers. We used pre-
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19 91 specified inclusion criteria to further screen the full-text articles. Disagreements were discussed during a consensus meeting or, if
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21 92 necessary, by including the third and fourth researchers (MW and TG) to make the final decision for the selection of studies to be
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23 93 included in the systematic review and meta-analysis.

24 25 94 **Inclusion and exclusion criteria**

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27 95 Those studies had reported the proportion of male and/or female among COVID-19 confirmed patients and published in the English
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29 96 language. Studies which didn't report the prevalence of male and/or female among COVID-19 confirmed patients were excluded.
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31 97 Citations without abstract and/or full-text, anonymous reports, editorials, and qualitative studies were excluded from the analysis. The
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33 98 Prevalence of male and female as the proportion of male and/or female among COVID-19 confirmed cases within a specific
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35 99 population and multiply by 100 to be prevalence report in both case.

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3 100 **Patient and Public Involvement:** Patients or the public WERE NOT involved in the design, or conduct, or reporting, or
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5 101 dissemination plans of our research
6

7 102 **Quality assessment**

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9 103 Using the Joanna Briggs Institute (JBI) quality appraisal checklist the authors appraised the quality of included studies (26). There was
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11 104 a team of four reviewers and the papers were split amongst the team. Each paper was then assessed by two reviewers and any
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13 105 disagreements were discussed with the third and the fourth reviewers. Studies were considered as low risk or good quality when it
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15 106 scored 4 and above (26), whereas the studies scored 3 and below were considered as high risk or poor quality (Table S2).
16

17 107 **Data extraction**

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19 108 The authors developed a data extraction form on the excel sheet and the following data were extracted from eligible studies: author,
20
21 109 country, sample size, number female patients, and the number of male patients. The data extraction sheet was piloted using 4 papers
22
23 110 randomly, and it was adjusted after piloted the template. Two of the authors extracted the data using the extraction form in
24
25 111 collaboration. The third and fourth authors checked the correctness of the data independently. Any disagreements between reviewers
26
27 112 were resolved through discussions with third and fourth reviewers when required. The mistyping of data was resolved through
28
29 113 crosschecking with the included papers. The case definition considered was as follows: confirmed case: detection of SARS-CoV-2
30
31 114 nucleic acid in a clinical specimen; possible case: any person with at least one of the following symptoms: cough, fever, shortness
32
33 115 of breath, sudden onset of anosmia, ageusia or dysgeusia; probable case: any person with at least one of the following symptoms :
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35 116 cough, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia, with close contact with a confirmed COVID-19
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37 117 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,
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119 **Synthesis of results**

120 The authors transformed the data to STATA 14 for analysis after it was extracted in an excel sheet considering prevalence male and
121 female reported. We pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the
122 heterogeneity of effect size using the Q statistic and the I² statistics. In this study, the I² statistic value of zero indicates true
123 homogeneity, whereas the value 25, 50, and 75% represented low, moderate and high heterogeneity, respectively. Subgroup analysis
124 was done by the study country and sample size. Sensitivity analysis was employed to examine the effect of a single study on the
125 overall estimation. Publication bias was checked by the funnel plot and more objectively through Egger's regression test.

126 **Result**

127 **Study selection**

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

134 **Characteristics of included studies**

135 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
136 The studies included participants ranging from 9 (74) to 78771 (44) (Table1).

137 **Meta-analysis**

138 **Prevalence of COVID-19 among male**

139 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
140 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

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3 141 from those studies revealed that, the pooled prevalence of COVID-19 confirmed cases is 55.00(51.43-58.58; $I^2=99.5\%$; $p<0.001$)
4 142 (Fig.2).

143 **Subgroup analysis of COVID-19 confirmed cases among male**

144 The subgroup analysis was done through stratification by country, providences, sample size and quality score. Based on this, the
145 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),
146 50.00(26.90-73.10) in China, Africa, Italy, Korea, and Singapore respectively (Table 2 and Supplementary Fig 1).

147 The pooled prevalence of COVID-19 among male in Wuhan, Shanghai, Hubei, Zhonghua, outside china, Zhejiang, Shenzhen, Jiangsu,
148 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) ; $I^2=66.7$;
149 $P= 0.001$, 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-
150 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
151 52.20(95% CI:47.95-56.44) ; $I^2=65.1$, $P= 0.09$) respectively (Table 2 and Supplementary Fig 2).

152 Regarding quality score the pooled prevalence of COVID-19 among male in studies which scored greater than or equal to seven was
153 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
154 seven from JBI quality appraisal checklist(Table 2 and Supplementary Fig 3).

155 Regarding sample size the pooled prevalence of COVID-19 among male in studies which have sample size greater than or equal to
156 384 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
157 than seven from JBI quality appraisal checklist(Table 2 and Supplementary figure 4).

158 **Sensitivity analysis**

159 We employed a leave-one-out sensitivity analysis to identify the impact of individual research on the pooled prevalence of severe
160 illness among COVID-19 confirmed cases. The results of this sensitivity analysis showed that our findings were not dependent on a

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3 161 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)
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5 162 Yanping Z ET al after the deletion of a single study (Figure 3).
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7 163 **Publication Bias**

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10 164 We have also checked publication bias and, a funnel plot showed symmetrical distribution. Egger's regression test p-value was 0.599.
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12 165 Both the symmetric funnel plot and the insignificant p-value (<0.05) indicates the absence of publication bias.
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14 166 **Meta-regression**

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16 167 Univariate meta-regression analyses revealed that the prevalence of smoking was found to be high in males. This contributed for high
17 168 prevalence of COVID-19 among males ($P=0.002$). Comorbidities like hypertension (0.042), diabetic mellitus (0.012, chronic
18 169 respiratory disease (0.021), and cardio vascular disease (0.001) were also found to be higher in males and these significantly increases
19 170 the prevalence of COVID-19. Besides, higher proportion of sever/critical illness (0.003) and death (0.001) were also observed among
20 171 males (Table 3).
22

23 172 **Discussion**

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26 173 This systematic review and meta-analysis were conducted to assess the sex difference in getting COVID -19 diseases. Fifty seven
27 174 studies were included in the final analysis. The result of this systematic review and meta-analysis revealed that the pooled prevalence
28 175 of COVID -19 confirmed cases among males and females was found to be 55.00(51.43-56.58; $I^2=99.5\%$; $p<0.001$) and 45.00(41.42-
29 176 48.57) respectively. This indicates COVID -19 is prevalent in males than females.
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34 177 This finding was also reported by other studies (75, 76). A study in Ontario, Canada showed that men were more likely to test
35 178 positive(77, 78). In Pakistan 72% of COVID-19 cases were male(79). According to Global Health 5050 data gathering, the number of
36 179 COVID-19 confirmed cases and the death rate due to COVID-19 is high among males in different countries (15-17).
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39 180 This might be due to behavioral factors and roles which increase the risk of acquiring COVID-19 tend to occur more among men.
40 181 Male are more involved in different risky behaviors like alcohol consumption (80-82), key activities in burial rites; as employees in
41 182 basic sectors and occupations that continue being active and require them to work outside the home and interact with other people
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3 183 during the containment phase (e.g., food or pharmacy manufacturing and sales, agriculture or food production and distribution,
4 184 transportation, and security). Because of such behaviors males mostly don't stay at home, sit together, and remove their mask while
5 185 they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease. In China 50% of
6 186 men in smoke, but because it is not considered acceptable for women to smoke, only 2% of them do so. Smoking is associated with
7 187 adverse outcomes of COVID-19: for instance, the combined results of five studies showed that smokers were 1.4 times more likely
8 188 than non-smokers to have severe symptoms of COVID-19 (83). Besides, smoking is related to higher expression of ACE2 (the
9 189 receptor for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), which might be the reason for the higher prevalence of
10 190 COVID-19 in this subgroup of patients than in women (84).

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14 191 Men tended to develop more symptomatic and serious cases than women, according to the clinical classification of severity. Similar
15 192 occasions occurred during previous coronavirus epidemics: men had worse outcomes of illness from severe acute respiratory
16 193 syndrome (SARS), (85) and a higher risk of dying from Middle East respiratory syndrome (MERS)(86). Biological sex variation is said
17 194 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
18 195 more vigorous immune response to infections and vaccinations(88). Some previous studies on coronaviruses in mice have suggested
19 196 that the hormone estrogen may have a protective role. Estrogens suppress the escalation phase of the immune response that leads to
20 197 increased cytokine release(89). The authors showed that female mice treated with an estrogen receptor antagonist died at close to the
21 198 same rate as the male mice(90).

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26 199 The X chromosome is known to contain the largest number of immune-related genes in the whole genome(80). With their XX
27 200 chromosome, women have a double copy of key immune genes compared to the single copy in XY men. This boost extends to both
28 201 the general reaction to infection (the innate response) and also to the more specific response to microbes including antibody formation
29 202 (adaptive immunity)(86). Thus women's immune systems are generally more responsive to infections. This might mean women are
30 203 able to tackle the novel coronavirus more effectively but this has not yet been proven.

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35 204 Besides, the above listed behavioral factors like smoking and alcohol consumption tend to occur more among men, those behaviors
36 205 predisposes males for cardiac and respiratory diseases. This may also explain the overall higher mortality rates among men (84, 91,
37 206 92). A systematic review and meta-analysis revealed that comorbid disease, such as respiratory system disease, hypertension, and
38 207 cardiovascular disease as risk a risk factors for death compared with patients without comorbidity(93).

