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

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1	Sex difference in coronavirus disease (COVID-19): A systematic review and meta-analysis	0-040
2	Biruk Beletew Abate ^{1*} , Ayelign Mengesha Kasie ¹ , Mesfin Wudu Kassaw ¹ , Teshome Gebremeskel ¹	136/bmjopen-2020-040129 on 6
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11	*Corresponding Author: Biruk Beletew Abate; E-mail: <u>birukkelemb@gmail.com</u>	njope
12	<i>Running title</i> : Sex difference in coronavirus disease (COVID-19)	n.b.m.
13	Abstract	Downloaded from http://bmjopen.bmj.com/
14	Objective: To assess the sex difference in the prevalence of coronavirus disease (COVID-19) confirmed cas	
15	Design: Systematic review and meta-analysis.	pril 19, 2
16 17 18 19 20	Setting: PubMed, Cochrane library, and Google Scholar were searched for related information. The authors extraction form on the excel sheet and the following data were extracted for eligible studies: author, country female patients, and the number of male patients. Using STATA 14 for analysis authors pooled the overall p female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q st Subgroup and sensitivity analysis was done Publication bias was also checked.	Sample size, number valence male and/or distic and the I ² statistics.
21	Participants: Studies with COVID-19 confirmed cases were included.	stected by copyright.
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2 3 4	22	Intervention: sex (male/female) of COVID-19 confirmed cases were considered
5 6	23	Primary and secondary outcome measures: Primary outcomes were prevalence of COVID-19 among males and females.
7 8	24	Result: A total of 57 studies with 221195 participants were used for analysis. The pooled prevalence of COV 2D-19 among males was
9 10	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
11 12	26	study. Moreover a funnel plot showed symmetrical distribution. Egger's regression test p-value was not sign B cant, which indicates
13 14	27	the absence of publication bias in both outcomes.
15	28	Conclusions: The prevalence of COVID-19 is higher among males than females. This can be explained with the hormonal and
16 17	29	chromosomal variation between males and females. In addition the high prevalence of smoking and alcohol ansumption has
18 19	30	contributed for increased high prevalence of COVID-19 among males. Additional studies regarding discrepancy in severe illness and
20	31	mortality due to COVID-19 among males and females and factors which determine the exposure, severity and mortality due to
21 22	32	COVID-19 is recommended.
23 24	33	Keywords: COVID-19; sex difference; Systematic review; Meta-analysis
25 26	34	Background
27 28	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
29 30	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
31 32	37	the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19) (5, 6). The virus has now been named Sever Acute
33	38	Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Virus (ICTV) (7). COVID-19
34 35	39	has now been declared as a Public Health Emergency of International Concern by the WHO on 30th January 2020(8).
36 37	40	COVID-19 affects people differently, in terms of infection with the virus SARS-CoV-2 and mortality rates $(9\frac{24}{2}10)$.
38 39	41	Susceptibility to COVID-19 seems to be associated with age, biological sex, and comorbidities (11). Although the COVID-19 causes
40 41 42 43	42	a mild illness in a majority of cases, severe illness requiring hospital admission is not uncommon (12). Besides, it has the potential to
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3 4	43	precipitate a life-threatening critical illness, characterized by respiratory failure, circulatory shock, sepsis or other organ failure,
5	44	requiring intensive care(13, 14).
6 7	45	According to Global Health 5050 data gathering, the highest ratio of male to female deaths, as a result of COVID-19, is in Denmark
8	46	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 2.1 to 1, and Norway,
9 10	47	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
10	48	countries have more cases among men than they do among women. Norway, Sweden, and Germany have a 50/2-50% case ratio while
12	49	Switzerland (53% of women to 47% of men), Spain (51% to 49%), The Netherlands (53% to 47%), Belgium (\$5% to 45%), South
13 14	50	Korea (60% to 40%),Portugal (57% to 43%),Canada (52% to 48%),Republic of Ireland (52% to 45%) and a bggher number of
15	51	confirmed cases have been observed among men than women in Greece, Italy, Peru, China, and Australia $(16\frac{5}{8}17)$.
16 17	52	The report in The Lancet reads, "Knowing the degree to which outbreaks upsets women and men in different way is a important step
18	53	for generating effective, equitable policies and interventions." Men and women tend to react differently to postential vaccines and
19	54	treatments, so having access to sex-disaggregated data is crucial for conducting safe clinical trials(18). Under and ing sex difference in
20 21	55	world health is a core component of ensuring effective and equitable national and global health systems that work for everyone.
22 23 24	56	National governments and global health organizations must urgently face up to this reality.
25	57	Since the occurrence of COVID-19 infection in Wuhan, China, in December 2019 (19), it has quickly spread across China and
26	58	numerous other countries(20-24). So far, 2019-nCoV has affected more than 210 countries with 2, 733,591 confirmed cases, including
27 28	59	191185 deaths and 751,404 recovery (25). Given the rapid spread of COVID-19 and its health related impacts many research articles
20	60	have been done already been published about this epidemic (26). Global Health 5050 summarize in their artifie, Sex-disaggregated
30	61	data are essential for understanding the distributions of risk, infection, and disease in the population, and the extent to which sex and
31 32	62	gender affect clinical outcomes. Even though, some previously published papers haven showed the sex variation, some indicates males
33	63	are at high risk than female while others indicate females are at high risk for COVID-19. Therefore the findings are not conclusive due
34	64	to inconsistency in prevalence of COVID-19 among males and females. Moreover, there is lack of systematigreview and meta-
35 36	65	analysis which indicated the worldwide clear picture of sex variation on the risk of COVID-19. Hence, this systematic review and
37 38	66	meta-analysis was conducted to assess the pooled prevalence of COVID-19 among males and females.
39	67	Review question The review questions of this systematic review and meta-analysis were: Open to assess the pooled prevalence of COVID-19 among males and remales. Open to assess the pooled prevalence of COVID-19 among males and remales.
40 41	68	The review questions of this systematic review and meta-analysis were:
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70 Methods

71 Search strategy

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

83 Study selection and screening

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

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Inclusion and exclusion criteria

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

95 Patient and Public Involvement: Patients or the public WERE NOT involved in the design, or conduct, or not provide a second s