208 **Conclusions**

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

217 **Abbreviations**

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

221 **Declarations**

222 **Ethics approval and consent to participate**

223 Not applicable

224 **Consent for publication**

225 Not applicable

226 **Availability of data and material**

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3 227 The datasets analyzed during the current study are available from the corresponding author upon reasonable request.
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5
6 228 **Competing interests**

7
8 229 We have confirmed that we have no competing interests.
9

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11 230 **Funding**

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13 231 No funding was obtained for this study
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21 234 **Authors' contributions**

22
23 235 BB, AM, MW, and TG: developed the study design and protocol, literature review, selection of studies, quality assessment, data
24 236 extraction, statistical analysis, interpretation of the data and developing the initial drafts of the manuscript and prepared the final draft
25 237 of the manuscript. All authors read and approved the final manuscript.
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29
30 238 **Acknowledgments**

31
32 239 We would like to thank the authors of the included primary studies.
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34

35 240 **References**

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407 **Table Legend**

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

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

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3 410 Table 3: a meta-regression analysis showing factors which have effect on the sex difference of COVID-19
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13 419 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	(2)
2.	Liu Y et al	China	Jan11-Jan20	12	8	4	9/9	(2)
3.	Liu Y et al	China	Jan23-Feb8	109	59	50	6/9	(2)
4.	Liu J et al	China	Jan-Feb	40	15	25	8/9	(3)
5.	Wu J et al	China	Jan22-Feb14	80	39	41	8/9	(3)
6.	Xu X et al	China	Jan10-Jan26	62	36	26	8/9	(1)
7.	Xu Y et al	China	Jan-Feb	50	29	21	6/9	(3)
8.	Yao et al	China	Jan01-Feb07	195	115	80	8/9	(3)
9.	Young et al	China	Jan22-Jan31	18	9	9	6/9	(3)
10.	Zhang J et al	China	Jan16-Feb03	140	71	69	8/9	(3)
11.	Zhang M et al	China	Jan18-Feb03	9	5	4	7/9	(3)
12.	Zhao et al	China	Jan16-Feb03	101	56	45	8/9	(3)
13.	Zhu et al	China	Dec01-Feb15	12	8	4	7/9	(3)
14.	Yanping Z et al	China	February 2020	44672	22981	21691	8/9	(3)
15.	W. Guan et al	China	February 2020	1099	640	459	7/9	(4)
16.	WHO ,2020	Africa	March 2020	482	189	177	7/9	(4)
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	(3)
19.	Wang et al	China	March 2020	138	75	63	7/9	(2)

3	420	20.	Kaiyuan S et al	China	February, 2020	507	281	201	6/9
4		21.	AL Giwa et al	China	March, 2020	78771	57482	21289	9/9
5	421	22.	Qian G et al	China	March, 2020	91	37	54	8/9
6		23.	Livingston E et al	Italy	March, 2020	22512	13462	9050	7/9
7		24.	Wang Y et al	China	March, 2020	110	48	62	6/9
8	422	25.	KSID,2020	Korea	February, 2020	4212	1591	2621	9/9
9		26.	Su YJ et al	China	March, 2020	10	7	3	6/9
10		27.	Jennifer B et al	China	March, 2020	59600	30000	29600	8/9
11	423	28.	Kui et al	China	March, 2020	137	61	76	8/9
12		29.	Deng L et al	China	March, 2020	33	17	16	8/9
13		30.	Dong X et al	China	March, 2020	135	72	63	6/9
14	424	31.	Xiaobo et al	China	March, 2020	52	35	17	8/9
15		32.	Zhou F et al	China	March, 2020	191	119	72	6/9
16		33.	Wu Y et al	China	March, 2020	297	147	150	8/9
17	425	34.	Gao Q et al	China	January to February ,2020	213	108	105	7/9
18		35.	Chen X et al	China	February 2020	291	145	146	8/9
19	426	36.	Zhang G et al	China	December 2019	221	108	113	7/9
20		37.	Wu W et al	China	March, 2020	21	10	11	8/9
21		38.	Cao M et al	China	February, 2020	128	60	68	7/9
22	427	39.	Chung et al	China	March, 2020	20	13	7	7/9
23		40.	Xiao F et al	China	March, 2020	73	41	32	7/9
24		41.	Qi D et al	China	January to February ,2020	267	149	118	6/9
25	428	42.	Liang et al	China	China	1590	911	679	7/9
26		43.	Wang Y et al	China	February, 2020	55	22	23	6/9
27		44.	Nicholas E et al	UK	April 2020	68	32	36	9/9
28	429	45.	Mizumoto K et al	Japan	March, 2020	634	321	313	8/9
29		46.	Chen X et al	China	March, 2020	48	37	11	7/9
30	430	47.	Cheng J et al	China	March, 2020	1079	573	505	6/9
31		48.	Li J et al	China	March, 2020	47	28	19	9/9
32		49.	Tian S et al	China	April 2020	262	127	135	8/9
33	431	50.	Li et al	China	March, 2020	425	240	185	7/9
34		51.	Liu Y et al	China	February, 2020	109	59	50	6/9
35	432	52.	Cao W et al	China	February, 2020	198	101	97	9/9
36		53.	Chaolin et al	China	February, 2020	41	30	11	6/9
37		54.	Yang X et al	China	February, 2020	52	35	17	8/9
38	433	55.	Liu L et al	China	February, 2020	51	32	19	8/9
39		56.	Huang C et al	China	February, 2020	41	30	11	8/9
40	434	57.	Wang D et al	China	February, 2020	138	75	63	6/9

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438 Table 2

439	Variables	Characteristics	Pooled prevalence (95% CI)	I²(P-value)
440	By province in china	Wuhan	72.05 (71.71-72.35)	96.6 (0.00)
441		Shanghai	51.01 (44.05-57.97)	-
442		Hubei	50.40 (50.1-50.80)	66.7 (0.001)
443		Zhonghua	54.07 (95% CI:51.63-56.51)	37.9 (0.139)
444		Zhejiang	46.45 (39.10-53.81)	99.4 (0.00)
445		Shenzhen	63.52 (51.64-75.40)	0.0 (0.796)
446		Jiangsu	44.84 (35.99-53.68)	29 (0.235)
447		Chongqing	52.20 (47.95-56.44)	65.1 (0.09)
448		outside china	53.17 (52.81-53.53)	99.4 (0.00)
449		By country	China	55.99(51.99-59.99)
450	Africa		39.21(34.85-43.84)	-
451	Italy		59.80(59.16-60.44)	-
452	Korea		37.77(36.31-39.24)	-
453	Singapore		50.00(26.90-73.10)	-
454	By JBI quality score	≥ 7	53.66 (95% CI:49.23-58.09)	99.5 (0.00)
455		< 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)

456 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

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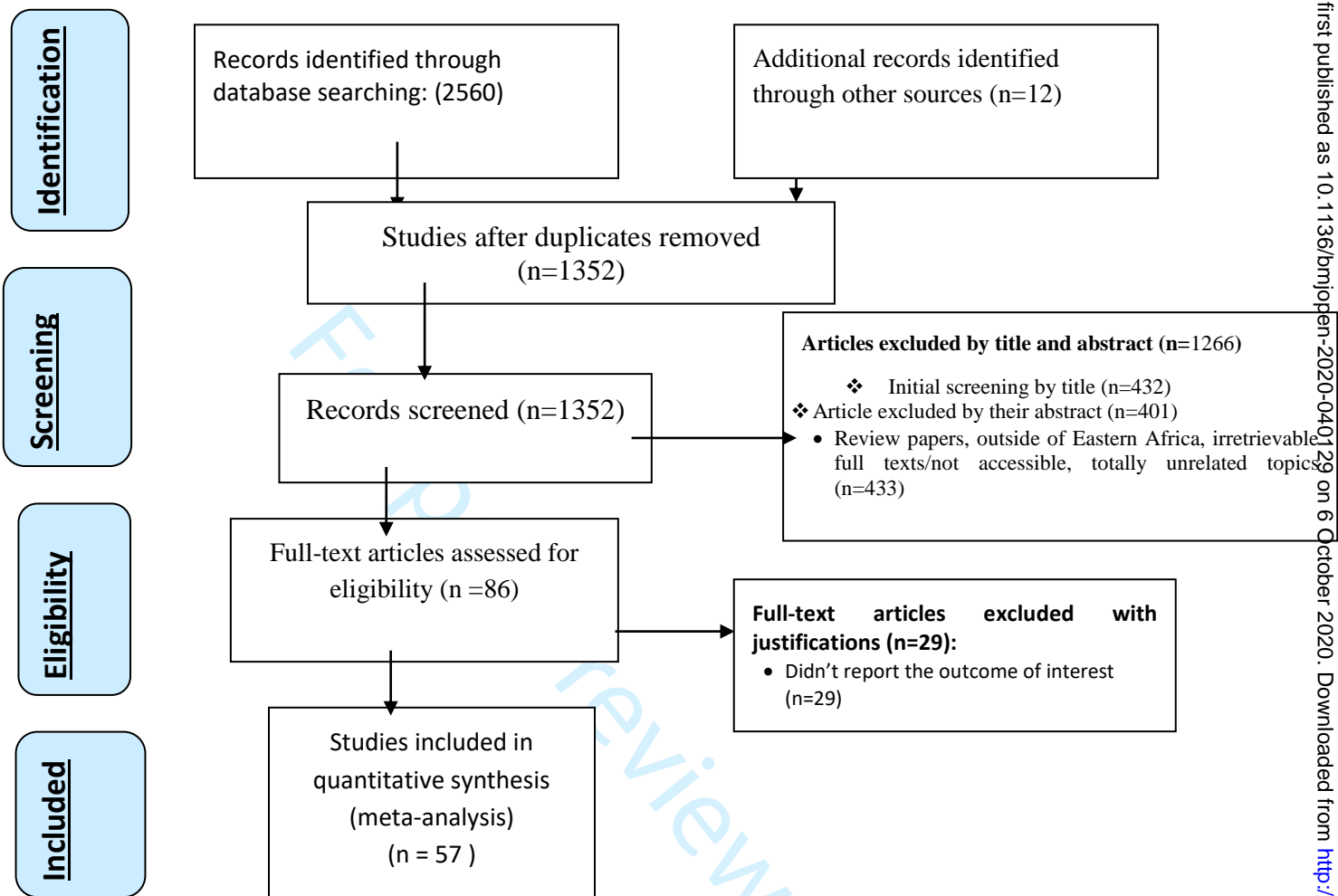


Figure 1: PRISMA flow diagram showed the results of the search and reasons for exclusion

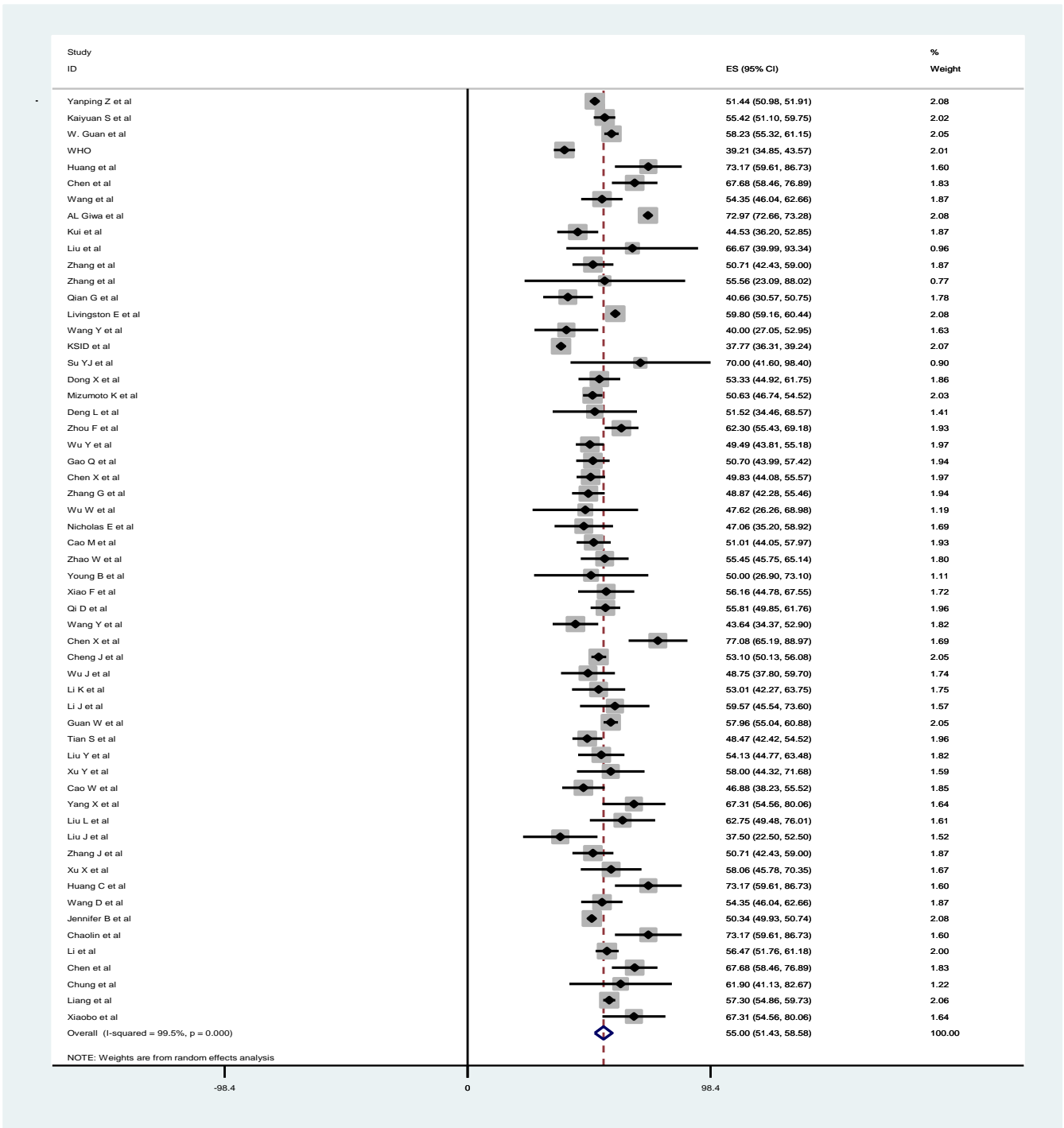
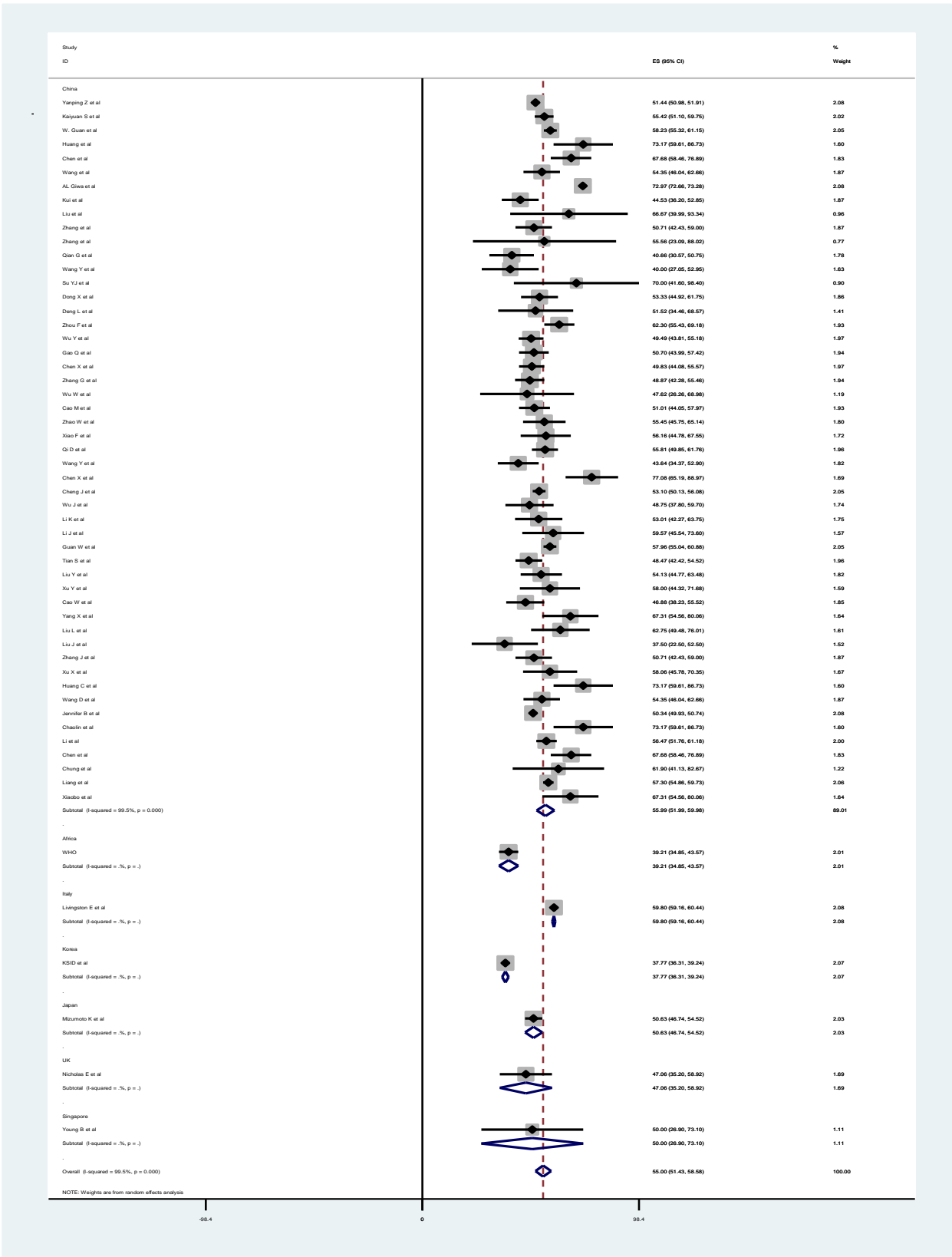


Figure 2: Forest plot showing the pooled prevalence of COVID-19 confirmed cases among male

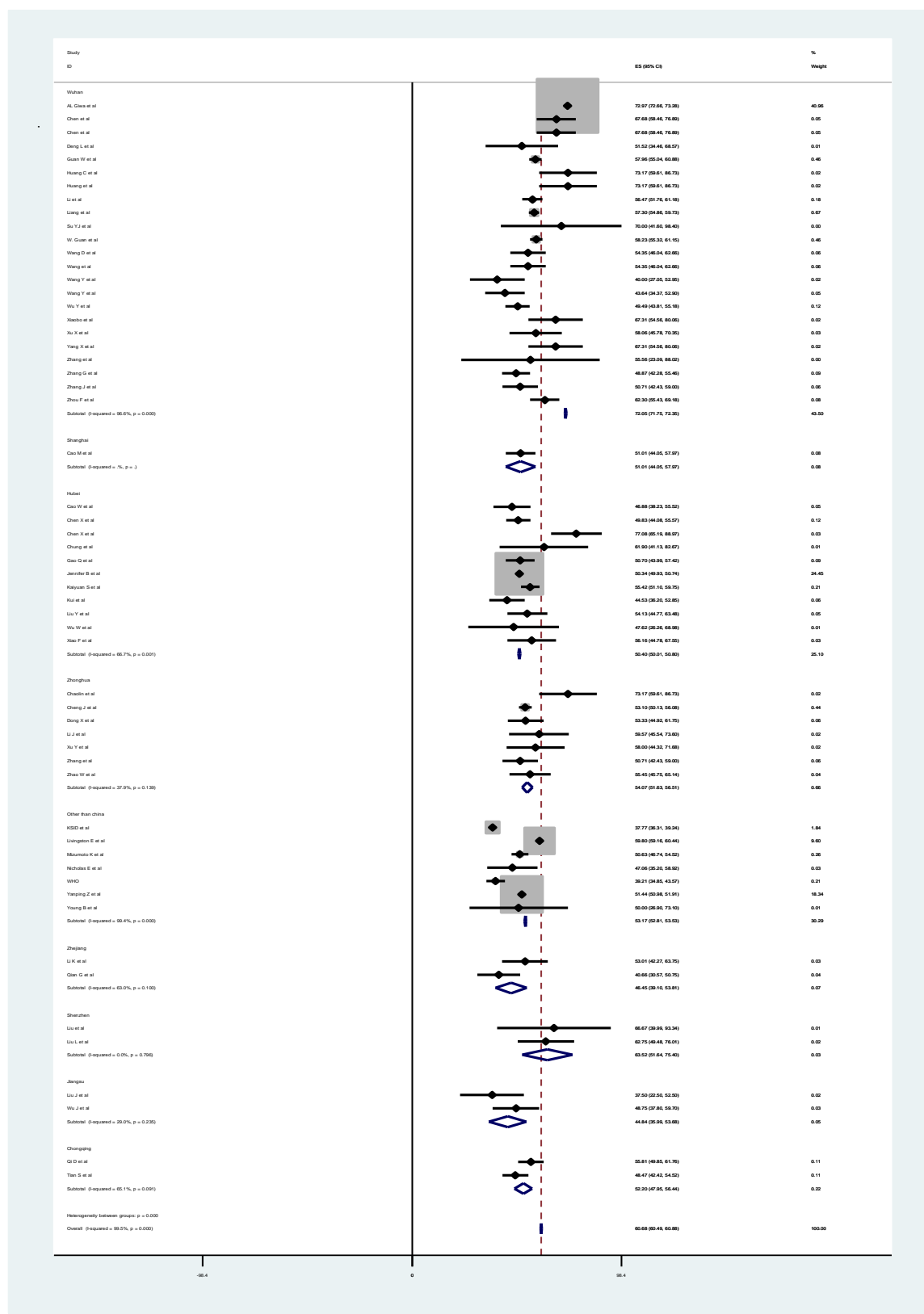
Study omitted	Coef.	[95% Conf. Interval]
Cheng J et al	20.732838	20.445127 21.020546
Xu X et al	17.418531	17.156216 17.680845
Liu L et al	17.381458	17.119438 17.643478
Yao et al	17.516275	17.25304 17.77951
wang Yet al	17.346966	17.085199 17.608732
Wu J et al	17.362354	17.100435 17.624273
Xia W et al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