96 dissemination plans of our research

97 Quality assessment

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

102 Data extraction

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

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1 2		Synthesis of results
3 4	109	Synthesis of results
5	110	The authors transformed the data to STATA 14 for analysis after it was extracted in an excel sheet considering prevalence male and
6 7	111	female reported. We pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the
8 9	112	heterogeneity of effect size using the Q statistic and the I ² statistics. In this study, the I ² statistic value of zero indicates true
10 11	113	homogeneity, whereas the value 25, 50, and 75% represented low, moderate and high heterogeneity, respectively. Subgroup analysis
12	114	was done by the study country and sample size. Sensitivity analysis was employed to examine the effected a single study on the
13 14	115	overall estimation. Publication bias was checked by the funnel plot and more objectively through Egger's regession test.
15 16	116	Result
17	117	Study selection
18 19	118	A total of 2574 studies were identified using electronic searches (through Database searching (n = 2560)) and other sources (n =12)).
20 21	119	After duplication removal, a total of 1352 articles remained (1222 duplicated). Finally, 86 studies were screened for full-text review
22 23	120	and, 57 articles (n=221195 patients) were selected for the analysis (Fig.1).
24 25	121	Characteristics of included studies
26 27	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
28 29	123	The studies included participants ranging from 9 (75)to 78771 (45) (Table1).
30	124	Meta-analysis
31 32	125	Prevalence of COVID-19 among male
33 34	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
35	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
36 37	128	pooled prevalence of severe illness is $55.00(51.43-56.58; I^2=99.5\%; p<0.001)$ (Fig.2).
38 39 40	129	pooled prevalence of severe illness is 55.00(51.43-56.58; I ² =99.5%; p<0.001) (Fig.2). Subgroup analysis of COVID-19 confirmed cases among male
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1 2		
3 4	130	The subgroup analysis was done through stratification by country. Based on this, the prevalence of severe illness was found to be
5 6	131	61.34 in china and 29.9 in Italy (Supplementary Fig 1).
7 8 9	132	Sensitivity analysis
10	133	We employed a leave-one-out sensitivity analysis to identify the impact of individual research on the poeled prevalence of sever
11 12	134	illness among COVID-19confirmed cases. The results of this sensitivity analysis showed that our findings were not dependent on
13 14	135	single study. Our pooled estimated prevalence of severe illness varied between 22.83 (19.12-26.53) Li J ET and 25.0 (19.87-30.13)
15 16	136	Yanping Z ET al after the deletion of a single study (Figure 3).
17 18 19	137	Publication Bias
20 21	138	We have also checked publication bias and, a funnel plot showed symmetrical distribution. Egger's regression test p-value was 0.599
22 22 23	139	which indicates the absence of publication bias (Figure 4).
24 25	140	Discussion
26 27	141	Recently, following the COVID-19 outbreak, numerous questions have been raised; comprising what is their sex difference in getting
28 29	142	COVID-19?. This systematic review and meta-analysis were conducted to assess the sex difference in getting COVID -19 disease and
30 31	143	this review revealed the pooled prevalence of COVID-19 among males and females.
32 33	144	Fifty seven studies were included in the final analysis. The pooled prevalence COVID -19 confirmed cases approach males and females
34 35	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
36 37 38 39 40 41 42 43 44	146	(76, 77).
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2		N
3 4	147 148	Biological sex variation is said to be one of the reason for the sex discrepancy of COVID-19(78). Women's ignate immune response affected by sex chromosomes and sex hormones plays a role. As a result, women are in general able to moung a more vigorous
5 6 7	149	immune response to infections [and] vaccinations(79).
8	150	Some previous studies on coronaviruses in mice have suggested that the hormone estrogen may have a prote $\hat{\mathbf{g}}$ ive role. Estrogens
9 10 11	151 152	suppress the escalation phase of the immune response that leads to increased cytokine release(80). The authors showed that female mice treated with an estrogen receptor antagonist died at close to the same rate as the male mice(81).
12 13	153	In addition behavioral factors, like smoking and alcohol consumption, which tend to occur more among mengthose behaviors
14 15	154	predisposes males for cardiac and respiratory diseases. This may also explain the overall higher mortality rates among men (82-84).
16 17	155	A systematic review and meta-analysis revealed that comorbid disease, such as respiratory system disease, here pertension, and
18 19	156	cardiovascular disease as risk a risk factors for death compared with patients without comorbidity(85).
20 21	157	Strength and limitations
22 23	158	This systematic review and meta- analysis has several strengths: we used a pre-specified protocol for search strategy and data
24 25	159	abstraction and used internationally accepted tools for a critical appraisal system for quality assessment of individual studies. Besides
26 27	160	we employed subgroup analysis, publication bias and sensitivity analysis Nevertheless, this review had some limitations: because of
28	161	the inclusion of studies which are published in English only, language bias is likely. In addition most included are from China due to \mathbb{R}
29 30	162	lack of literatures from other countries in the world which reported the outcome of interest. However, the data in this review permit to
31 32	163	systematically review and analyze the pooled prevalence of severe illness and mortality among COVID-19 confirmed patients
33 34 35	164	Conclusions
36 37	165	The prevalence of COVID-19 is higher among males than females. This can be explained with the hormonal $\frac{g}{2}$ and chromosomal
38	166	variation between males and females. In addition the high prevalence of smoking and alcohol consumption has contributed for
39 40	167	increased high prevalence of COVID-19 among males. Although there has been a rapid surge in research in the outbreak
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3 4	168	of COVID-19, additional studies regarding discrepancy in severe illness and mortality due to COVID-19 amo	10
5 6	169	and factors which determine the exposure, severity and mortality due to COVID-19 is recommended. Everyc	ge should take actions,
7	170	such as hand washing with sanitizer, social distancing, avoid crowding (2m apart if coming together is must)	Savoid smoking and
8 9	171	alcohol consumption especially among men to help slow the spread of COVID-19.	Octo
10 11	172	Abbreviations	ber 202
12 13	173	COVID-19: coronavirus disease 2019; WHO: World Health Organization; ICTV: International Committee	of Taxonomy of Viruses;
14 15	174	SARS-CoV-2: Sever Acute Respiratory Syndrome Coronavirus 2; CI: Confidence Interval; AOR: Adjusted	Bodds ratio; ARTI: Acute
16 17	175	Respiratory Tract Infections	aded frc
18 19 20	176	Declarations	m http://
21 22 23	177	Ethics approval and consent to participate	(bmjoper
24 25	178	COVID-19: coronavirus disease 2019; WHO: World Health Organization; ICTV: International Committee SARS-CoV-2: Sever Acute Respiratory Syndrome Coronavirus 2; CI: Confidence Interval; AOR: Adjusted Respiratory Tract Infections Declarations Ethics approval and consent to participate Not applicable Consent for publication Not applicable Availability of data and material The datasets analyzed during the current study are available from the corresponding author upon reasonable	n.bmj.co
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29 30 31	180	Not applicable	pril 19, 2
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39 40 41 42 43	184	We have confirmed that we have no competing interests.	st. Protected by copyright.
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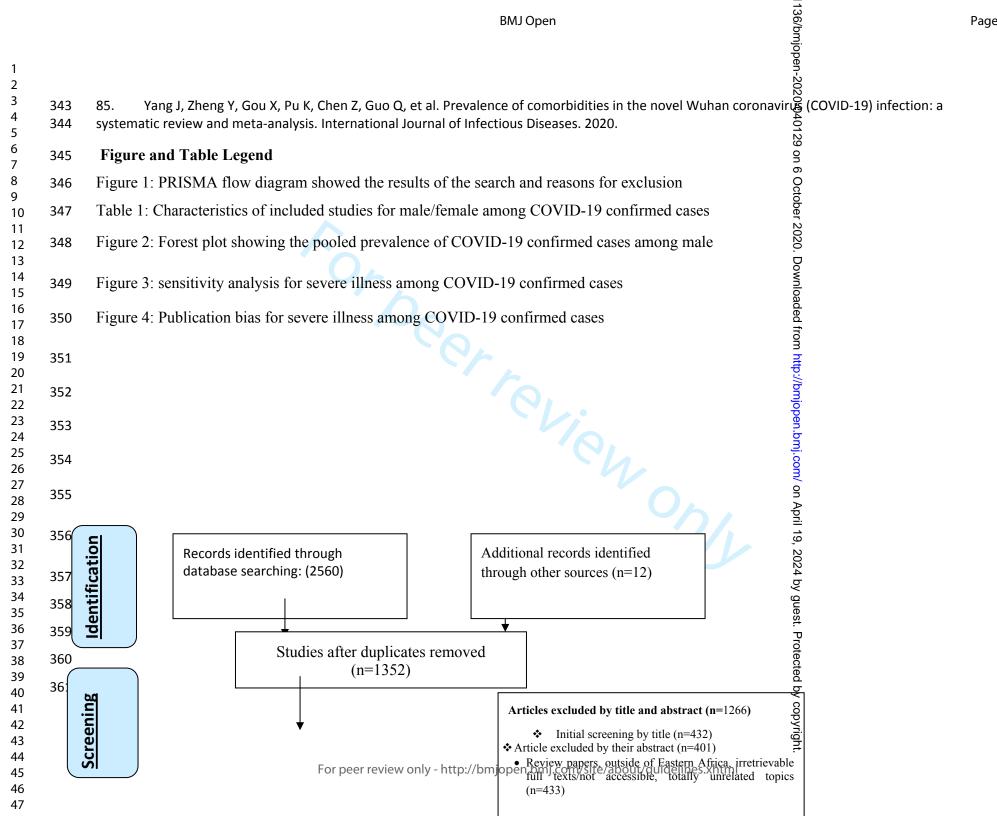
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10 11 12	188	BB, AM, MW, and TG: developed the study design and protocol, literature review, selection of studies,	e
12 13	189	extraction, statistical analysis, interpretation of the data and developing the initial drafts of the manuscript and	ed prepared the final draft
14 15	190	of the manuscript. All authors read and approved the final manuscript.	ownic
16 17 18	191	Acknowledgments	oaded from
19 20	192	We would like to thank the authors of the included primary studies.	http://t
21 22 23	193	References	http://bmioper
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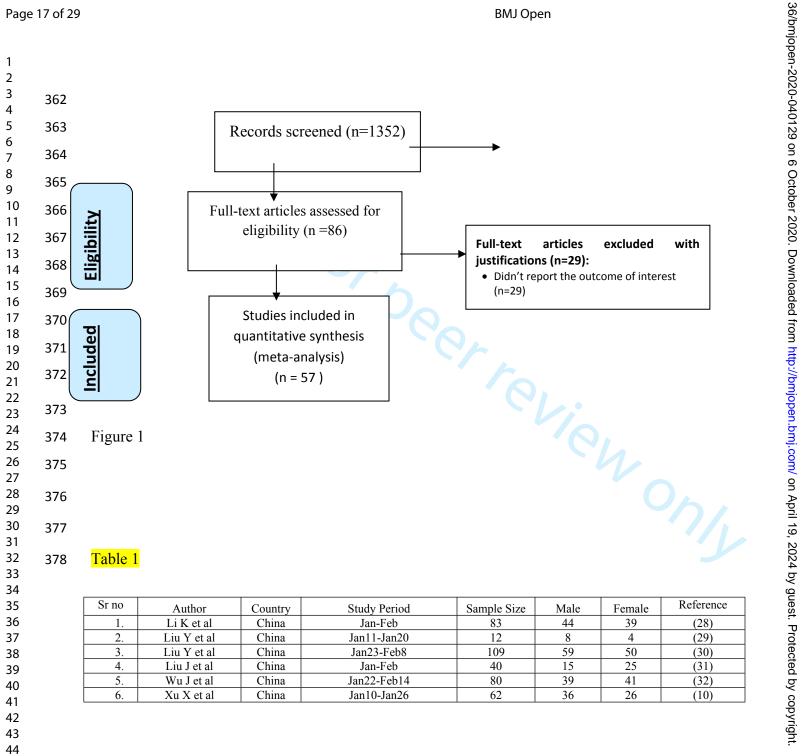
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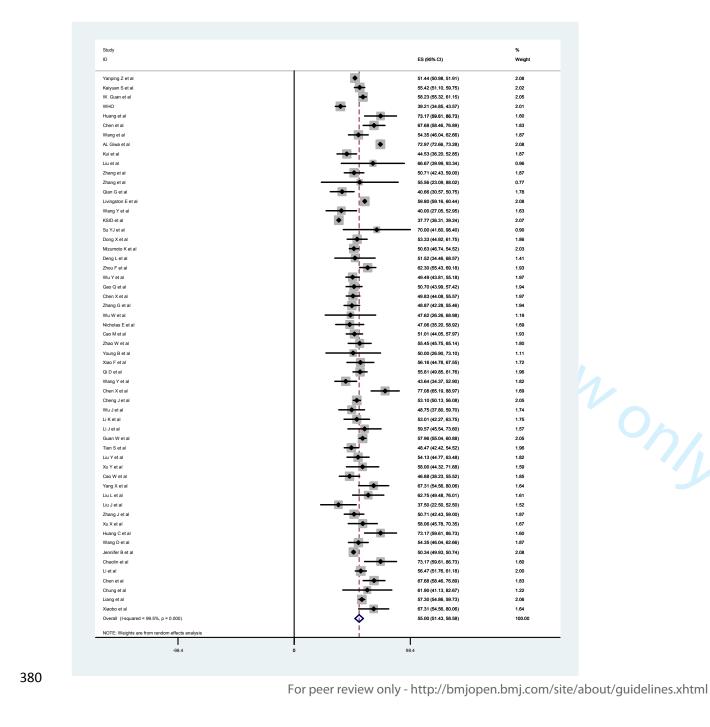
7.	Xu Y et al	China	Jan-Feb	50	29	21	(3
8.	Yao et al	China	Jan01-Feb07	195	115	80	(3
9.	Young et al	China	Jan22-Jan31	18	9	9	(.
10.	Zhang J et al	China	Jan16-Feb03	140	71	69	(.
11.	Zhang M et al	China	Jan18-Feb03	9	5	4	(
12.	Zhao et al	China	Jan16-Feb03	101	56	45	(
13.	Zhu et al	China	Dec01-Feb15	12	8	4	(
14.	Yanping Z et al	China	February 2020	44672	22981	21691	(•
15.	W. Guan et al	China	February 2020	1099	640	459	(
16.	WHO ,2020	Africa	March 2020	482	189	177	(
17.	Huang et al	China	Jan, 2020	41	30	11	
18.	Chen et al	China	December 2020	99	67	32	(
19.	Wang et al	China	March 2020	138	75	63	(
20.	Kaiyuan S et al		February, 2020	507	281	201	(
21.	AL Giwa et al	China	March, 2020	78771	57482	21289	(·
22.	Qian G et al	China	March, 2020	91	37	54	(·
23.	Livingston E et al	Italy	March, 2020	22512	13462	9050	(·
24.	Wang Y et al	China	March, 2020	110	48	62	(·
25.	KSID,2020	Korea	February, 2020	4212	1591	2621	(
26.	Su YJ et al	China	March, 2020	10	7	3	(
27.	Jennifer B et al	China	March, 2020	59600	30000	29600	(
28.	Kui et al	China	March, 2020	137	61	76	(
29.	Deng L et al	China	March, 2020	33	17	16	(
30.	Dong X et al	China	March, 2020	135	72	63	(
31.	Xiaobo et al	China	March, 2020	52	35	17	(
32.	Zhou F et al	China	March, 2020	191	119	72	(
33.	Wu Y et al	China	March, 2020	297	147	150	(
34.	Gao Q et al	China	January to February ,2020	213	108	105	
35.	Chen X et al	China	February 2020	291	145	146	(
36.	Zhang G et al	China	December 2019	221	108	113	(
37.	Wu W et al	China	March, 2020	21	10	11	(
38.	Cao M et al	China	February, 2020	128	60	68	(
39.	Chung et al	China	March, 2020	20	13	7	(
40.	Xiao F et al	China	March, 2020	73	41	32	(
41.	Qi D et al	China	January to February ,2020	267	149	118	(
42.	Liang et al	China	China	1590	911	679	(
43.	Wang Y et al	China	February, 2020	55	22	23	(
44.	Nicholas E et al	UK	April 2020	68	32	36	(
45.	Mizumoto K et al	Japan	March, 2020	634	321	313	(•
46.	Chen X et al	China	March, 2020	48	37	11	(
47.	Cheng J et al	China	March, 2020	1079	573	505	(
48.	Li J et al	China	March, 2020	47	28	19	(