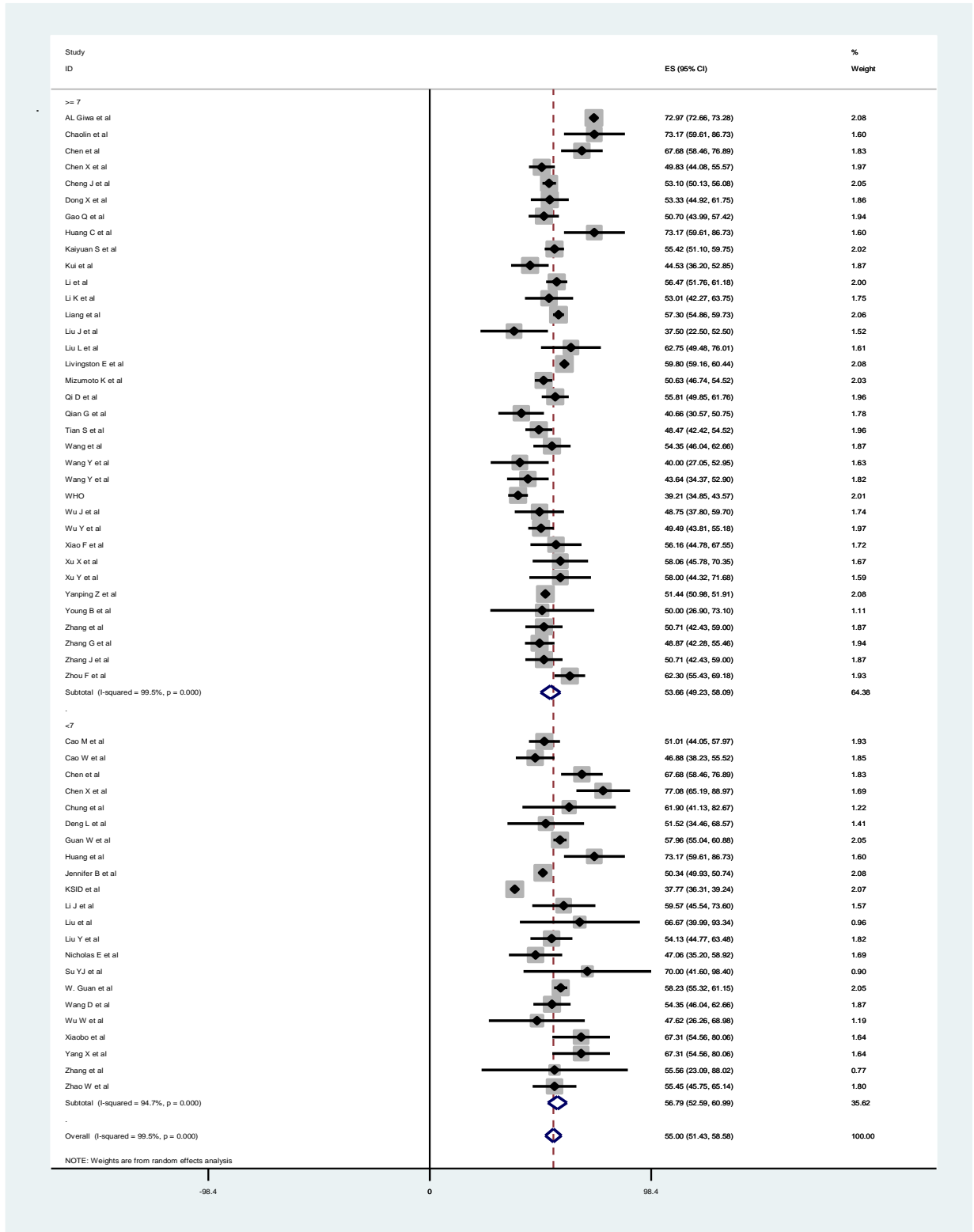


Supplementary Figure 1: Subgroup analysis for prevalence of COVID-19 among males by countries

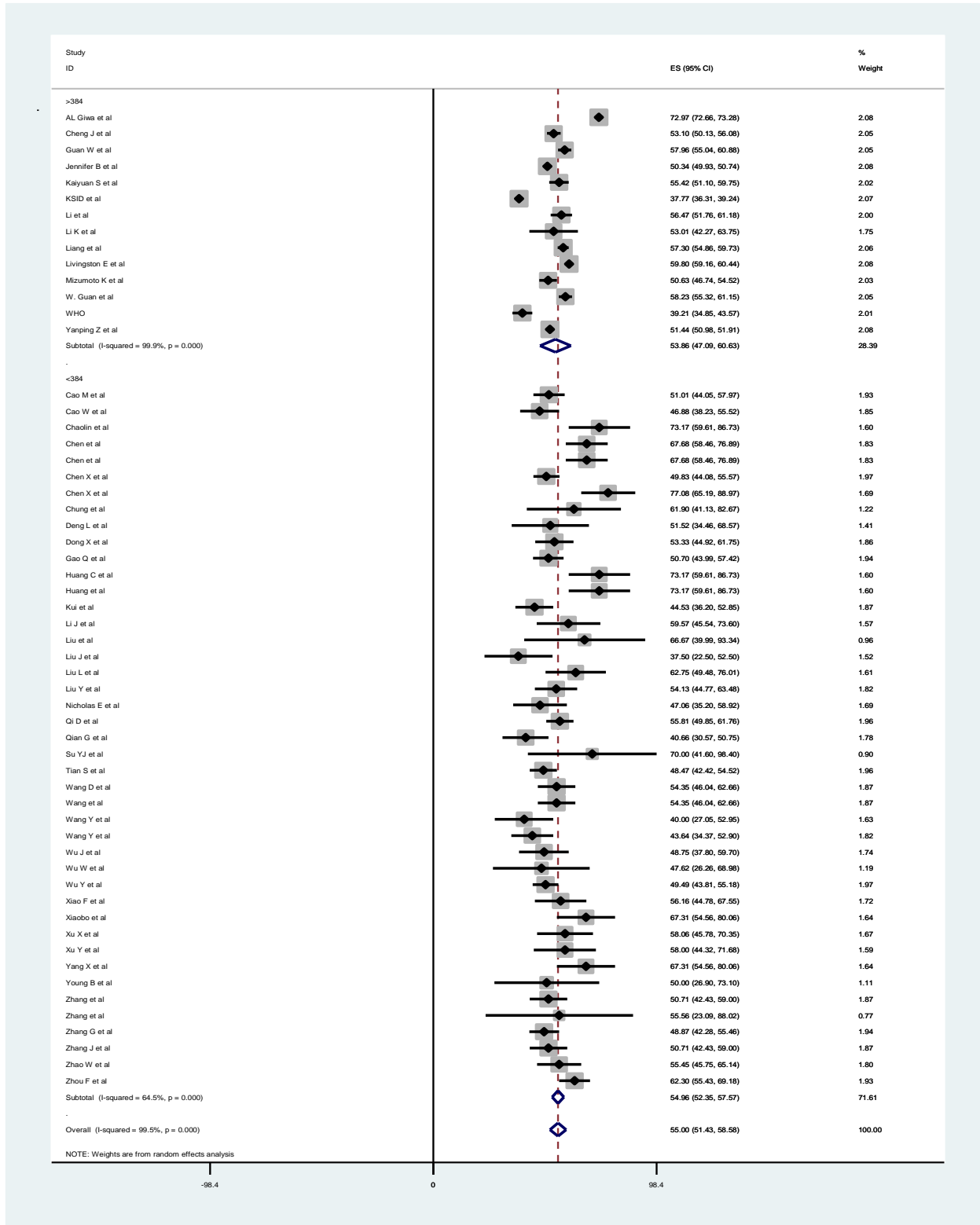
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Supplementary Figure 2: Subgroup analysis of the prevalence of COVID-19 by province in china



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

3	40. Xiao F et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
4	41. Qi D et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
5	42. Liang et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included
6	43. Wang Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
7	44. Nicholas E et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
8	45. Mizumoto K et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
9	46. Chen X et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
10	47. Cheng J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
11	48. Li J et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
12	49. Tian S et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
13	50. Li et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
14	51. Liu Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
15	52. Cao W et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
16	53. Chaolin et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
17	54. Yang X et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
18	55. Liu L et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
19	56. Huang C et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
20	57. Wang D et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
21	58. Cheng J et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
22	59. Wu J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
23	60. Li K et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
24	61. Li J et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
25	62. Guan W et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
26	63. Tian S et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
27	64. Liu Y et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
28	65. Xu Y et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
29	66. Cao W et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
30	67. Yang X et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
31	68. Liu L et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
32	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

1 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?				

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

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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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3 1 **Sex difference in coronavirus disease (COVID-19): A systematic review and meta-analysis**

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33 16 **Running title:** Sex difference in coronavirus disease (COVID-19)

34
35 17 **Abstract**

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37 18 **Objective:** To assess the sex difference in the prevalence of coronavirus disease (COVID-19) confirmed cases

38
39 19 **Design:** Systematic review and meta-analysis.

20 **Setting:** PubMed, Cochrane library, and Google Scholar were searched for related information. The authors developed a data
21 extraction form on the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number
22 female patients, and the number of male patients. Using STATA 14 for analysis authors pooled the overall prevalence male and/or
23 female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I² statistics.
24 Subgroup and sensitivity analysis was done Publication bias was also checked.

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

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

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

28 **Result:** A total of 57 studies with 221195 participants were used for analysis. The pooled prevalence of COVID-19 among males was
29 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
30 study. Moreover a funnel plot showed symmetrical distribution. Egger's regression test p-value was not significant, which indicates
31 the absence of publication bias in both outcomes.

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

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

36 Article summary

37 Strength and limitations

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

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

43 **Background**

44 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
45 indicated by the substantial rise in the number of cases and the fast geographical spread of the disease (1-4). The WHO announced that
46 the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19) (5, 6). The virus has now been named Severe
47 Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) (7).
48 COVID-19 has now been declared as a Public Health Emergency of International Concern by the WHO on 31st January 2020(8).
49 COVID-19 affects people differently, in terms of infection with the virus SARS-CoV-2 and mortality rates(9-10).
50 Susceptibility to symptomatic COVID-19 seems to be associated with age, biological sex, and comorbidities(11). Although the
51 COVID-19 causes a mild illness in a majority of cases, severe illness requiring hospital admission is not uncommon (12). Besides, it
52 has the potential to precipitate a life-threatening critical illness, characterized by respiratory failure, circulatory shock, sepsis or other
53 organ failure, requiring intensive care(13, 14). According to Global Health 5050 data gathering, the number of COVID-19 confirmed
54 cases and the death rate due to COVID-19 is high among males in different countries (15-17).

55 The report in the lancet and Global Health 5050 summarize, sex-disaggregated data are essential for understanding the distributions of
56 risk, infection, and disease in the population, and the extent to which sex and gender affect clinical outcomes(18). Besides, knowing
57 the degree to which outbreaks upsets women and men in different way is an important step for generating effective, equitable policies
58 and interventions. Since the occurrence of COVID-19 infection in Wuhan, China, in December 2019 (19), it has quickly spread across
59 China and numerous other countries(20-24). So far, 2019-nCoV has affected more than 193 countries with 2,733,591 confirmed
60 cases, including 191185 deaths and 751,404 recovery (25). Even though, some previously published papers have shown the sex

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3 61 variation, those findings are not conclusive due to inconsistency in prevalence of COVID-19 among males and females. Moreover,
4 62 there is lack of systematic review and meta-analysis which indicated the worldwide clear picture of sex variation on the risk of
5 63 COVID-19. Hence, this systematic review and meta-analysis was conducted to assess the pooled prevalence of COVID-19 among
6 64 males and females.
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10 65 **Review question**

11 66 The review questions of this systematic review and meta-analysis were:

- 12
13 67 Are men more susceptible to getting symptomatic COVID-19?
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16 68 **Methods**

17 18 69 ***Search strategy***

19 70 This systematic review and meta-analysis identified studies that revealed data on the proportion of sex in COVID-19 confirmed case.
20 71 We used the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines to search electronic databases
21 72 it presents as a supplementary file ("PRISMA checklist COVID with SEX.pdf (v1.0). We retrieved studies from Google Scholar,
22 73 PubMed, Scopus, Web of Sciences Cochrane library, research gate, and institutional repositories as described in detail previously (26,
23 74 27). The search included keywords that are the combinations of population, condition/outcome, and context. A snowball searching for
24 75 the references of relevant papers for linked articles was also performed. Those search terms or phrases including were: The search
25 76 terms used were: "Novel coronavirus," "Novel coronavirus 2019", "2019 nCoV", "COVID-19", "Wuhan coronavirus," "Wuhan
26 77 pneumonia," and "SARS-CoV-2." Articles published in English language were considered from January 1, 2020. The searches were
27 78 concluded by March 27, 2020, and four different researchers independently evaluated search results. Using those key terms, the
28 79 following search map was applied: (prevalence OR proportion OR magnitude) AND (Male OR Female) AND (Novel coronavirus OR
29 80 Novel coronavirus 2019 OR 2019 nCoV OR COVID-19 OR Wuhan coronavirus OR Wuhan pneumonia OR SARS-CoV-2) AND
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3 81 COVID-19 confirmed patients on PubMed database (Table S1). Thus, the PubMed search combines #1 AND #2 AND #3 AND #4
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5 82 (Table S1). The searching date was January 2000 to December 2019.
6
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8 83 **Study selection and screening**

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10 84 The retrieved studies were exported to Endnote version 8 reference managers to remove duplicate studies as described in detail
11 85 previously (26, 27). Two investigators (BB and AM) independently screened the selected studies using article's title and abstracts
12 86 before retrieval of full-text papers. We used pre-specified inclusion criteria to further screen the full-text articles. Disagreements were
13 87 discussed during a consensus meeting or, if necessary, by including the third and fourth researchers (MW and TG) to make the final
14 88 decision for the selection of studies to be included in the systematic review and meta-analysis.
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19 89 **Inclusion and exclusion criteria**

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21 90 Those studies had reported the proportion of male and/or female among COVID-19 confirmed patients and published in the English
22 91 language. Studies which didn't report the prevalence of male and/or female among COVID-19 confirmed patients were excluded.
23 92 Citations without abstract and/or full-text, anonymous reports, editorials, and qualitative studies were excluded from the analysis. The
24 93 Prevalence of male and female as the proportion of male and/or female among COVID-19 confirmed cases within a specific
25 94 population and multiply by 100 to be prevalence report in both case.
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30 95 **Patient and Public Involvement:** Patients or the public WERE NOT involved in the design, or conduct, or reporting, or
31 96 dissemination plans of our research
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35 97 **Quality assessment**

36 98 Using the Joanna Briggs Institute (JBI) quality appraisal checklist the authors appraised the quality of included studies (28). There was
37 99 a team of four reviewers and the papers were split amongst the team. Each paper was then assessed by two reviewers and any
38 100 disagreements were discussed with the third and the fourth reviewers. Studies were considered as low risk or good quality when it
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3 101 scored 4 and above (28), whereas the studies scored 3 and below were considered as high risk or poor quality as described in detail
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5 102 previously (26, 27) (Table S2).
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7 103 **Data extraction**

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9 104 The authors developed a data extraction form on the excel sheet and the following data were extracted for eligible studies: author,
10
11 105 country, sample size, number female patients, and the number of male patients as described in detail previously (26, 27). The data
12
13 106 extraction sheet was piloted using 4 papers randomly, and it was adjusted after piloted the template as described in detail previously
14
15 107 (26, 27). Two of the authors extracted the data using the extraction form in collaboration. The third and fourth authors checked the
16
17 108 correctness of the data independently. Any disagreements between reviewers were resolved through discussions with third and fourth
18
19 109 reviewers when required as described in detail previously (26, 27). The mistyping of data was resolved through crosschecking with the
20
21 110 included papers. The case definition considered was as follows: confirmed case: detection of SARS-CoV-2 nucleic acid in a clinical
22
23 111 specimen; possible case: any person with at least one of the following symptoms: cough, fever, shortness of breath, sudden
24
25 112 onset of anosmia, ageusia or dysgeusia; probable case: any person with at least one of the following symptoms : cough, fever,
26
27 113 shortness of breath, sudden onset of anosmia, ageusia or dysgeusia, with close contact with a confirmed COVID-19 case in the 14
28
29 114 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
30
31 115 institution for vulnerable people where ongoing COVID-19 transmission has been confirmed.

31 116 **Synthesis of results**

32
33 117 The authors transformed the data to STATA 14 for analysis after it was extracted in an excel sheet considering prevalence male and
34
35 118 female reported. We pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the
36
37 119 heterogeneity of effect size using the Q statistic and the I² statistics. In this study, the I² statistic value of zero indicates true
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39 120 homogeneity, whereas the value 25, 50, and 75% represented low, moderate and high heterogeneity, respectively. Subgroup analysis
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121 was done by the study country and sample size. Sensitivity analysis was employed to examine the effect of a single study on the
122 overall estimation. Publication bias was checked by the funnel plot and more objectively through Egger's regression test.

123 **Result**

124 **Study selection**

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

131 **Characteristics of included studies**

132 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
133 The studies included participants ranging from 9 (76) to 78771 (46) (Table1).

134 **Meta-analysis**

135 **Prevalence of COVID-19 among male**

136 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
137 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
138 from those studies revealed that, the pooled prevalence of COVID-19 confirmed cases is 55.00(51.43-59.58; I²=99.5%; p<0.001)
139 (Figure 2).

140 **Subgroup analysis of COVID-19 confirmed cases among male**

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3 141 The subgroup analysis was done through stratification by country, providences, sample size and quality score. Based on this, the
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5 142 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),
6
7 143 50.00(26.90-73.10) in China, Africa, Italy, Korea, and Singapore respectively (Table 2 and Supplementary Fig 1).

8
9 144 The pooled prevalence of COVID-19 among male in Wuhan, Shanghai, Hubei, Zhonghua, outside china, Zhejiang, Shenzhen, Jiangsu,
10
11 145 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;
12
13 146 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-
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15 147 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
16
17 148 52.20(95% CI:47.95-56.44) ; I^2 =65.1, P= 0.09) respectively (Table 2 and Supplementary Fig 2).

18
19 149 Regarding quality score the pooled prevalence of COVID-19 among male in studies which scored greater than or equal to seven was
20
21 150 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
22
23 151 seven from JBI quality appraisal checklist(Table 2 and Supplementary Fig 3).

24
25 152 Regarding sample size the pooled prevalence of COVID-19 among male in studies which have sample size greater than or equal to
26
27 153 384 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
28
29 154 than seven from JBI quality appraisal checklist(Table 2 and Supplementary figure 4).

30 31 155 **Sensitivity analysis**

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33 156 We employed a leave-one-out sensitivity analysis to identify the impact of individual research on the pooled prevalence of severe
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35 157 illness among COVID-19confirmed cases. The results of this sensitivity analysis showed that our findings were not dependent on a
36
37 158 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)
38
39 159 Yanping Z ET al after the deletion of a single study (Figure 3).

40 41 160 **Publication Bias**

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3 161 We have also checked publication bias and, a funnel plot showed symmetrical distribution. Egger's regression test p-value was 0.599.
4
5 162 Both the symmetric funnel plot and the insignificant p-value (<0.05) indicates the absence of publication bias.
6

7 163 **Meta-regression**

8
9 164 Univariate meta-regression analyses revealed that the prevalence of smoking was found to be high in males. This contributed for high
10 prevalence of COVID-19 among males (P=0.002). Comorbidities like hypertension (0.042), diabetic mellitus (0.012, chronic
11 165 respiratory disease (0.021), and cardio vascular disease (0.001) were also found to be higher in males and these significantly increases
12 166 the prevalence of COVID-19. Besides, higher proportion of sever/critical illness (0.003) and death (0.001) were also observed among
13 167 males (Table 3).
14
15 168

169 **Discussion**

170 This systematic review and meta-analysis were conducted to assess the sex difference in getting COVID -19 diseases. Fifty seven
171 studies were included in the final analysis. The result of this systematic review and meta-analysis revealed that the pooled prevalence
172 of COVID -19 confirmed cases among males and females was found to be 55.00(51.43-56.58; I2=99.5%; p<.001) and 45.00(41.42-
173 48.57) respectively. This indicates COVID -19 is prevalent in males than females.

174 This finding was also reported by other studies (77, 78). A study in Ontario, Canada showed that men were more likely to test
175 positive(79, 80). In Pakistan 72% of COVID-19 cases were male(81). According to Global Health 5050 data gathering, the number of
176 COVID-19 confirmed cases and the death rate due to COVID-19 is high among males in different countries (15-17).

177 This might be due to behavioral factors and roles which increase the risk of acquiring COVID-19 tend to occur more among men.
178 Male are more involved in different risky behaviors like alcohol consumption (82-84), key activities in burial rites; as employees in
179 basic sectors and occupations that continue being active and require them to work outside the home and interact with other people
180 during the containment phase (e.g., food or pharmacy manufacturing and sales, agriculture or food production and distribution,

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3 181 transportation, and security). Because of such behaviors males mostly don't stay at home, sit together, and remove their mask while
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5 182 they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease. In China 50% of
6
7 183 men in smoke, but because it is not considered acceptable for women to smoke, only 2% of them do so. Smoking is associated with
8
9 184 adverse outcomes of COVID-19: for instance, the combined results of five studies showed that smokers were 1.4 times more likely
10
11 185 than non-smokers to have severe symptoms of COVID-19 (85). Besides, smoking is related to higher expression of ACE2 (the
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13 186 receptor for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), which might be the reason for the higher prevalence of
14
15 187 COVID-19 in this subgroup of patients than in women (86).

16
17 188 Men tended to develop more symptomatic and serious cases than women, according to the clinical classification of severity. Similar
18
19 189 occasions occurred during previous coronavirus epidemics: men had worse outcomes of illness from severe acute respiratory
20
21 190 syndrome (SARS), (87) and a higher risk of dying from Middle East respiratory syndrome (MERS)(88). Biological sex variation is said
22
23 191 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
24
25 192 more vigorous immune response to infections and vaccinations(90). Some previous studies on coronaviruses in mice have suggested
26
27 193 that the hormone estrogen may have a protective role. Estrogens suppress the escalation phase of the immune response that leads to
28
29 194 increased cytokine release(91). The authors showed that female mice treated with an estrogen receptor antagonist died at close to the
30
31 195 same rate as the male mice(92).