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49. 50.	Tian S et al	China	April 2020	262	127	135	(69)
	Li et al	China	March, 2020	425	240	185	
51.	Liu Y et al	China	February, 2020	109	59	50	` ´
52.	Cao W et al	China	February, 2020	198	101	97	(69) (70) (1) (71) (72) (13) (73) (1) (74)
53.	Chaolin et al	China	February, 2020	41	30	11	
54.	Yang X et al	China	February, 2020	52	35	17	
55.	LinLatal	China	Echrupry 2020	51	22	10	(72)
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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6		Study ommited	Coef.	[95% Conf.	Interval]	129 on 6 October 2020. Downloaded from http://bmjopen.bmj.com/ on April 19, 2024 by guest. Protected
7		Cheng J et al	20.732838	20.445127	21.020546	 6
8		Xu X et al	17.418531	17.156216	17.680845	0
9		Liu L et al	17.381458	17.119438	17.643478	욙
-		Yao et al	17.516275	17.25304	17.77951	8
10		Wang Yet al	17.346966	17.085199	17.608732	er
11		Wujetal	17.362354	17.100435	17.624273	N
		xia w_et al	17.317913	17.056414	17.579412	22
12		Xiao F et al	17.338419	17.076689	17.600149	.0
13		Cao M Qian G et al	17.340126 17.322186	17.078194 17.060547	17.60206 17.583824	
14		Liu C et al	17.322180	17.049721	17.57266	Ş
		Zhao et al	17.313881	17.052284	17.57548	ň
15		Yang et al	17.312496	17.050829	17.574163	ō
16		Gao Q et al	17.313957	17.052176	17.575737	ad
		Guan W	17.332129	17.068779	17.595478	e
17		Cao W et al	17.310188	17.048569	17.571806	Ť
18		Chen X	17.309149	17.04727	17.571028	õ
		Tian et al	17.307884	17.046061	17.569708	Ц
19		Tian S et al	17.307884	17.046061	17.569708	
20		Yanping z et al	16.002106	15.621832	16.382381	5
		Qi D et al	17.304249	17.042439	17.566059	
21		W. Guan et al	17.256212	16.993301	17.519123	¥
22		Liu K et al Liu W et al	17.298866 17.30262	17.037294 17.041122	17.56044 17.564116	j
23		Li Y et al	17.304375	17.042908	17.565842	ğ
		Xu Y et al	17.304667	17.043205	17.56613	, Ľ
24		Wang D et al	17.297497	17.035929	17.559065	ġ
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		Wu Y et al	17.280704	17.018961	17.54245	ġ
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27		Li K et al	17.299694	17.0382	17.561188	<
		Li K et al	17.299694	17.0382	17.561188	n
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31		Zhang Jet al	17.283909	17.022371	17.545444	Ň
32		Zhang Jet al	17.283909	17.022371	17.545444	õ
		Wu W et al	17.30135	17.039911	17.56279	4
33		Chen L et al	17.302288	17.040859	17.563717	g
34		Liu Y et al	17.284363	17.02286	17.545866) C
		Chen X et al 🛛 🛛	17.295172	17.033726	17.556618	Ĵ
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36		Liu Y et al	17.302118	17.040703	17.563536	<u> </u>
37		Li J et al	17.256153	16.994654	17.517653	
		Yang X et al	17.308687	17.047285	17.570087	 ote
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3 4	383	Figure 3						
5 6		Tests for Publ	ication Bias					
7 8		Begg's Test						
9		adi Kendall	's Score (P-	2) = 30 5				
10 11		Std.	Dev. of Scor	re = 105.62	(correct	ted for t	ies)	
12		Num	ber of Studi	es = 46 z = 2.89				
13			Pr >	z = 0.004				
14 15			Pr >	z = 2.88 z = 0.004	(contin	uity corr uity corr	ected)	
16			rii	-	8		,	
17		Egger's test	5			510 - 510		100
18 19		Std_Eff	Coef.	Std. Err.	t	P> t	[95% Conf.	Interval]
20		slope	16.85592	1.704925	9.89	0.000	13.41986	20.29197
21		bias	. 9970979	1.884806	0.53	0.599	-2.801478	4.795674
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	Study			%
	10 		ES (95% CI)	Weight
	China			
	Yanping Z et al	•	51.44 (50.98, 51.91)	2.08
	Kalyuan Setal W. Guan et al		55.42 (51.10, 59.75) 58.23 (55.32, 61.15)	2.02
)	Huang et al		73.17 (59.61, 86.73)	1.60
	Chen et al	1-8-	67.68 (58.46, 76.89)	1.83
1	Wang et al		54.35 (46.04, 62.66) 72.97 (72.66, 73.28)	1.87
2	Kui et al		44.53 (36.20, 52.85)	1.87
3	Liu et al		66.67 (39.99, 93.34)	0.96
1	Zhang et al		50.71 (42.43, 59.00)	1.87
5	Zhang et al Qian G et al		55.56 (23.09, 88.02) 40.66 (30.57, 50.75)	0.77
	Wang Y et al	i	40.00 (27.05, 52.95)	1.63
5	Su YJ et al		70.00 (41.60, 98.40)	0.90
,	Dong X et al Deng L et al		53.33 (44.92, 61.75) 51.52 (34.46, 68.57)	1.86
	Zhou F et al		62.30 (55.43, 69.18)	1.93
	Wu Y et al		49.49 (43.81, 55.18)	1.97
	Gao Q et al Chen X et al		50.70 (43.99, 57.42) 49.83 (44.08, 55.57)	1.94
)	Zhang G et al		49.83 (44.08, 55.57) 48.87 (42.28, 55.46)	1.97
	Wu W et al		47.62 (26.26, 68.98)	1.19
2	Cao M et al		51.01 (44.05, 57.97)	1.93
3	ZhaoWetal XiaoFetal		55.45 (45.75, 65.14) 56.16 (44.78, 67.55)	1.80
1	Qi D et al		55.81 (49.85, 61.76)	1.96
	Wang Y et al		43.64 (34.37, 52.90)	1.82
5	Chen X et al Cheng J et al		77.08 (65.19, 88.97) 53.10 (50.13, 56.08)	1.69 2.05
5	Wu Jetal		48.75 (37.80, 59.70)	1.74
7	Li K et al		53.01 (42.27, 63.75)	1.75
3	Li J et al		59.57 (45.54, 73.60)	1.57
9	Guan W et al Tian S et al	*	57.96 (55.04, 60.88) 48.47 (42.42, 54.52)	2.05
	Liu Y et al		54.13 (44.77, 63.48)	1.82
)	Xu Yetal		58.00 (44.32, 71.68)	1.59
1	Cao W et al		46.88 (38.23, 55.52)	1.85
2	Yang X et al		 67.31 (54.56, 80.06) 62.75 (49.48, 76.01) 	1.64
3	Liu J et al		37.50 (22.50, 52.50)	1.52
1	Zhang J et al		50.71 (42.43, 59.00)	1.87
	Xu X et al Huang C et al		58.06 (45.78, 70.35) 73.17 (59.61, 86.73)	1.67
5	Wang D et al		54.35 (46.04, 62.66)	1.87
5	Jennifer B et al	•	50.34 (49.93, 50.74)	2.08
7	Chaolin et al		73.17 (59.61, 86.73) 56.47 (51.76, 61.18)	1.60
3	Chen et al	· · · · ·	67.68 (58.46, 76.89)	1.83
)	Chung et al		61.90 (41.13, 82.67)	1.22
	Liang et al	•	57.30 (54.86, 59.73)	2.06
)	Xiaobo et al Subtotal (I-squared = 99.5%, p = 0.000)		 67.31 (54.56, 80.06) 55.99 (51.99, 59.98) 	1.64 89.01
		i i		
	Africa			
3	WHO Subtotal (I-squared = .%, p = .)	*	39.21 (34.85, 43.57) 39.21 (34.85, 43.57)	2.01
		· · · ·	v	
	Italy			
	Livingston E et al Subtotal (I-squared = %, p = .)	· · · · · · · · · · · · · · · · · · ·	59.80 (59.16, 60.44)	2.08
5	constant (redunation = -36, b) = -1		59.80 (59.16, 60.44)	2.08
7	Korea	i		
3	KSID et al		37.77 (36.31, 39.24)	2.07
	Subtotal (I-squared = .%, p = .)	•	37.77 (36.31, 39.24)	2.07
9	Japan			
)	Mizumoto K et al	•	50.63 (46.74, 54.52)	2.03
	Subtotal (I-squared = .%, p = .)		50.63 (46.74, 54.52)	2.03
	UK			
	Nicholas E et al		47.06 (35.20, 58.92)	1.69
3	Subtotal (l-squared = .%, p = .)		47.06 (35.20, 58.92)	1.69
1	- Signature			
5	Singapore Young B et al	<u> </u>	50.00 (26.90, 73.10)	1.11
	Subtotal (I-squared = .%, p = .)		50.00 (26.90, 73.10)	1.11
5				
5				100.00
3	Overall (I-squared = 99.5%, p = 0.000)		55.00 (51.43, 58.58)	100.00
	Ovenal (H-aquared = 99.9%, p = 0.000) NOTE: Weights are from random effects analysis		55.00 (51.43, 58.58)	

Medline/PubMed			
	Search terms		
<u>Group</u>	Non-MeSH terms	MeSH (sub-terms in MeSH)	Citat
#1	Magnitude	Prevalence	
	Epidemiology		
	proportion		
#2	Female	Male	
#3	Novel coronavirus	COVID-19	
	Novel coronavirus 2019		
	2019 nCoV		
	Wuhan coronavirus		
	Wuhan pneumonia		
	SARS-CoV-2		
11.4			
#4		COVID-19 confirmed	
#1 AND #2 AND #3 AN	D #4	patients	
	oportion OR magnitude) AND (Male C	R Female) AND (Novel coronav	irus
· ·	irus 2019 OR 2019 nCoV OR COVID-	<i>,</i> , , , , , , , , , , , , , , , , , ,	
-	RS-CoV-2) AND COVID-19 confirme	· · · · · · · · · · · · · · · · · · ·	ea
database (Table SI). Thus, the PubMed search combines #	#1 AND #2 AND #3 AND #4	

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Joanna Briggs	mstit	ule (JI	31) qu	lanty	appra	aisal	cnec	Klist						
Author				Qu	ality as	sessmei	nt ques	tions						
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	60	Q10	Q11	Yes Total	Quality status	Overall appraisa
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			<u>6</u> /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	Ν			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
2020, 16. WHO	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	Ν			7/9	Low risk	Included
18. Chen et al	UC	Y	Y	Y	Y	N	Y	Y	Y			<mark>6</mark> /9	Low risk	Included
19. Wang et al	Y	Y	Y	Y	Y	N	Y	Y	Ν			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	Ν	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			<mark>6</mark> /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	Ν	Y	Y	Y		<mark>6</mark> /9	Low risk	Included
42. Liang et al	Y	Y	Y	Y	Y	Ν	Y	Y	Ν		7/9	Low risk	Included
43. Wang Y et al	N	Y	Ν	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	Ν	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	Ν	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	Ν	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	Ν	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	 	<u>6/9</u>	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=n	io, UC⁼	=unclea	ar, Q=(Juesti	on								



9 Checklist Checklist item Checklist item Identify the report as a systematic review, meta-analysis, or both. Provide a structured summary including, as applicable: background; objectives; data sources; stady eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. Describe the rationale for the review in the context of what is already known. Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons,	Reported on page #1112
Identify the report as a systematic review, meta-analysis, or both. O Identify the report as a systematic review, meta-analysis, or both. O Provide a structured summary including, as applicable: background; objectives; data sources; stedy eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. O Describe the rationale for the review in the context of what is already known. O	on page # 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Provide a structured summary including, as applicable: background; objectives; data sources; stady eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1 1 1 2
Provide a structured summary including, as applicable: background; objectives; data sources; stady eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1 1 2
participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. Implications; conclusions and operations; conclusions; conclusions and operations; conclusions; conclusin; conclusions; conclusions; conclusions; c	2
participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. Implications; conclusions and operations; conclusions; conclusions and operations; conclusions; conclusin; conclusions; conclusions; conclusions; c	1
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Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons,	
outcomes, and study design (PICOS).	3
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
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
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
Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
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
State the principal summary measures (e.g., risk ratio, difference in means).	7
	5
ir D fo L s D d	Active din the meta-analysis).

Page 29 of 29

Page 1 of 2

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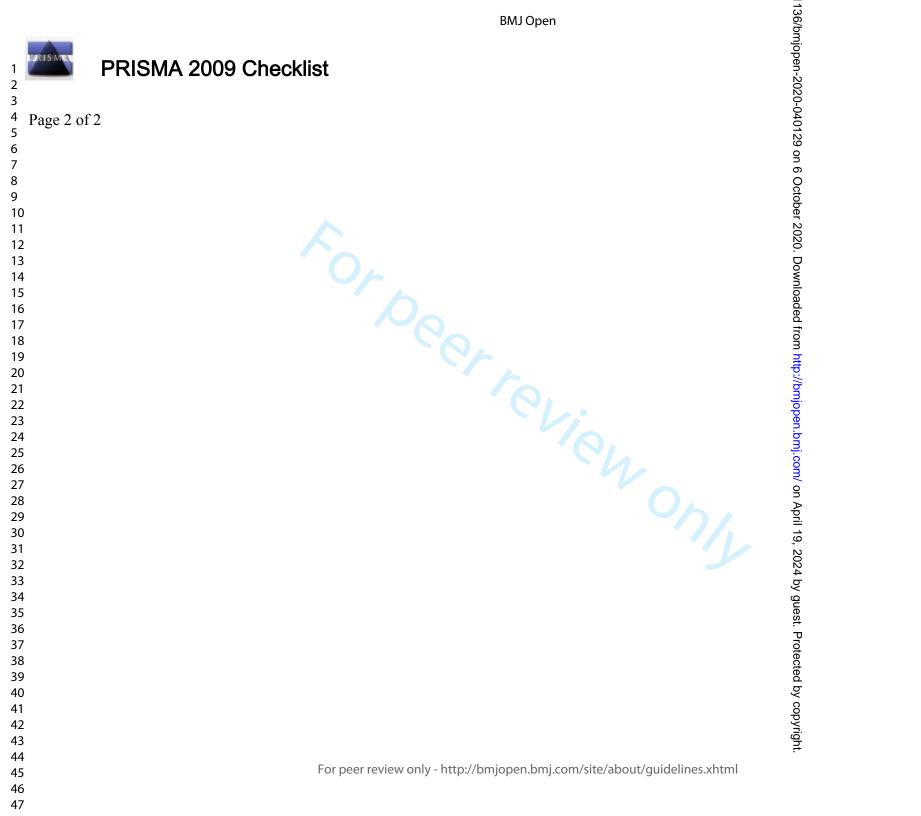
PRISMA 2009 Checklist

6 7 Section/topic 8	#	Checklist item	Reported on page #
9 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
1 Additional analyses 12 13	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
¹⁴ RESULTS			
15 Study selection 17	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions ateach stage, ideally with a flow diagram.	6
18 19 Study characteristics 20	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
23 Results of individual studies 24	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
25 Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	5
27 Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	5
28 29 29	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	5
DISCUSSION		ů, Q	
32 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
34 Limitations 35	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., in complete retrieval of identified research, reporting bias).	13
36 Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
³ 7 FUNDING			
38 Funding 39	27	N/A g	
40	•	by	
41 42 <i>From:</i> Moher D, Liberati	A, Tet	tzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Me	ta-Analyses:
12		Ied 6(7): e1000097. doi:10.1371/journal.pmed1000097 Image: Constraint of the second	2

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- 46 47



BMJ Open

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

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





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	BMJ Open	136/bmjo
1 2	Sex difference in coronavirus disease (COVID-19): A systematic review and meta-analysis Biruk Beletew Abate ^{1*} , Ayelign Mengesha Kasie ¹ , Mesfin Wudu Kassaw ¹ , Teshome Gebremeskel ²	136/bmjopen-2020-040129 on 6
3		
4	¹ Woldia University, College of Health Sciences, Department of Nursing, P.O.Box 400, Woldia, Ethiopia:	October
5		2020.
6		
7	¹ BB= E-mail: <u>birukkelemb@gmail.com</u> ; Tel: +251922898070	Downloaded
8	¹ AM= E-mail: <u>Ayelignmengesha59@gmail.com</u> ; Tel: +251937384459	ed fro
9		from htt
10	² TG= <u>E-mail:teshomefirst12@gmail.com; Tel:+251929397251</u>	tp://br
11	*Corresponding Author: Biruk Beletew Abate; E-mail: <u>birukkelemb@gmail.com</u>	njope
12	<i>Running title</i> : Sex difference in coronavirus disease (COVID-19)	5.b 3
13	Abstract	http://bmjopen.bmj.com/
14	Objective: To assess the sex difference in the prevalence of coronavirus disease (COVID-19) confirmed cas	on&r
15		oril 19, 2
16	Setting: PubMed, Cochrane library, and Google Scholar were searched for related information. The authors	Reveloped a data
17	extraction form on the excel sheet and the following data were extracted for eligible studies: author, country,	ample size, number
18	female patients, and the number of male patients. Using STATA 14 for analysis authors pooled the overall pr	valence male and/or
19	female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q sta	$\mathbf{\tilde{s}}_{\mathbf{\tilde{s}}}$ istic and the I ² statistics.
20	Subgroup and sensitivity analysis was done Publication bias was also checked.	d by
		by copyright
		ight.