32
33 196 The X chromosome is known to contain the largest number of immune-related genes in the whole genome(88). With their XX
34
35 197 chromosome, women have a double copy of key immune genes compared to the single copy in XY men. This boost extends to both
36
37 198 the general reaction to infection (the innate response) and also to the more specific response to microbes including antibody formation
38
39 199 (adaptive immunity)(88). Thus women's immune systems are generally more responsive to infections. This might mean women are
40
41 200 able to tackle the novel coronavirus more effectively but this has not yet been proven.

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

205 **Conclusions**

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

214 **Abbreviations**

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

218 **Declarations**

219 **Ethics approval and consent to participate**

220 Not applicable

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3 221 **Consent for publication**
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6 222 Not applicable
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8 223 **Availability of data and material**
9

10 224 The datasets analyzed during the current study are available from the corresponding author upon reasonable request.
11
12

13 225 **Competing interests**
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15
16 226 We have confirmed that we have no competing interests.
17

18 227 **Funding**
19

20
21 228 No funding was obtained for this study
22

23 229 **Authors' contributions**
24

25
26 230 BB, AM, MW, TG and SA: developed the study design and protocol, literature review, selection of studies, quality assessment, data
27 231 extraction, statistical analysis, interpretation of the data and developing the initial drafts of the manuscript and prepared the final draft
28 232 of the manuscript. All authors read and approved the final manuscript.
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407 Figure Legends

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

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

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

411 Table Legends

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

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

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

415 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	(2)
2.	Liu Y et al	China	Jan11-Jan20	12	8	4	9/9	(3)
3.	Liu Y et al	China	Jan23-Feb8	109	59	50	6/9	(3)
4.	Liu J et al	China	Jan-Feb	40	15	25	8/9	(3)
5.	Wu J et al	China	Jan22-Feb14	80	39	41	8/9	(3)
6.	Xu X et al	China	Jan10-Jan26	62	36	26	8/9	(1)
7.	Xu Y et al	China	Jan-Feb	50	29	21	6/9	(3)
8.	Yao et al	China	Jan01-Feb07	195	115	80	8/9	(3)
9.	Young et al	China	Jan22-Jan31	18	9	9	6/9	(3)
10.	Zhang J et al	China	Jan16-Feb03	140	71	69	8/9	(3)
11.	Zhang M et al	China	Jan18-Feb03	9	5	4	7/9	(3)
12.	Zhao et al	China	Jan16-Feb03	101	56	45	8/9	(3)
13.	Zhu et al	China	Dec01-Feb15	12	8	4	7/9	(4)
14.	Yanping Z et al	China	February 2020	44672	22981	21691	8/9	(4)
15.	W. Guan et al	China	February 2020	1099	640	459	7/9	(4)
16.	WHO ,2020	Africa	March 2020	482	189	177	7/9	(5)
17.	Huang et al	China	Jan, 2020	41	30	11	7/9	(1)

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3	416	18.	Chen et al	China	December 2020	99	67	32	6/9
4		19.	Wang et al	China	March 2020	138	75	63	7/9
5	417	20.	Kaiyuan S et al	China	February, 2020	507	281	201	6/9
6		21.	AL Giwa et al	China	March, 2020	78771	57482	21289	9/9
7		22.	Qian G et al	China	March, 2020	91	37	54	8/9
8	418	23.	Livingston E et al	Italy	March, 2020	22512	13462	9050	7/9
9		24.	Wang Y et al	China	March, 2020	110	48	62	6/9
10		25.	KSID,2020	Korea	February, 2020	4212	1591	2621	9/9
11	419	26.	Su YJ et al	China	March, 2020	10	7	3	6/9
12		27.	Jennifer B et al	China	March, 2020	59600	30000	29600	8/9
13		28.	Kui et al	China	March, 2020	137	61	76	8/9
14	420	29.	Deng L et al	China	March, 2020	33	17	16	8/9
15		30.	Dong X et al	China	March, 2020	135	72	63	6/9
16		31.	Xiaobo et al	China	March, 2020	52	35	17	8/9
17	421	32.	Zhou F et al	China	March, 2020	191	119	72	6/9
18		33.	Wu Y et al	China	March, 2020	297	147	150	8/9
19		34.	Gao Q et al	China	January to February ,2020	213	108	105	7/9
20	422	35.	Chen X et al	China	February 2020	291	145	146	8/9
21		36.	Zhang G et al	China	December 2019	221	108	113	7/9
22		37.	Wu W et al	China	March, 2020	21	10	11	8/9
23	423	38.	Cao M et al	China	February, 2020	128	60	68	7/9
24		39.	Chung et al	China	March, 2020	20	13	7	7/9
25		40.	Xiao F et al	China	March, 2020	73	41	32	7/9
26	424	41.	Qi D et al	China	January to February ,2020	267	149	118	6/9
27		42.	Liang et al	China	China	1590	911	679	7/9
28	425	43.	Wang Y et al	China	February, 2020	55	22	23	6/9
29		44.	Nicholas E et al	UK	April 2020	68	32	36	9/9
30	426	45.	Mizumoto K et al	Japan	March, 2020	634	321	313	8/9
31		46.	Chen X et al	China	March, 2020	48	37	11	7/9
32		47.	Cheng J et al	China	March, 2020	1079	573	505	6/9
33	427	48.	Li J et al	China	March, 2020	47	28	19	9/9
34		49.	Tian S et al	China	April 2020	262	127	135	8/9
35		50.	Li et al	China	March, 2020	425	240	185	7/9
36	428	51.	Liu Y et al	China	February, 2020	109	59	50	6/9
37		52.	Cao W et al	China	February, 2020	198	101	97	9/9
38		53.	Chaolin et al	China	February, 2020	41	30	11	6/9
39	429	54.	Yang X et al	China	February, 2020	52	35	17	8/9
40		55.	Liu L et al	China	February, 2020	51	32	19	8/9
41	430	56.	Huang C et al	China	February, 2020	41	30	11	8/9
42		57.	Wang D et al	China	February, 2020	138	75	63	6/9
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434 Table 2

435	Variables	Characteristics	Pooled prevalence (95% CI)	I²(P-value)
436	By province in china	Wuhan	72.05 (71.71-72.35)	96.6 (0.00)
437		Shanghai	51.01 (44.05-57.97)	-
438		Hubei	50.40 (50.1-50.80)	66.7 (0.001)
439		Zhonghua	54.07 (95% CI:51.63-56.51)	37.9 (0.139)
440		Zhejiang	46.45 (39.10-53.81)	99.4 (0.00)
441		Shenzhen	63.52 (51.64-75.40)	0.0 (0.796)
442		Jiangsu	44.84 (35.99-53.68)	29 (0.235)
443		Chongqing	52.20 (47.95-56.44)	65.1 (0.09)
444		outside china	53.17 (52.81-53.53)	99.4 (0.00)
445		By country	China	55.99(51.99-59.99)
446	Africa		39.21(34.85-43.84)	-
447	Italy		59.80(59.16-60.44)	-
448	Korea		37.77(36.31-39.24)	-
449	Singapore		50.00(26.90-73.10)	-
450	By JBI quality score	>=7	53.66 (95% CI:49.23-58.09)	99.5 (0.00)
451		<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)

452 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

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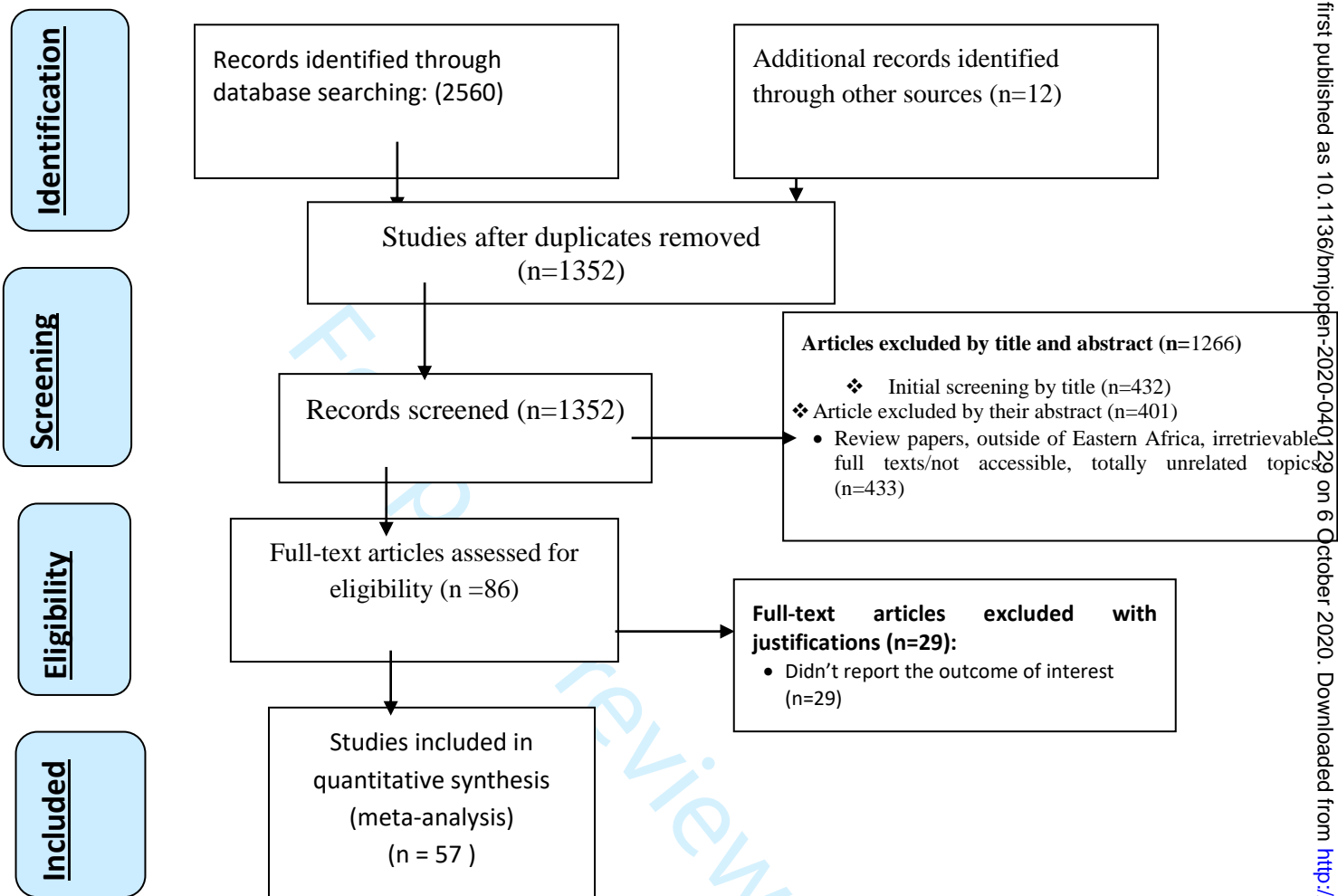


Figure 1: PRISMA flow diagram showed the results of the search and reasons for exclusion