Page 3 of 34		BMJ Open
1		
2 3 4 5 6 7 8 9 10 11 12 13 14 15	21	BMJ Open BMJ Open Participants: Studies with COVID-19 confirmed cases were included. BMJ Open Intervention: sex (male/female) of COVID-19 confirmed cases were considered BMJ Open
	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
	24	Result: A total of 57 studies with 221195 participants were used for analysis. The pooled prevalence of COV 2D-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 sign
16	27	the absence of publication bias in both outcomes.
17 18	28	Conclusions: The prevalence of symptomatic COVID-19 is higher among males than females. The high pregalence of smoking and
19 20 21 22 23 24 25 26 27 28 29 30 31	29	alcohol consumption has contributed for increased high prevalence of COVID-19 among males. Additional sudies regarding
	30	discrepancy in severe illness and mortality due to COVID-19 among males and females and factors which determine the exposure,
	31	severity and mortality due to COVID-19 is recommended.
	32	Keywords: COVID-19; sex difference; Systematic review; Meta-analysis
	33	Keywords: COVID-19; sex difference; Systematic review; Meta-analysis Image: Covid Strength and limitations Strength and limitations Image: Covid Strength and Strength a
	34	This systematic review and meta- analysis has several strengths: we used a pre-specified protocol for $\frac{g}{2}$ earch strategy and data
	35	abstraction and used internationally accepted tools for a critical appraisal system for quality assessment of individual studies. Besides
32 33	36	we employed subgroup analysis, publication bias and sensitivity analysis. Nevertheless, this review had some limitations: because of
34	37	the inclusion of studies which are published in English only, language bias is likely. In addition most inclueed are from China due to
35 36	38	lack of literatures from other countries in the world which reported the outcome of interest. However, the data in this review permit to
37 38	39	systematically review and analyze the pooled prevalence of COVID-19 among males.
39 40 41 42 43 44	40	systematically review and analyze the pooled prevalence of COVID-19 among males.

Background

136/bmjopen-2020-0401 A COVID-19, first identified in Wuhan, China in late 2019, has rapidly evolved resulted in a pandemic by the first quarter of 2020, as indicated by the substantial rise in the number of cases and the fast geographical spread of the disease (1-4). The WHO announced that the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19) (5, 6). The virus has novel been named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) (7). COVID-19 has now been declared as a Public Health Emergency of International Concern by the WHO on 30th January 2020(8). COVID-19 affects people differently, in terms of infection with the virus SARS-CoV-2 and mortality rates ($9 \le 10$). Susceptibility to symptomatic COVID-19 seems to be associated with age, biological sex, and comorbidities (11). Although the COVID-19 causes a mild illness in a majority of cases, severe illness requiring hospital admission is not uncommon (12). Besides, it has the potential to precipitate a life-threatening critical illness, characterized by respiratory failure, circulatory shock, sepsis or other organ failure, requiring intensive care(13, 14). According to Global Health 5050 data gathering, the number of COVID-19 confirmed cases and the death rate due to COVID-19 is high among males in different countries (15-17). The report in the lancet and Global Health 5050 summarize, sex-disaggregated data are essential for understanding the distributions of risk, infection, and disease in the population, and the extent to which sex and gender affect clinical outcomes (18). Besides, knowing the degree to which outbreaks upsets women and men in different way is an important step for generating effective, equitable policies and interventions. Since the occurrence of COVID-19 infection in Wuhan, China, in December 2019 (19), it has quickly spread across China and numerous other countries(20-24). So far, 2019-nCoV has affected more than 193 countries with 23,591 confirmed cases, including 191185 deaths and 751,404 recovery (25). Even though, some previously published papers have showed the sex variation, those findings are not conclusive due to inconsistency in prevalence of COVID-19 among males and females. Moreover, there is lack of systematic review and meta-analysis which indicated the worldwide clear picture of sex variagion on the risk of by copyright. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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Page 5 of 34		BMJ Open	
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2 3	61	COVID-19. Hence, this systematic review and meta-analysis was conducted to assess the pooled prevalence	S f COVID-19 among
4 5 6 7			
	62	males and females.	
/ 8	63	Review question	2 2
9 10	64	The review questions of this systematic review and meta-analysis were:	
11	65	Are men more susceptible to getting symptomatic COVID-19?	r 90000
12 13	66	Methods	
14 15	67	Search strategy	
16 17	68	This systematic review and meta-analysis identified studies that revealed data on the proportion of sex in C	VID-19 confirmed case.
18 19 20 21	69	We retrieved studies from Google Scholar, PubMed, Scopus, Web of Sciences Cochrane library, researed	h gate, and institutional
	70	repositories. The search included keywords that are the combinations of population, condition/outcome,	and context. A snowball
22 23	71	searching for the references of relevant papers for linked articles was also performed. Those search terms	phrases including were:
24	72	The search terms used were: "Novel coronavirus," "Novel coronavirus 2019", "2019 nCoV", "COVID-19	", "Wuhan coronavirus,"
25 26	73	"Wuhan pneumonia," and "SARS-CoV-2." Articles published in English language were considered from	m January 1, 2020. The
27 28	74	searches were concluded by March 27, 2020, and four different researchers independently evaluated search	Fresults. Using those key
29	75	terms, the following search map was applied: (prevalence OR proportion OR magnitude) AND (Male d	R Female) AND (Novel
30 31 32 33	76	coronavirus OR Novel coronavirus 2019 OR 2019 nCoV OR COVID-19 OR Wuhan coronavirus OR Wuha	n pneumonia OR SARS-
	77	CoV-2) AND COVID-19 confirmed patients on PubMed database (Table S1). Thus, the PubMed search co	mbines #1 AND #2 AND
34 35	78	#3 AND #4 (Table S1). The searching date was January 2000 to December 2019.	
36 37 28	79	Study selection and screening	
38 39	80	The retrieved studies were exported to Endnote version 8 reference managers to remove duplicate studies.	wo investigators (BB and
40 41 42 43	81	AM) independently screened the selected studies using article's title and abstracts before retrieval of full-	

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

Inclusion and exclusion criteria

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

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

Quality assessment

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

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Data extraction

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

BMJ Open were resolved through discussions with third and fourth reviewers when required. The mistyping of data was resolved through crosschecking with the included papers. The case definition considered was as follows: confirmed case: detection of SARS-CoV-2 nucleic acid in a clinical specimen; possible case: any person with at least one of the following symptoms: wugh, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia; probable case: any person with at least one of the following symptoms : cough, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia, with close contact with a confirmed COVID-19 case in the 14 days prior to onset of symptom or having been a resident or a staff member, in the 14 days prefor to onset of symptoms, in a residential institution for vulnerable people where ongoing COVID-19 transmission has been confirmed.

Synthesis of results

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

Result

Study selection

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

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2 3 4 5 6 7 8 9 10 11 12 13 14	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) (Table1).
	128	Meta-analysis
14 15	129	Prevalence of COVID-19 among male
16	130	All studies (n=57) with a total of 2,21195 patients had reported the sex proportion of COVID-19 (1, 1) 13, 14, 24, 27-73). The
17 18 19 20 21 22 23 24 25 26 27 28 29 30	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(51.43-5, 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\vert 4), 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 $F_{\underline{g}}^{\underbrace{B}}$ 1).
31 32	138	The pooled prevalence of COVID-19 among male in Wuhan, Shanghai, Hubei, Zhonghua, outside china, Zhonghua, Shenzhen, Jiangsu,
33 34	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;
35	140	$P=0.001, 54.07 (95\% \text{ CI:}51.63-56.51) ; I^2 = 37.9 ; P=0.139, 53.17 (95\% \text{ CI:}52.81-53.53) ; I^2 = 99.4, P=0 \underbrace{1000}{1000} 0, 46.45 (95\% \text{ CI:}39.10-1000) ; I^2 = 1000 \text{ CI:}51.63-56.51 ; I^2 = 10000 \text{ CI:}51.53-56.51 ; I^2 = 10000 \text{ CI:}51.53-56.51 ; I^2 = 100000 \text{ CI:}51.53-56.51 ; I^2 = 100000000000000000000000000000000000$
36 37	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) \vec{P} ; $I^2 = 29$, P= 0.235, and
38 39 40 41 42	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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2		1-2020
3 4	143	Regarding quality score the pooled prevalence of COVID-19 among male in studies which scored greater than or equal to seven was
5	144	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
6 7 8	145	seven from JBI quality appraisal checklist(Table 2 and Supplementary Fig 3).
9 10	146	Regarding sample size the pooled prevalence of COVID-19 among male in studies which have sample size greater than or equal to
11	147	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 and studies scored less
12 13	148	than seven from JBI quality appraisal checklist(Table 2 and Supplementary figure 4).
14 15 16	149	Sensitivity analysis
17 18	150	We employed a leave-one-out sensitivity analysis to identify the impact of individual research on the pogled prevalence of severe
19 20	151	illness among COVID-19confirmed cases. The results of this sensitivity analysis showed that our findings were not dependent on a
21 22	152	single study. Our pooled estimated prevalence of severe illness varied between 22.83 (19.12-26.53) Li J ET and 25.0 (19.87-30.13)
23	153	Yanping Z ET al after the deletion of a single study (Figure 3).
24 25 26 27 28 29 30 31 32	154	Publication Bias
	155	We have also checked publication bias and, a funnel plot showed symmetrical distribution. Egger's regression test p-value was 0.599.
	156	Both the symmetric funnel plot and the insignificant p-value (<0.05) indicates the absence of publication bias
	157	Meta-regression 224
33 34 25	158	Univariate meta-regression analyses revealed that the prevalence of smoking was found to be high in males. This contributed for high
35 36	159 160	prevalence of COVID-19 among males (P=0.002). Comorbidities like hypertension (0.042), diabetic mellitus (0.012, chronic respiratory disease (0.021), and cardio vascular disease (0.001) were also found to be higher in males and the significantly increases
37 38	161	the prevalence of COVID-19. Besides, higher proportion of sever/critical illness (0.003) and death (0.001) were also observed among
39	162	males (Table 3)
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3 4	163	Discussion
5 6	164	This systematic review and meta-analysis were conducted to assess the sex difference in getting COVID -19 giseases. Fifty seven
7 8	165	studies were included in the final analysis. The result of this systematic review and meta-analysis revealed that the pooled prevalence
9	166	of COVID -19 confirmed cases among males and females was found to be $55.00(51.43-56.58; I2=99.5\%; p < 0.01)$ and $45.00(41.42-$
10 11	167	48.57) respectively. This indicates COVID -19 is prevalent in males than females.
12 13		
14	168	This finding was also reported by other studies (75, 76). A study in Ontario, Canada showed that men were not be the studies of the studies o
15 16	169	positive(77, 78). In Pakistan 72% of COVID-19 cases were male(79). According to Global Health 5050 datagethering, the number of
17	170	COVID-19 confirmed cases and the death rate due to COVID-19 is high among males in different countries $\frac{1}{2}$ 5-17).
18 19	171	This might be due to behavioral factors and roles which increase the risk of acquiring COVID-19 tend to occur more among men.
20	172	Male are more involved in different risky behaviors like alcohol consumption (80-82), key activities in buria frites; as employees in
21 22	173	basic sectors and occupations that continue being active and require them to work outside the home and interact with other people
22	174	during the containment phase (e.g., food or pharmacy manufacturing and sales, agriculture or food production and distribution,
24	175	transportation, and security). Because of such behaviors males mostly don't stay at home, sit together, and remove their mask while
25 26	176	they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease. In China 50% of
20	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
28	178	adverse outcomes of COVID-19: for instance, the combined results of five studies showed that smokers were 1.4 times more likely
29 30	179	than non-smokers to have severe symptoms of COVID-19 (83). Besides, smoking is related to higher expression of ACE2 (the
31	180	receptor for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), which might be the reason for the higher prevalence of COVID 10 in this subgroup of patients than in woman (84)
32 33	181	COVID-19 in this subgroup of patients than in women (84).
33 34	182	Men tended to develop more symptomatic and serious cases than women, according to the clinical classification of severity. Similar
35	183	occasions occurred during previous coronavirus epidemics: men had worse outcomes of illness from severe a gute respiratory
36 37	184	syndrome (SARS), (85)and a higher risk of dying from Middle East respiratory syndrome (MERS)(86). Biological sex variation is said
38	185	to be one of the reason for the sex discrepancy of COVID-19 cases, severity and mortality (87). Women are $in \frac{1}{2}$ general able to mount a
39	186	more vigorous immune response to infections and vaccinations(88). Some previous studies on coronaviruses and mice have suggested
40 41	187	that the hormone estrogen may have a protective role. Estrogens suppress the escalation phase of the immune response that leads to
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3 4 5	188 189	increased cytokine release(89). The authors showed that female mice treated with an estrogen receptor antagen ist died at close to the same rate as the male mice(90).
6 7	190	The X chromosome is known to contain the largest number of immune-related genes in the whole genome($8\hat{\theta}$). With their XX
8 9	191	chromosome, women have a double copy of key immune genes compared to the single copy in XY men. This boost extends to both
10 11	192	the general reaction to infection (the innate response) and also to the more specific response to microbes including antibody formation
12	193	(adaptive immunity)(86). Thus women's immune systems are generally more responsive to infections. This might mean women are
13 14 15	194	able to tackle the novel coronavirus more effectively but this has not yet been proven.
16 17	195	Besides, the above listed behavioral factors like smoking and alcohol consumption tend to occur more among men, those behaviors
18	196	predisposes males for cardiac and respiratory diseases. This may also explain the overall higher mortality rates among men (84, 91,
19 20	197	92). A systematic review and meta-analysis revealed that comorbid disease, such as respiratory system disease, hypertension, and
21 22	198	cardiovascular disease as risk a risk factors for death compared with patients without comorbidity(93).
23 24 25	199	Conclusions
26 27	200	The prevalence of symptomatic COVID-19 is higher among males than females. This can be explained with prevalent behaviors
28 29	201	which increase the risk of acquiring COVID-19 are among males. Males are more involved in different risky behaviors like alcohol
30	202	consumption (3-5), and occupational exposures because of which males mostly don't stay at home, sit together, remove their mask
31 32	203	while they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVIB-19 disease; that is why
33 34	204	it is more prevalent in male. Smoking and drinking alcohol reduce your overall health and therefore make your more susceptible to
35	205	symptomatic COVID-19 infection. Although there has been a rapid surge in research in response to the outbread at a coving of the coving at the coving of the coving at the coving of the coving at the
36 37	206	additional studies regarding discrepancy in severe illness and mortality due to COVID-19 among males and generative market which
38 39	207	determine the exposure, severity and mortality due to COVID-19 is recommended.
40 41 42 43	208	determine the exposure, severity and mortality due to COVID-19 is recommended. Mathematical Structure Abbreviations Mathematical Structure
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1 2		jopen-20
2 3 4	209	COVID-19: coronavirus disease 2019; WHO: World Health Organization; ICTV: International Committee of Taxonomy of Viruses;
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 10	212	Declarations
11 12 13	213	Ethics approval and consent to participate
14 15	214	Not applicable
16 17 18	215	Ethics approval and consent to participate Description Not applicable Consent for publication Not applicable Availability of data and material
19 20	216	Not applicable
21 22 23	217	Availability of data and material
24 25	218	The datasets analyzed during the current study are available from the corresponding author upon reasonable request.
26 27 28	219	Competing interests
29 30 31	220	Competing interests Ve have confirmed that we have no competing interests. Ve have confirmed that w
32 33	221	Funding
34 35 36	222	No funding was obtained for this study
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1 2 3 4	225	BMJ Open 36000000000000000000000000000000000000
5 6	226	BB, AM, MW, and TG: developed the study design and protocol, literature review, selection of studies \vec{p}_{p} quality assessment, data
7 8	227	extraction, statistical analysis, interpretation of the data and developing the initial drafts of the manuscript and prepared the final draft
9 10	228	of the manuscript. All authors read and approved the final manuscript.
10 11 12 13	229	Acknowledgments
14 15	230	We would like to thank the authors of the included primary studies.
16 17 18	231	References for the formation of the form
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Table 1

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_	Sr no	Author	Country	Study Period	Sample Size	Male	Female	Quality score	Refere
	1.	Li K et al	China	Jan-Feb	83	44	39	6/9	(27
	2.	Liu Y et al	China	Jan11-Jan20	12	8	4	9/9	(28
	3.	Liu Y et al	China	Jan23-Feb8	109	59	50	6/9	(2 g
	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. 7	Xu X et al	China	Jan10-Jan26	62 50	36	26	8/9 6/0	
	7. 8.	Xu Y et al Yao et al	China China	Jan-Feb Jan01-Feb07	50 195	29 115	21 80	6/9 8/9	(3Z) (3E)
	o. 9.	Young et al	China	Jan22-Jan31	195	9	9	8/9 6/9	
). 10.	Zhang J et al	China	Jan16-Feb03	140	71	69	8/9	(37
	11.	Zhang M et al	China	Jan18-Feb03	9	5	4	7/9	(36
	12.	Zhao et al	China	Jan16-Feb03	101	56	45	8/9	
	12.	Zhu et al	China	Dec01-Feb15	12	8	43	7/9	(38
	14.	Yanping Z et al	China	February 2020	44672	22981	21691	8/9	(3 9
	15.	W. Guan et al	China	February 2020	1099	640	459	7/9	(46)
	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	(42
	19.	Wang et al	China	March 2020	138	75	63	7/9	(24
	20.	Kaiyuan S et al	China	February, 2020	507	281	201	6/9	(4)
	21.	AL Giwa et al	China	March, 2020	78771	57482	21289	9/9	(44
	22.	Qian G et al	China	March, 2020	91	37	54	8/9	(45
	23.	Livingston E et al	Italy	March, 2020	22512	13462	9050	7/9	(46
	24.	Wang Y et al	China	March, 2020	110	48	62	6/9	(42
	25.	KSID,2020	Korea	February, 2020	4212	1591	2621	9/9	(48
	26. 27	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	()()
	28. 29.	Kui et al	China China	March, 2020	137 33	61	76 16	8/9 8/9	() []
	29. 30.	Deng L et al	China	March, 2020	135	17 72	10 63	6/9	(32
	30. 31.	Dong X et al Xiaobo et al	China	March, 2020	52	35	03 17	8/9	(12)
	31.	Zhou F et al	China	March, 2020 March, 2020	52 191	119	72	6/9	
	32. 33.	Wu Y et al	China	March, 2020	297	119	150	8/9	(14) (5 4)
	33. 34.	Gao Q et al	China	January to February ,2020	213	108	105	7/9	(5) (5)
	34. 35.	Chen X et al	China	February 2020	213	145	105	8/9	(55) (56) (57)
	35. 36.	Zhang G et al	China	December 2019	221	108	113	7/9	(5 6
	30. 37.	Wu W et al	China	March, 2020	21	100	115	8/9	(১৭) (১ম
	38.	Cao M et al	China	February, 2020	128	60	68	7/9	55(9)(6)(6)(6)(6)(6)(7)(7)(7)(7)(7)(7)(7)(7)(7)(7)(7)(7)(7)
	39.	Chung et al	China	March, 2020	20	13	7	7/9	(Second
	40.	Xiao F et al	China	March, 2020	73	41	32	7/9	(6 0
	41.	Qi D et al	China	January to February ,2020	267	149	118	6/9	(8) (6)
	42.	Liang et al	China	China	1590	911	679	7/9	62
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5	412	45. 46.	Mizumoto K et al Chen X et al	Japan China	March, 2020 March, 2020	634 48	321 37	313 11	8/9 7/9	(39) (39) (689)
7 8	413	47. 48. 49.	Cheng J et al Li J et al Tian S et al	China China China	March, 2020 March, 2020 April 2020	1079 47 262	573 28 127	505 19 135	6/9 9/9 8/9	(6 9 (2 9) (6 0)
9 10 11	414	50. 51. 52.	Li et al Liu Y et al Cao W et al	China China China	March, 2020 February, 2020 February, 2020	425 109 198	240 59 101	185 50 97	7/9 6/9 9/9	(6 8) (1 8) (7 0)
11 12 13	415	53. 54. 55.	Chaolin et al Yang X et al Liu L et al	China China China	February, 2020 February, 2020 February, 2020	41 52 51	30 35 32	11 17 19	6/9 8/9 8/9	(78) (19) (79)
14 15	416	56. 57.	Huang C et al Wang D et al	China China	February, 2020 February, 2020 February, 2020	41 138	30 75	11 63	8/9 6/9	(1¥17) (7) (7)
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Variables	Characteristics	Pooled prevalence (95% CI)	I ² (P-value)
By province in	Wuhan	72.05 (71.71-72.35)	96.6 (0.00)
china	Shanghai	51.01 (44.05-57.97)	-
	Hubei	50.40 (50.1-50.80)	66.7 (0.001)
	Zhonghua	54.07 (95% CI:51.63-56.51)	37.9 (0.139)
	Zhejiang	46.45 (39.10-53.81)	99.4 (0.00)
	Shenzhen	63.52 (51.64-75.40)	0.0 (0.796)
	Jiangsu	44.84 (35.99-53.68)	29 (0.235)
	Chongqing	52.20 (47.95-56.44)	65.1 (0.09)
	outside china	53.17 (52.81-53.53)	99.4 (0.00)
By country	China	55.99(51.99-59.99)	99.5 (0.00)
	Africa	39.21(34.85-43.84)	-
	Italy	59.80(59.16-60.44)	-
	Korea	37.77(36.31-39.24)	-
	Singapore	50.00(26.90-73.10)	-
By JBI quality	>=7	53.66 (95% CI:49.23-58.09)	99.5 (0.00)
score	<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)
U I	<384	54.96 (52.35-57.57)	64.5(0.00)

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Table 3

Variable	Event	Total	Male	Studies	Male (%)	Female (%)	P value
Smoking Comorbidities	2863	11590	8693	19	75	25	0.002
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	20120	150070	105222	40	(())	227	0.002
Sever / critical illness Death	38128 699028	158870 158870	105322 125322	49 46	66.3 78.8	33.7 21.2	0.003 0.001

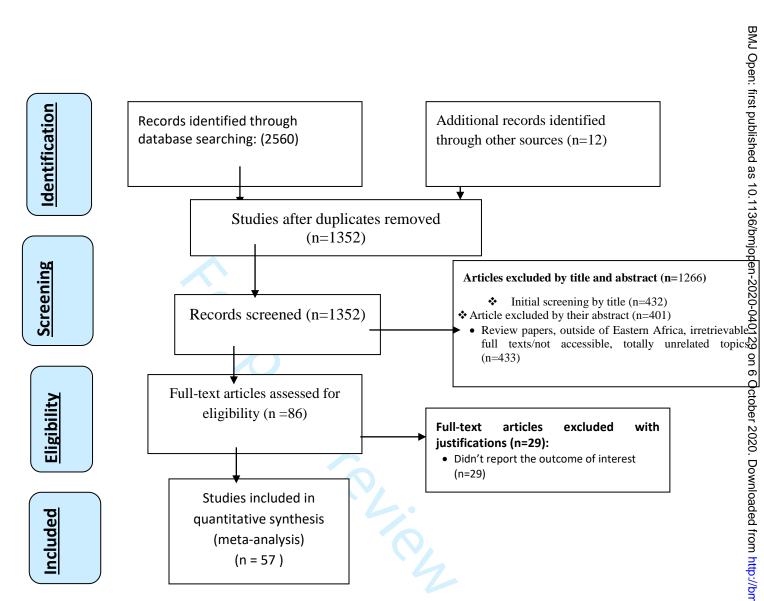


Figure 1: PRISMA flow diagram showed the results of the search and reasons for exclusion



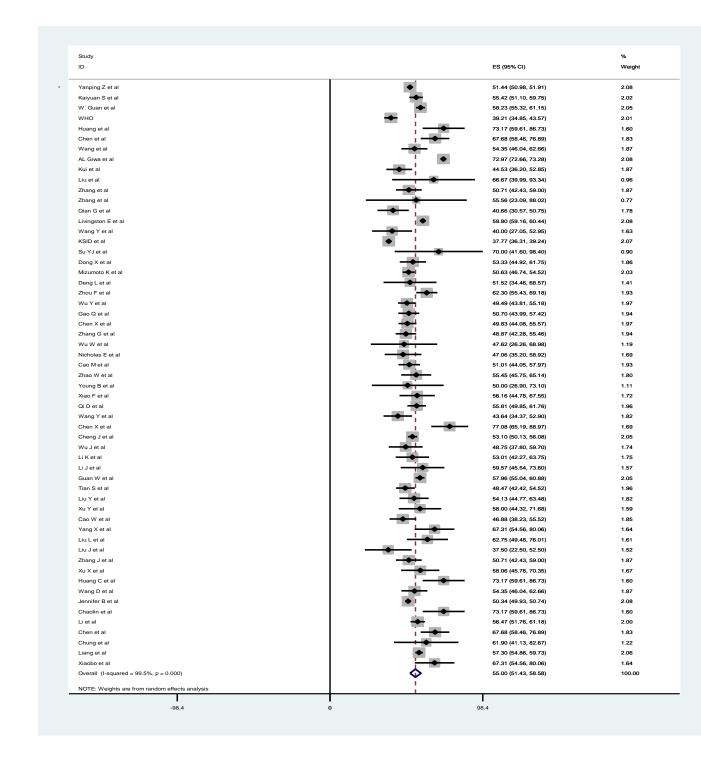
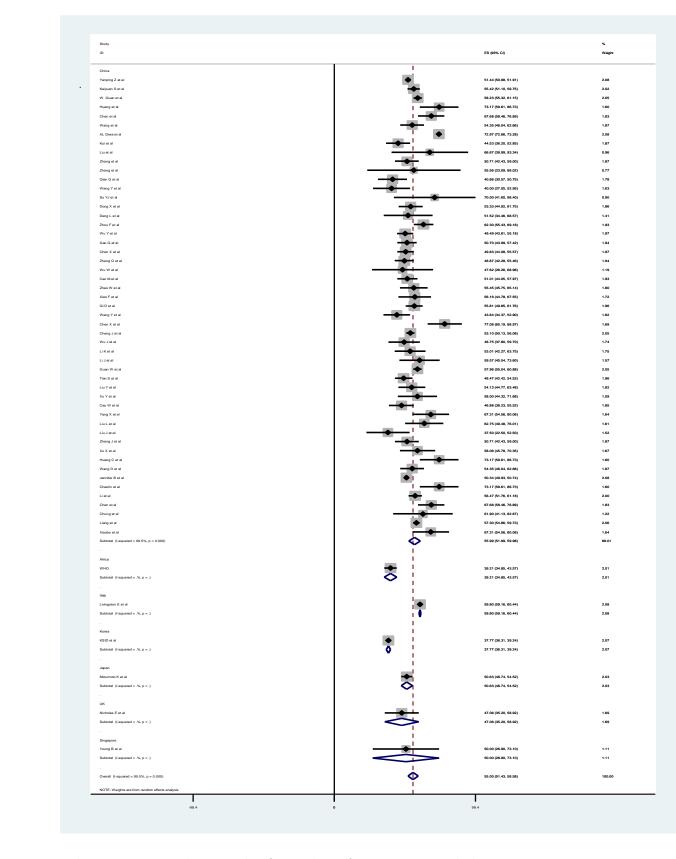