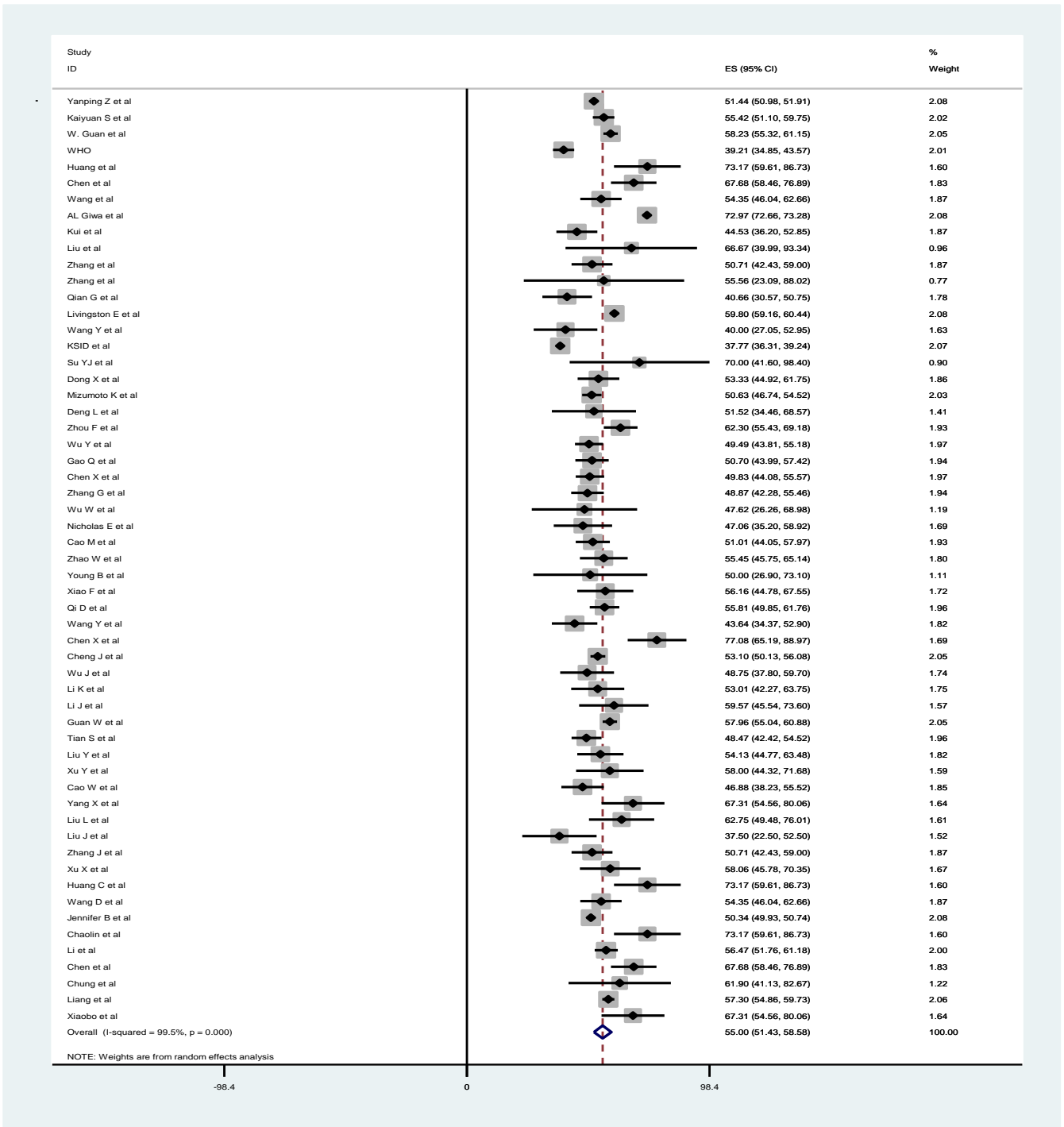
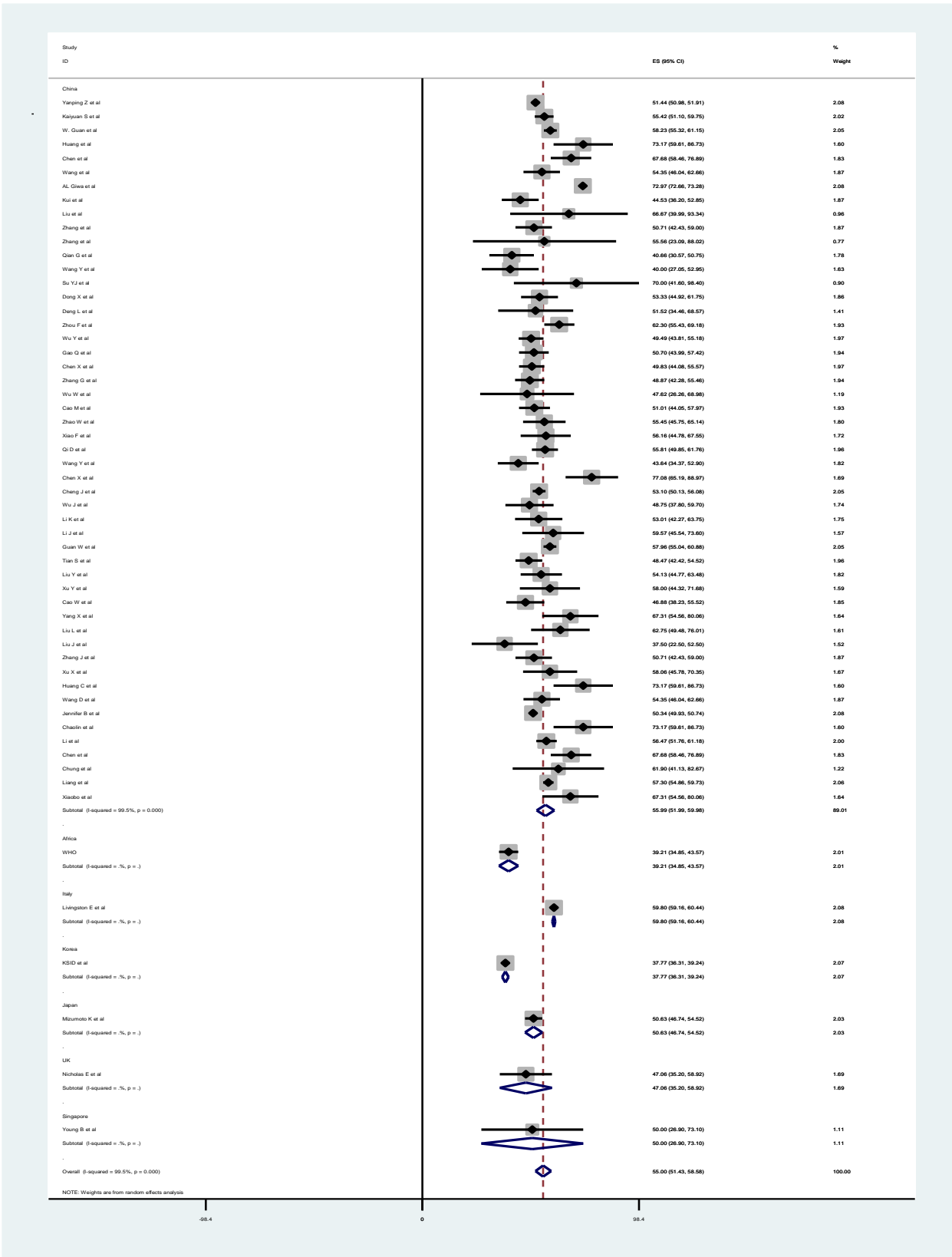


Figure 2: Forest plot showing the pooled prevalence of COVID-19 confirmed cases among male

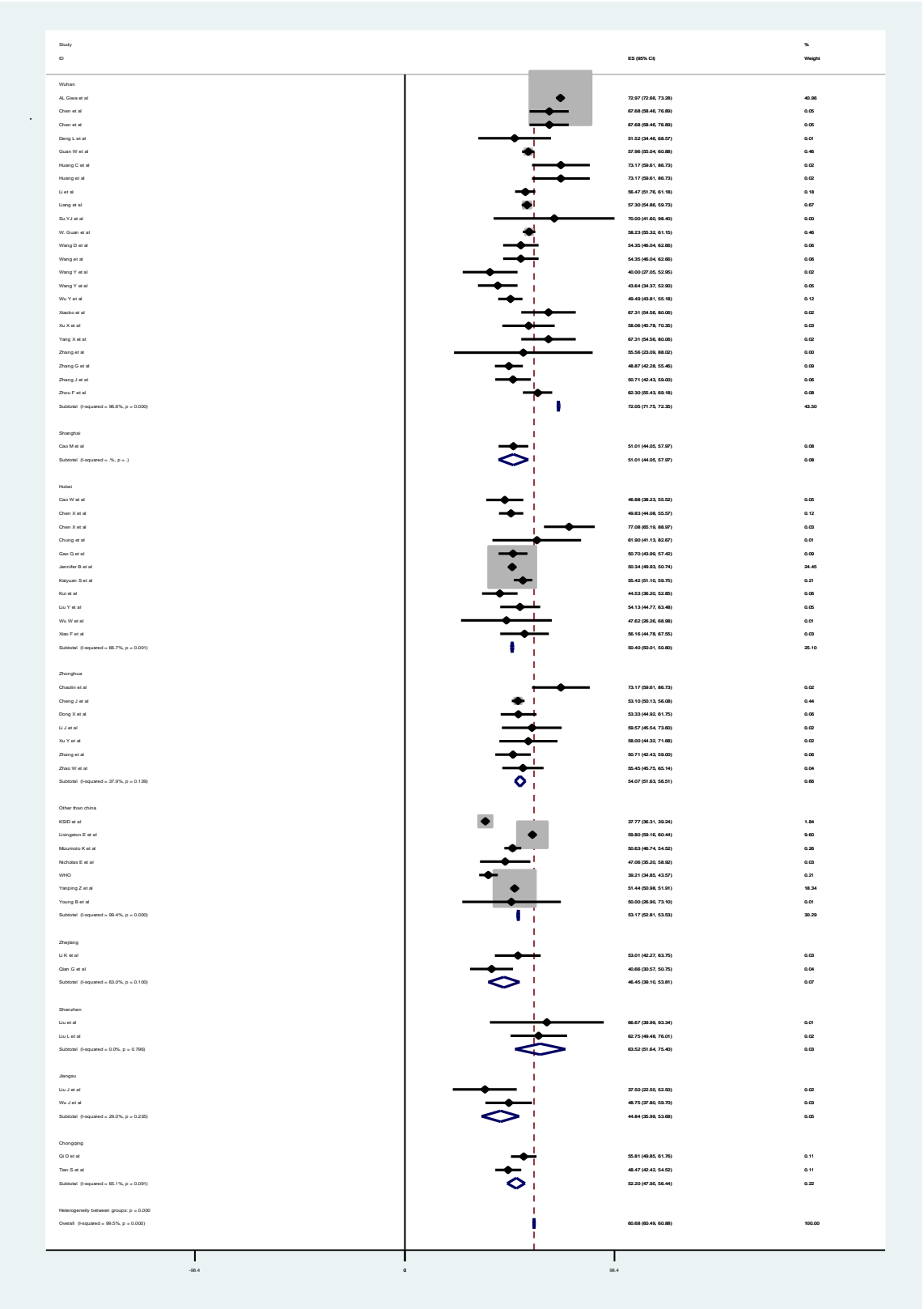
Study omitted	Coef.	[95% Conf. Interval]
Cheng J et al	20.732838	20.445127 21.020546
Xu X et al	17.418531	17.156216 17.680845
Liu L et al	17.381458	17.119438 17.643478
Yao et al	17.516275	17.25304 17.77951
wang Yet al	17.346966	17.085199 17.608732
Wu J et al	17.362354	17.100435 17.624273
Xia W et al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