Figure 2: Forest plot showing the pooled prevalence of COVID-19 confirmed cases among male

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4	Study ommited	Coef.	[95% Conf.	Interval]
5	Cheng J et al	20.732838	20.445127	21.020546
6	xu x et al	17.418531	17.156216	17.680845
7	Liu L et al	17.381458	17.119438	17.643478
8	Yao et al	17.516275	17.25304	17.77951
9	Wang Yet al	17.346966	17.085199	17.608732
	Wu J et al		17.100435	17.624273
10	Xia W et al Xiao F et al	17.317913 17.338419	17.056414 17.076689	17.579412 17.600149
11	Cao M	17.330419	17.078194	17.60206
12	Qian G et al	17.322186	17.060547	17.583824
13	Liu C et al	17.311192	17.049721	17.57266
14	zhao et al	17.313881	17.052284	17.57548
15	Yang et al	17.312496	17.050829	17.574163
16	Gao Q et al	17.313957	17.052176	17.575737
	Guan W		17.068779	17.595478
17	Cao W et al Chen X	17.310188	17.048569 17.04727	17.571806 17.571028
18	Tian et al	17.307884	17.046061	17.569708
19	Tian S et al	17.307884	17.046061	17.569708
20	Yanping Z et al	16.002106	15.621832	16.382381
21	Qi D et al	17.304249	17.042439	17.566059
22	W. Guan et_al	17.256212	16.993301	17.519123
23	Liu K et al	17.298866	17.037294	17.56044
23	Liu W et al Li Y et al	17.30262 17.304375	17.041122 17.042908	17.564116 17.565842
	Xu Y et al	17.304575	17.042908	17.56613
25	Wang D et al	17.297497	17.035929	17.559065
26	Wang D et al	17.297497	17.035929	17.559065
27	Wu Y et al	17.280704	17.018961	17.54245
28	Livingston E et al	14.335077	14.044443	14.625712
29	Li K et al	17.299694	17.0382	17.561188
30	Li K et al Chen W et al	17.299694 17.301987	17.0382 17.040525	17.561188 17.56345
31	Huang C et al	17.303835	17.040323	17.565281
32	Wu W et al	17.305992	17.044569	17.567415
	Young et al	17.306377	17.044958	17.567799
33	Wang Y et al	17.293758	17.032244	17.555273
34	zhang J et al	17.283909	17.022371	17.545444
35	Zhang J et al		17.022371	17.545444
36	Wu W et al Chen L et al	17.30135 17.302288	17.039911 17.040859	17.56279 17.563717
37	Liu Y et al	17.284363	17.02286	17.545866
38	Chen X et al	17.295172	17.033726	17.556618
39	zhou F et al	17.243504	16.981913	17.505095
	Liu Y et al	17.302118	17.040703	17.563536
40	Li J et al	17.256153	16.994654	17.517653
41	Yang X et al	17.308687	17.047285	17.570087
42	Combined	17.308687	17.047285	17.570088
43				
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Figure 3: sensitivity analysis for pooled prevalence of COVID-19 confirmed cases among males



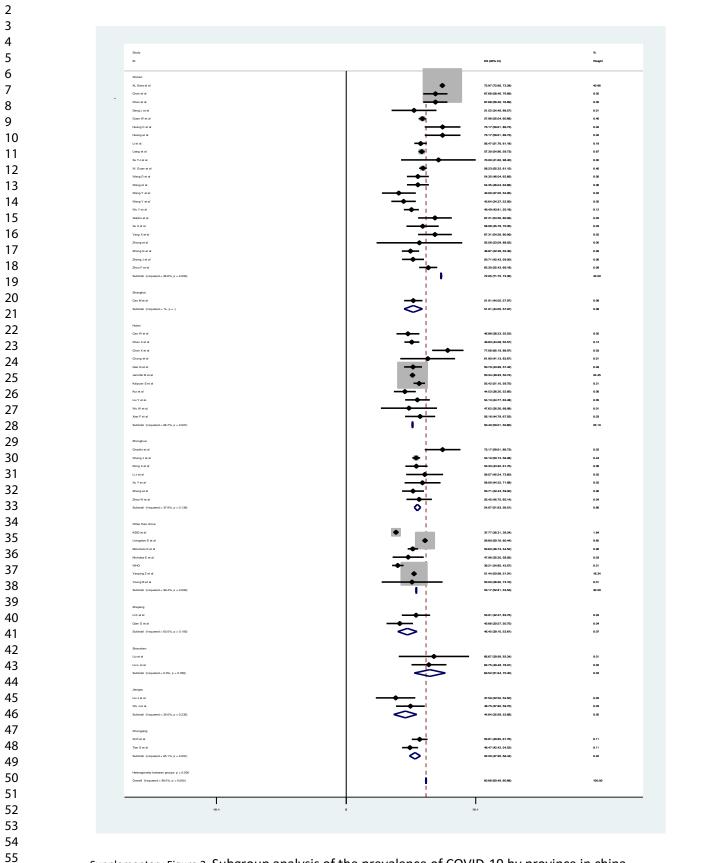
Supplementary Figure 1: Sub group analysis for prevalence of COVID-19 among males by countries

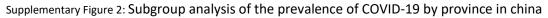
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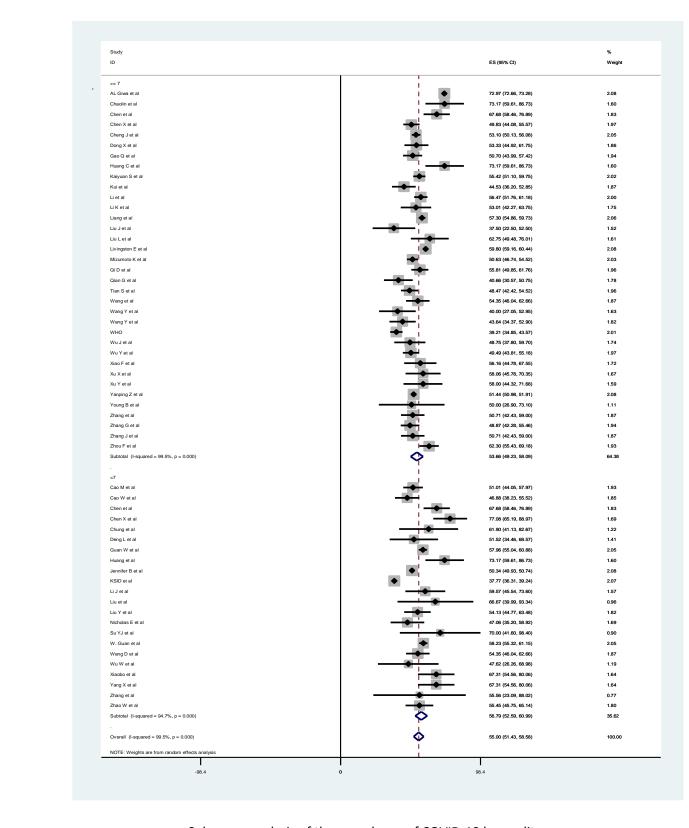
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Supplementary Figure 3: Subgroup analysis of the prevalence of COVID-19 by quality score

Study ID		ES (95% CI)	% Weight
>384	•		
AL Giwa et al Cheng J et al	· · · ·	72.97 (72.66, 73.28) 53.10 (50.13, 56.08)	2.08
Guan W et al	•	57.96 (55.04, 60.88)	2.05
Jennifer B et al	•	50.34 (49.93, 50.74)	2.08
Kaiyuan S et al	+	55.42 (51.10, 59.75)	2.02
KSID et al	• •	37.77 (36.31, 39.24)	2.07
Lietal LiKetal		56.47 (51.76, 61.18) 53.01 (42.27, 63.75)	2.00 1.75
Lincetal		53.01 (42.27, 63.75) 57.30 (54.86, 59.73)	1.75
Livingston E et al	•	59.80 (59.16, 60.44)	2.08
Mizumoto K et al	•	50.63 (46.74, 54.52)	2.03
W. Guan et al	•	58.23 (55.32, 61.15)	2.05
WHO KING THE REPORT	• •	39.21 (34.85, 43.57)	2.01
Yanping Z et al Subtotal (I-squared = 99.9%, p = 0.000)		51.44 (50.98, 51.91) 53.86 (47.09, 60.63)	2.08 28.39
-		00.00 (47.00, 00.00)	20.00
<384	1		
Cao M et al		51.01 (44.05, 57.97)	1.93
Cao W et al		46.88 (38.23, 55.52)	1.85
Chaolin et al Chen et al		73.17 (59.61, 86.73) 67.68 (58.46, 76.89)	1.60
Chen et al		67.68 (58.46, 76.89) 67.68 (58.46, 76.89)	1.83 1.83
Chen X et al		49.83 (44.08, 55.57)	1.97
Chen X et al		77.08 (65.19, 88.97)	1.69
Chung et al		61.90 (41.13, 82.67)	1.22
Deng L et al		51.52 (34.46, 68.57)	1.41
Dong X et al Gao Q et al		53.33 (44.92, 61.75) 50.70 (43.99, 57.42)	1.86 1.94
Huang C et al		73.17 (59.61, 86.73)	1.60
Huang et al	·	73.17 (59.61, 86.73)	1.60
Kui et al		44.53 (36.20, 52.85)	1.87
Li J et al		59.57 (45.54, 73.60)	1.57
Liu et al		66.67 (39.99, 93.34) 37.50 (22.50, 52.50)	0.96
Liu L et al		62.75 (49.48, 76.01)	1.61
Liu Y et al		54.13 (44.77, 63.48)	1.82
Nicholas E et al		47.06 (35.20, 58.92)	1.69
Qi D et al	*	55.81 (49.85, 61.76)	1.96
Qian G et al Su YJ et al		40.66 (30.57, 50.75) 70.00 (41.60, 98.40)	1.78
Tian S et al		48.47 (42.42, 54.52)	1.96
Wang D et al		54.35 (46.04, 62.66)	1.87
Wang et al		54.35 (46.04, 62.66)	1.87
Wang Y et al		40.00 (27.05, 52.95)	1.63
Wang Yetal Wu Jetal		43.64 (34.37, 52.90) 48.75 (37.80, 59.70)	1.82
Wu Jetal		48.75 (37.80, 59.70) 47.62 (26.26, 68.98)	1.74
Wu Y et al		49.49 (43.81, 55.18)	1.97
Xiao F et al		56.16 (44.78, 67.55)	1.72
Xiaobo et al		67.31 (54.56, 80.06)	1.64
Xu X et al		58.06 (45.78, 70.35)	1.67
Xu Yetal Yang Xetal		58.00 (44.32, 71.68) 67.31 (54.56, 80.06)	1.59
Young B et al		50.00 (26.90, 73.10)	1.11
Zhang et al		50.71 (42.43, 59.00)	1.87
Zhang et al		55.56 (23.09, 88.02)	0.77
Zhang G et al		48.87 (42.28, 55.46)	1.94
Zhang J et al Zhao W et al		50.71 (42.43, 59.00) 55.45 (45.75, 65.14)	1.87
Zhao w et al Zhou F et al		55.45 (45.75, 65.14) 62.30 (55.43, 69.18)	1.80
Subtotal (I-squared = 64.5%, p = 0.000)	o	54.96 (52.35, 57.57)	71.61
Overall (I-squared = 99.5%, p = 0.000)	▲	55.00 (51.43, 58.58)	100.00
NOTE: Weights are from random effects analysis			
-98.4	0	98.4	

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Table S1. Search strategy used for one of the databases

Medline/PubMed			
	Search terms		
<u>Group</u>	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	
щл			
#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

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Table S2: Quality appraisal result of included studies in East Africa, from 2002-2019. Using

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BMJ Open: first Joanna Briggs Institute (JBI) quality appraisal checklist 5 6 published Author Quality assessment questions 7 Overall appraisal Yes Quality status 8 Q10 Total Q11 62 63 Q5 Q6 5 Q8 69 9 5 9 as 10 **Cross-sectional studies** 10.1136/bmjopen-2020-0401 11 Ν Y Ν Y Y Ν Y Y Y 6/9 Low risk Included Li K et al 1. 12 Y Y Y Y Y Y Y 9/9 Y Y Low risk Included Liu Y et al 2. 13 Y Y UC Y Y Ν Y Y Ν 6/9 Low risk Included 3. Liu Y et al 14 Y Y Y Y Y UC Y Y Y 8/9 Low risk Included 4. Liu J et al 15 Y Y Y Y Ν Y Y Y 8/9 Y Included 16 Low risk 5. Wu J et al 17 Y UC 8/9 Y Y Y Ν Υ Υ Y Low risk Included 6. Xu X et al 18 UC Y Y Y Y Ν Y Y Ν 6/9 Low risk Included 7. Xu Y et al 19 Y Y Y Y Y Ν Y Y Y 8/9 Low risk Included Yao et al 8. 20 29 Ν Ν Y Y Y Ν Y Y 6/9 Low risk Included 9. Young et al Υ 21 on Y Y Y Y Y Y Y Y Ν 8/9 Low risk Included 10. Zhang J et al 22 <u>б</u> Y Y UC Y Y Ν Y Y Y 7/9 Low risk Included 23 October 2020 11. Zhang M et al 24 Y Y Y Y UC Y Y Y 8/9 Low risk Included 12. Zhao et al Y 25 Y Y Y Y Y Y Y UC Ν 7/9 Low risk Included 13. Zhu et al 26 Ν Y Y Y Y Y 8/9 Y Y Y Low risk Included 14. Yanping Z et al 27 Y UC Y Y Y Ν Y Y Y 7/9 Low risk Included 15. W. Guan et al 28 Downloaded Y UC Y Y Y Y 7/9Y Y Ν 16. WHO ,2020 Low risk Included 29 Y UC Y Y Y Y Y Y 7/9 Ν Low risk Included 30 17. Huang et al 31 UC Y Y Y Y N Y Y Y 6/9 Low risk Included 18. Chen et al 32 Y Y Y Y Y Ν Y Y Ν 7/9 Low risk Included 19. Wang et al trom 33 Y Ν Y Y Y Y Y Ν N 6/9 Included Low risk 20. Kaiyuan S et al 34 Υ Υ Υ Y Υ Υ Υ Υ Y 9/9 Low risk Included 21. AL Giwa et al 35 Y Y UC Y Y Ν Y Y Y 8/9 Low risk Included 22. Qian G et al 36 UC 7/9 Y Υ Y Υ Υ Ν 37 23. Livingston E et al Y Y Low risk Included pen Y Ν Y Y Y Y Y 38 Ν Ν 6/9 Low risk Included 24. Wang Y et al 39 Υ Υ Υ Y Y Υ Υ Υ Υ 9/9 Low risk Included B 25. KSID,2020 40 Y UC Y Y Y Ν Y Y Ν 6/9 Low risk Included 26. Su YJ et al 41 Y Y Y Y UC Y Y 8/9 Y Y Low risk Included 27. Jennifer B et al 42 on Y Y Y Y Y Ν Y Y Y 8/9 Low risk Included 28. Kui et al 43 April Y UC Y Y Y Ν Y Y Y 8/9 Low risk Included 29. Deng L et al 44 UC Y Y Y Y Ν Y Y Ν 6/9 Low risk Included 45 30. Dong X et al 19 46 Y Y Y Y Y Y Y Y Ν 8/9 Low risk Included 31. Xiaobo et al 2024 47 Ν Y Ν Y Y Ν Y Y Y 6/9 Low risk Included 32. Zhou F et al 48 by Y Y Y Y Y Y Y Y N 8/9 Low risk Included 33. Wu Y et al 49 ' guest UC 7/9 Y Y Y Y Y Y Y Included Ν Low risk 34. Gao Q et al 50 Y Y Y Y Y UC Y Y Y 8/9 Low risk Included 35. Chen X et al 51 Protected by copyright. Y UC Y Y Y Ν Y Y Y 7/9 Low risk Included 52 36. Zhang G et al 53 Y Ν Y Y 8/9 Low risk Included Y Y Y Y Y 37. Wu W et al 54 Y Y Y Y Y UC Y Y 7/9 Ν Low risk Included 38. Cao M et al 55 Y UC Y Y Y Ν Y Y Y 7/9 Low risk Included 39. Chung et al 56 57

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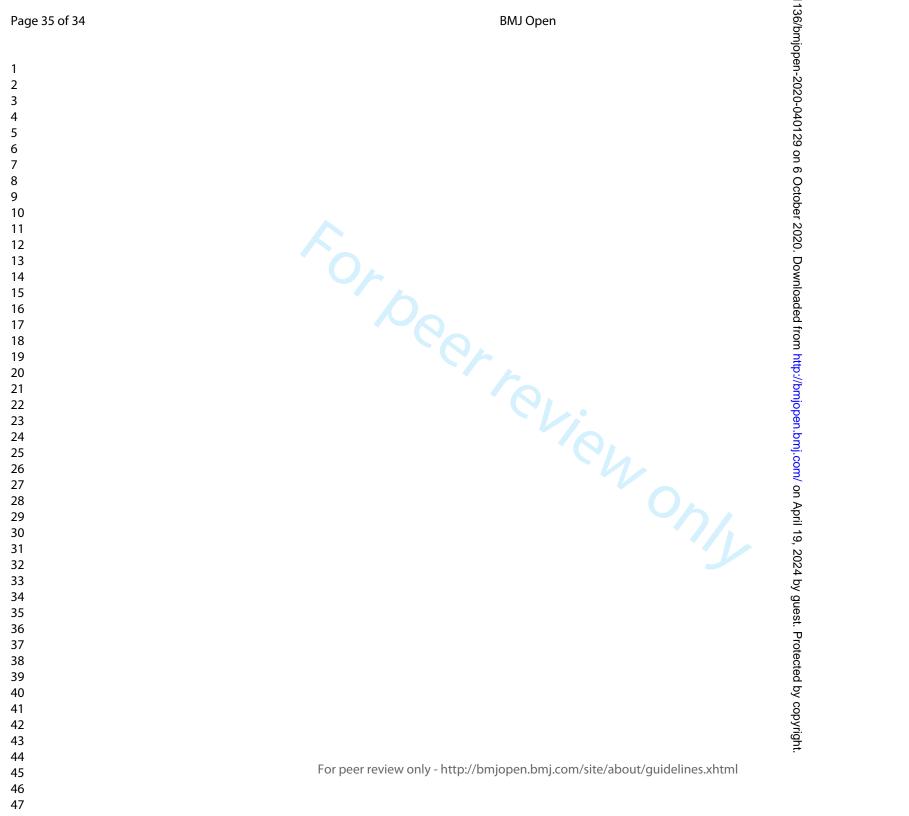
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 Key: Y=yes, N=no, UC=unclear, Q=Question Key: Y=yes, N=no, UC=unclear, Q=Question Key: Y=yes, N=no, UC=unclear, Q=Question
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JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data

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?				
response rate managed appropriately?				





BMJ Open

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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	BMJ Open	136/bmjo
1 2	Sex difference in coronavirus disease (COVID-19): A systematic review and meta-analysis Biruk Beletew Abate ^{1*} , Ayelign Mengesha Kasie ¹ , Mesfin Wudu Kassaw ¹ , Teshome Gebremeskel ²	136/bmjopen-2020-040129 on 6
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11	*Corresponding Author: Biruk Beletew Abate; E-mail: <u>birukkelemb@gmail.com</u>	njope
12	<i>Running title</i> : Sex difference in coronavirus disease (COVID-19)	5.b 3
13	Abstract	http://bmjopen.bmj.com/
14	Objective: To assess the sex difference in the prevalence of coronavirus disease (COVID-19) confirmed cas	on&r
15		oril 19, 2
16	Setting: PubMed, Cochrane library, and Google Scholar were searched for related information. The authors	Reveloped a data
17	extraction form on the excel sheet and the following data were extracted for eligible studies: author, country,	ample size, number
18	female patients, and the number of male patients. Using STATA 14 for analysis authors pooled the overall pr	valence male and/or
19	female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q sta	$\mathbf{\tilde{s}}_{\mathbf{\tilde{s}}}$ istic and the I ² statistics.
20	Subgroup and sensitivity analysis was done Publication bias was also checked.	d by
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Page 3	3 of 34	BMJ Open
1 2		BMJ Open Toppen Participants: Studies with COVID-19 confirmed cases were included. Toppen
3 4 5	21	Participants: Studies with COVID-19 confirmed cases were included.
6 7	22	Intervention: sex (male/female) of COVID-19 confirmed cases were considered
8 9	23	Primary and secondary outcome measures: Primary outcomes were prevalence of COVID-19 among males and females.
10 11	24	Result: A total of 57 studies with 221195 participants were used for analysis. The pooled prevalence of COV among males was
12 13	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
14 15	26	study. Moreover a funnel plot showed symmetrical distribution. Egger's regression test p-value was not sign
16	27	the absence of publication bias in both outcomes.
17 18	28	Conclusions: The prevalence of symptomatic COVID-19 found to be higher among males than females. The shigh prevalence of
19 20	29	smoking and alcohol consumption has contributed for high prevalence of COVID-19 among males. Addition gl studies regarding
21 22	30	discrepancy severity and mortality rate due to COVID-19 among males and females and associated factors is gecommended.
23	31	Keywords: COVID-19; sex difference; Systematic review; Meta-analysis
24 25	32	Article summary
26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44	 33 34 35 36 37 38 39 40 41 42 	 A total of 57 studies with 221195 participants were used for the systematic review and meta-analysis. The pooled prevalence of COVID-19 among males was found to be 55.00(51.43-56.58; 12=99.5%; p.0.001). The sensitivity analysis showed the findings were not dependent on a single study. Moreover a funnel plot showed symmetrical distribution. Egger's regression test p-value was not significant, which indicates the absence of publication bias in both outcomes. The prevalence of symptomatic COVID-19 found to be higher among males than females. The high prevalence of smoking and alcohol consumption has contributed for high prevalence of COVID-19 among males. Additional studies regarding discrepancy severity and mortality rate due to COVID-19 among males and associated factors is recommended.
44 45 46 47		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open This systematic review and meta- analysis has several strengths: we used a pre-specified protocol for gearch strategy and data abstraction and used internationally accepted tools for a critical appraisal system for quality assessment of individual studies. Besides we employed subgroup analysis, publication bias and sensitivity analysis. Nevertheless, this review had some limitations: because of the inclusion of studies which are published in English only, language bias is likely. In addition most included are from China due to lack of literatures from other countries in the world which reported the outcome of interest. However, the data in this review permit to systematically review and analyze the pooled prevalence of COVID-19 among males. 20. Downloaded from Jr De

Background

 A COVID-19, first identified in Wuhan, China in late 2019, has rapidly evolved resulted in a pandemic by the first quarter of 2020, as indicated by the substantial rise in the number of cases and the fast geographical spread of the disease (1-4). The WHO announced that the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19) (5, 6). The virus has now been named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) (7). COVID-19 has now been declared as a Public Health Emergency of International Concern by the WHO on 3th January 2020(8). COVID-19 affects people differently, in terms of infection with the virus SARS-CoV-2 and mortality rates ($9 \ge 10$). Susceptibility to symptomatic COVID-19 seems to be associated with age, biological sex, and comorbidities (11). Although the COVID-19 causes a mild illness in a majority of cases, severe illness requiring hospital admission is not uncommon (12). Besides, it has the potential to precipitate a life-threatening critical illness, characterized by respiratory failure, circulatory shock, sepsis or other organ failure, requiring intensive care(13, 14). According to Global Health 5050 data gathering, the number & COVID-19 confirmed cases and the death rate due to COVID-19 is high among males in different countries (15-17). rotected by copyright.