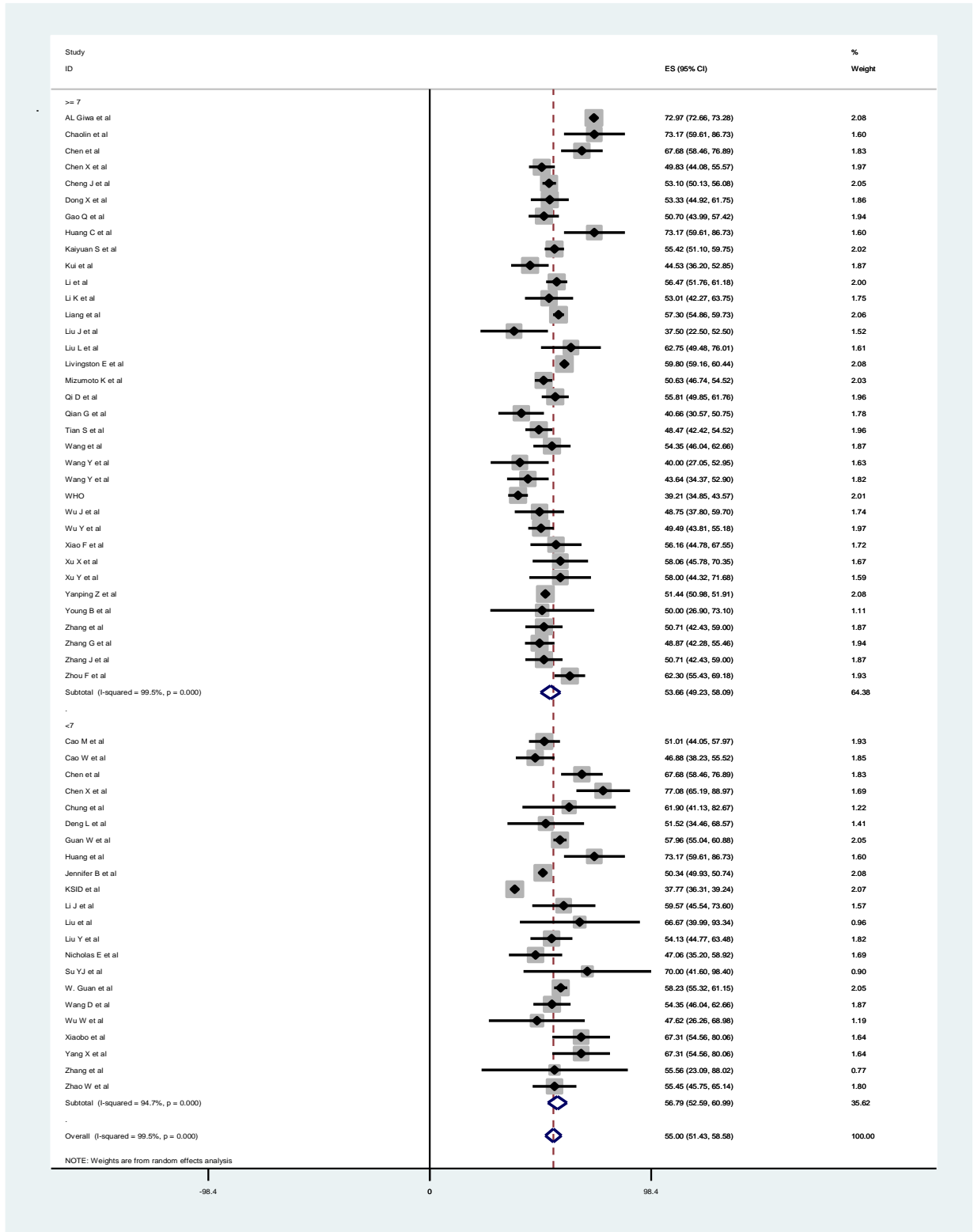


Supplementary Figure 1: Subgroup analysis for prevalence of COVID-19 among males by countries

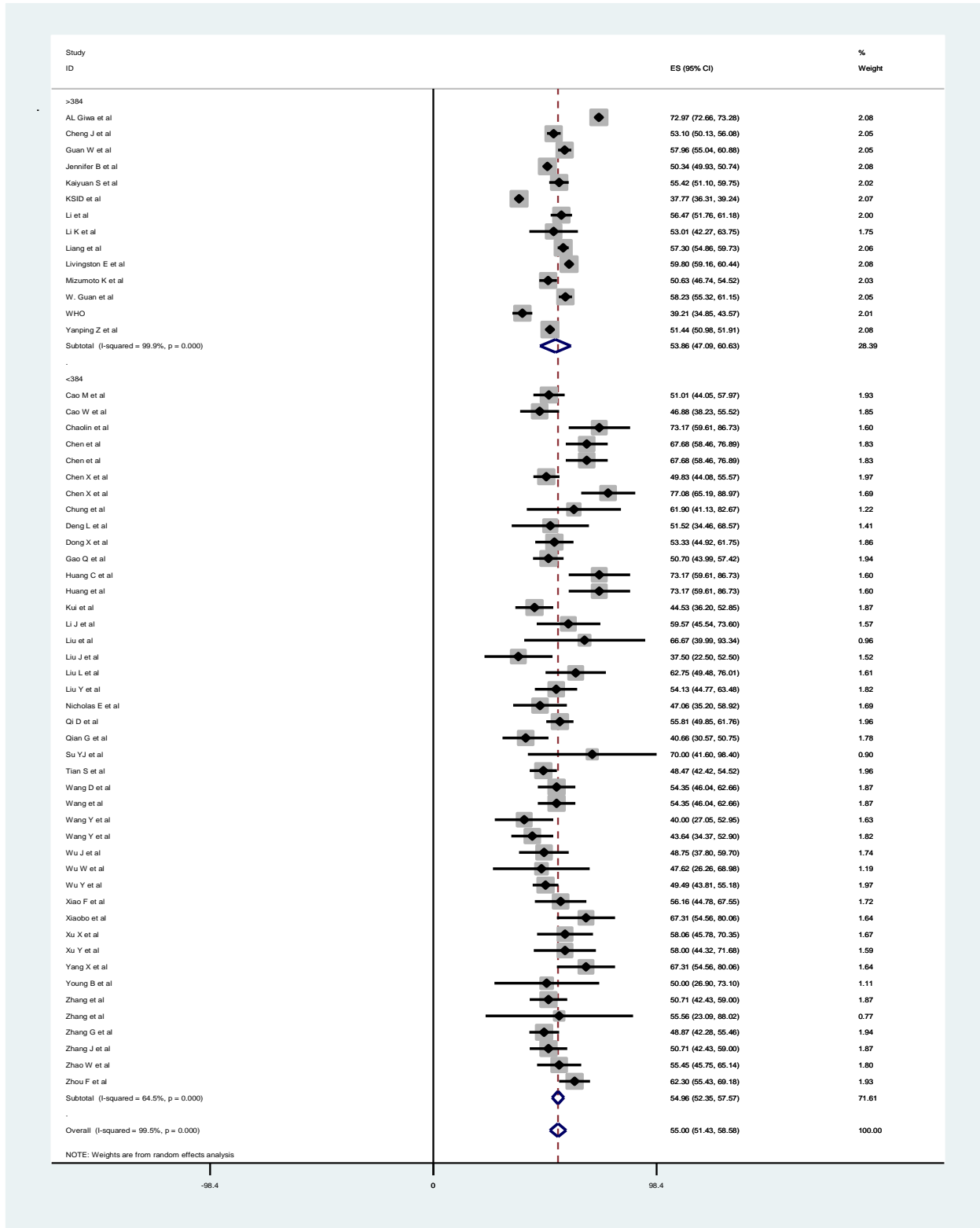
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Supplementary Figure 2: Subgroup analysis of the prevalence of COVID-19 by province in china



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			
Group	Search terms		Citations
	Non-MeSH terms	MeSH (sub-terms in MeSH)	
#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

3	40. Xiao F et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
4	41. Qi D et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
5	42. Liang et al	Y	Y	Y	Y	Y	N	Y	Y	N			7/9	Low risk	Included
6	43. Wang Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
7	44. Nicholas E et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
8	45. Mizumoto K et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
9	46. Chen X et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
10	47. Cheng J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
11	48. Li J et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
12	49. Tian S et al	Y	Y	UC	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
13	50. Li et al	Y	Y	Y	Y	Y	UC	Y	Y	N			7/9	Low risk	Included
14	51. Liu Y et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
15	52. Cao W et al	Y	Y	Y	Y	Y	Y	Y	Y	Y			9/9	Low risk	Included
16	53. Chaolin et al	Y	Y	UC	Y	Y	N	Y	Y	N			6/9	Low risk	Included
17	54. Yang X et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
18	55. Liu L et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
19	56. Huang C et al	Y	UC	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
20	57. Wang D et al	UC	Y	Y	Y	Y	N	Y	Y	N			6/9	Low risk	Included
21	58. Cheng J et al	Y	Y	Y	Y	Y	N	Y	Y	Y			8/9	Low risk	Included
22	59. Wu J et al	N	Y	N	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
23	60. Li K et al	Y	Y	Y	Y	Y	Y	Y	Y	N			8/9	Low risk	Included
24	61. Li J et al	Y	Y	UC	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
25	62. Guan W et al	Y	Y	Y	Y	Y	UC	Y	Y	Y			8/9	Low risk	Included
26	63. Tian S et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
27	64. Liu Y et al	Y	N	Y	Y	Y	Y	Y	Y	Y			8/9	Low risk	Included
28	65. Xu Y et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
29	66. Cao W et al	Y	UC	Y	Y	Y	N	Y	Y	Y			7/9	Low risk	Included
30	67. Yang X et al	Y	UC	Y	Y	Y	Y	Y	Y	N			7/9	Low risk	Included
31	68. Liu L et al	UC	Y	Y	Y	Y	N	Y	Y	Y			6/9	Low risk	Included
32	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

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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?				

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