BMJ Open The report in the lancet and Global Health 5050 summarize, sex-disaggregated data are essential for understanding the distributions of risk, infection, and disease in the population, and the extent to which sex and gender affect clinical outcomes (38). Besides, knowing the degree to which outbreaks upsets women and men in different way is an important step for generating effective, equitable policies and interventions. Since the occurrence of COVID-19 infection in Wuhan, China, in December 2019 (19), it has quickly spread across China and numerous other countries (20-24). So far, 2019-nCoV has affected more than 193 countries with 2,⁹733,591 confirmed cases, including 191185 deaths and 751,404 recovery (25). Even though, some previously published papers haven showed the sex variation, those findings are not conclusive due to inconsistency in prevalence of COVID-19 among males and females. Moreover, there is lack of systematic review and meta-analysis which indicated the worldwide clear picture of sex variagion 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. http://bmjopen.bmj.com/ on April **Review question** The review questions of this systematic review and meta-analysis were: en 01 □ Are men more susceptible to getting symptomatic COVID-19? Methods Search strategy This systematic review and meta-analysis identified studies that revealed data on the proportion of sex in CÖVID-19 confirmed case. We retrieved studies from Google Scholar, PubMed, Scopus, Web of Sciences Cochrane library, research gate, and institutional

repositories. The search included keywords that are the combinations of population, condition/outcome, and context. A snowball searching for the references of relevant papers for linked articles was also performed. Those search terms of phrases including were: The search terms used were: "Novel coronavirus," "Novel coronavirus 2019", "2019 nCoV", "COVID-1§", "Wuhan coronavirus,"

"Wuhan pneumonia," and "SARS-CoV-2." Articles published in English language were considered from January 1, 2020. The

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

Study selection and screening

The retrieved studies were exported to Endnote version 8 reference managers to remove duplicate studies. Tako investigators (BB and AM) independently screened the selected studies using article's title and abstracts before retrieval of full-ext papers. We used pre-specified inclusion criteria to further screen the full-text articles. Disagreements were discussed during a² consensus meeting or, if necessary, by including the third and fourth researchers (MW and TG) to make the final decision for the selection of studies to be included in the systematic review and meta-analysis.

Inclusion and exclusion criteria

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

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 Patient and Public Involvement: Patients or the public WERE NOT involved in the design, or conduct, or reporting, or

 0129 on 6 dissemination plans of our research

Quality assessment

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

Data extraction

The authors developed a data extraction form on the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number female patients, and the number of male patients. The data extraction sheet was piloted using 4 papers randomly, and it was adjusted after piloted the template. Two of the authors extracted the data using the extraction form in collaboration. The third and fourth authors checked the correctness of the data independently. Any disagreements between reviewers were resolved through discussions with third and fourth reviewers when required. The mistyping of data was resolved through crosschecking with the included papers. The case definition considered was as follows: confirmed case: detection of SARS-CoV-2 nucleic acid in a clinical specimen; possible case: any person with at least one of the following symptoms: Eugh, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia; probable case: any person with at least one of the following symptoms : cough, fever, shortness of breath, sudden onset of anosmia, ageusia or dysgeusia, with close contact with a confirmed COVID-19 case in the 14 days prior to onset of symptom or having been a resident or a staff member, in the 14 days pfeor to onset of symptoms, in a residential institution for vulnerable people where ongoing COVID-19 transmission has been confirmed. π

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 Synthesis of results
 The authors transformed the data to STATA 14 for analysis after it was extracted in an excel sheet considering prevalence male and

 female reported. We pooled the overall prevalence male and/or female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I² statistics. In this study, the I² statistic value of zero indicates true homogeneity, whereas the value 25, 50, and 75% represented low, moderate and high heterogeneity, respectively. Subgroup analysis was done by the study country and sample size. Sensitivity analysis was employed to examine the effected a single study on the overall estimation. Publication bias was checked by the funnel plot and more objectively through Egger's regression test.

Result

Study selection

A total of 2574 studies were identified using electronic searches (through Database searching (n = 2560)) and other sources (n = 12)). After duplication removal, a total of 1352 articles remained (1222 duplicated). Finally, 86 studies were screened for full-text review and, 57 articles (n=221195 patients) were selected for the analysis (Fig.1). This citation manager automatically identifies duplicates creates a separate group among imported references, which can be deleted. For those different citation for the same paper we screened and de-duplicated the citations by hand, which were recorded on a Microsoft Excel spreadsheet after assessing if they have the same author, title, publication date, volume, issue, sample size, etc we removed the duplicated one.) April 19

Characteristics of included studies

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

Meta-analysis

Prevalence of COVID-19 among male

All studies (n=57) with a total of 2,21195 patients had reported the sex proportion of COVID-19 (1, 16, 13, 14, 24, 27-73). The prevalence of COVID-19 among male ranges from 37.5 Liu J et al (30) to 77.08 Chen X et al (56) random-effects model analysis

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3	141	from those studies revealed that, the pooled prevalence of COVID-19 confirmed cases is $55.00(51.43-5658; I^2=99.5\%; p<0.001)$
4 5	142	(Fig.2).
6 7		
8	143	Subgroup analysis of COVID-19 confirmed cases among male
9 10	144	The subgroup analysis was done through stratification by country, providences, sample size and quality gcore. Based on this, the
11 12 13 14 15 16 17 18	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(4), 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, Zhagiang, 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); $I^2 = 66.7$;
18 19	149	$P = 0.001, 54.07 (95\% CI:51.63-56.51); I^2 = 37.9; P = 0.139, 53.17(95\% CI:52.81-53.53); I^2 = 99.4, P = 0.000, 46.45(95\% CI:39.10-100); I^2 = 10.000; I^2$
20 21	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
22 23	151	52.20(95% CI:47.95-56.44); $I^2 = 65.1$, P= 0.09) respectively (Table 2 and Supplementary Fig 2).
24 25	152	Regarding quality score the pooled prevalence of COVID-19 among male in studies which scored greater than or equal to seven was
26 27	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
28 29	154	seven from JBI quality appraisal checklist(Table 2 and Supplementary Fig 3).
30 31	155	Regarding sample size the pooled prevalence of COVID-19 among male in studies which have sample size \vec{s} greater than or equal to
32 33	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
34 35 36 37 38 39 40	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 poged prevalence of severe
41 42	160	illness among COVID-19confirmed cases. The results of this sensitivity analysis showed that our findings were not dependent on a
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2 3 4	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)
4 5 6	162	Yanping Z ET al after the deletion of a single study (Figure 3).
7 8	163	Publication Bias
9 10 11	164	We have also checked publication bias and, a funnel plot showed symmetrical distribution. Egger's regression test p-value was 0.599.
11 12 13	165	Both the symmetric funnel plot and the insignificant p-value (<0.05) indicates the absence of publication bia
13 14 15	166	Meta-regression Official Meta-regression
16 17	167 168	Univariate meta-regression analyses revealed that the prevalence of smoking was found to be high in males . This contributed for high prevalence of COVID-19 among males (P=0.002). Comorbidities like hypertension (0.042), diabetic mellitus (0.012, chronic
18 19 20	169 170	respiratory disease (0.021), and cardio vascular disease (0.001) were also found to be higher in males and these significantly increases the prevalence of COVID-19. Besides, higher proportion of sever/critical illness (0.003) and death (0.001) were also observed among
21 22	171	males (Table 3).
23 24 25	172	Discussion
25 26	173	This systematic review and meta-analysis were conducted to assess the sex difference in getting COVID -19 giseases. Fifty seven
27 28	174	studies were included in the final analysis. The result of this systematic review and meta-analysis revealed that the pooled prevalence
29 30	175	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-
31 32	176	48.57) respectively. This indicates COVID -19 is prevalent in males than females.
33 34	177	This finding was also reported by other studies (75, 76). A study in Ontario, Canada showed that men were the ore likely to test
35	178	positive(77, 78). In Pakistan 72% of COVID-19 cases were male(79). According to Global Health 5050 datage gathering, the number of
36 37	179	COVID-19 confirmed cases and the death rate due to COVID-19 is high among males in different countries $(\frac{1}{4}5-17)$.
38	180	This might be due to behavioral factors and roles which increase the risk of acquiring COVID-19 tend to occ
39 40	181	Male are more involved in different risky behaviors like alcohol consumption (80-82), key activities in buria Erites; as employees in
41 42 43	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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1 2 3 4	183 184	BMJ Open during the containment phase (e.g., food or pharmacy manufacturing and sales, agriculture or food production and distribution, transportation, and security). Because of such behaviors males mostly don't stay at home, sit together, and remove their mask while
5 6	184	they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease. In China 50% of
7	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
8 9	187	adverse outcomes of COVID-19: for instance, the combined results of five studies showed that smokers wered .4 times more likely
10	188	than non-smokers to have severe symptoms of COVID-19 (83). Besides, smoking is related to higher expression of ACE2 (the
11 12	189	receptor for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), which might be the reason for the higher prevalence of
13	190	COVID-19 in this subgroup of patients than in women (84).
14 15	191	Men tended to develop more symptomatic and serious cases than women, according to the clinical classification of severity. Similar
16	192	occasions occurred during previous coronavirus epidemics: men had worse outcomes of illness from severe acute respiratory
17 18	193	syndrome (SARS), (85)and a higher risk of dying from Middle East respiratory syndrome (MERS)(86). Biological sex variation is said
19	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
20 21	195	more vigorous immune response to infections and vaccinations(88). Some previous studies on coronaviruses in mice have suggested
22	196	that the hormone estrogen may have a protective role. Estrogens suppress the escalation phase of the immuneresponse that leads to
23 24	197 198	increased cytokine release(89). The authors showed that female mice treated with an estrogen receptor antagonist died at close to the same rate as the male mice(90).
25	150	
26 27	199	The X chromosome is known to contain the largest number of immune-related genes in the whole genome (8). With their XX
28	200	chromosome, women have a double copy of key immune genes compared to the single copy in XY men. This boost extends to both
29 30	201	the general reaction to infection (the innate response) and also to the more specific response to microbes including antibody formation
31 32	202	(adaptive immunity)(86). Thus women's immune systems are generally more responsive to infections. This might mean women are
33 34 35 36 37 38	203	able to tackle the novel coronavirus more effectively but this has not yet been proven.
	204	Besides, the above listed behavioral factors like smoking and alcohol consumption tend to occur more among men, those behaviors
	205	predisposes males for cardiac and respiratory diseases. This may also explain the overall higher mortality rat among men (84, 91,
39	206	92). A systematic review and meta-analysis revealed that comorbid disease, such as respiratory system disease, hypertension, and
40 41 42 43 44	207	cardiovascular disease as risk a risk factors for death compared with patients without comorbidity(93).

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3	208	Conclusions	
4 5			
6 7	209	The prevalence of symptomatic COVID-19 is higher among males than females. This can be explained with	frevalent behaviors
8	210	which increase the risk of acquiring COVID-19 are among males. Males are more involved in different risky	Behaviors like alcohol
9 10	211	consumption (3-5), and occupational exposures because of which males mostly don't stay at home, sit togeth	r, remove their mask
11	212	while they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVI	§ -19 disease; that is why
12 13	213	it is more prevalent in male. Smoking and drinking alcohol reduce your overall health and therefore make you	more susceptible to
14 15	214	symptomatic COVID-19 infection. Although there has been a rapid surge in research in response to the outbre	ak of COVID-19,
16	215	additional studies regarding discrepancy in severe illness and mortality due to COVID-19 among males and	males and factors which
17 18	216	determine the exposure, severity and mortality due to COVID-19 is recommended.	f
19 20	217	Abbreviations	
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22 23	218	COVID-19: coronavirus disease 2019; WHO: World Health Organization; ICTV: International Committee	D
24 25	219	SARS-CoV-2: Sever Acute Respiratory Syndrome Coronavirus 2; CI: Confidence Interval; AOR: Adjusted	odds ratio; ARTI: Acute
26	220	Respiratory Tract Infections	3
27 28	221	Declarations	
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30 31	222	Respiratory Tract Infections Declarations Ethics approval and consent to participate Not applicable	10 2
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35 36	224	Consent for publication The second	
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38 39	225	Not applicable	
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3 4 5	227	The datasets analyzed during the current study are available from the corresponding author upon reasonable request.
6 7	228	Competing interests
8 9	229	We have confirmed that we have no competing interests.
10 11 12	230	Funding
13 14	231	No funding was obtained for this study
15 16 17	232	oaded f
18 19 20	233	
20 21 22	234	We have confirmed that we have no competing interests. Funding No funding was obtained for this study Authors' contributions BB. AM. MW. and TG: developed the study design and protocol literature review, selection of studies equality assessment, data
23 24	235	BB, AM, MW, and TG: developed the study design and protocol, literature review, selection of studies quality assessment, data
25 26	236	extraction, statistical analysis, interpretation of the data and developing the initial drafts of the manuscript and prepared the final draft
27 28	237	of the manuscript. All authors read and approved the final manuscript.
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32 33	239	We would like to thank the authors of the included primary studies.
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38 39	408	Table Legend Potential Table 1: Characteristics of included studies for male/female among COVID-19 confirmed cases Potential
40	409	Table 2: Subgroup analysis of the pooled prevalence of COVID-19 by country, province, quality score, and sample size
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1 2 3	410	Table 3 [.]	a meta-regre	ssion analys	is showing factors	which have eff	fect on th	e sex dif	ference of CO	VID-1
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25		Sr no	Author	Country	Study Period	Sample Size	Male	Female	Quality score	Refei
26		1.	Li K et al	China	Jan-Feb	83	44	39	6/9	(2
27		2.	Liu Y et al	China	Jan11-Jan20	12	8	4	9/9	(2
28		3.	Liu Y et al	China	Jan23-Feb8	109	59	50	6/9	(2 (3
29		4.	Liu J et al	China	Jan-Feb	40	15	25	8/9	(3
30		5.	Wu J et al	China	Jan22-Feb14	80	39	41	8/9	(3
31		6. 7.	Xu X et al Xu Y et al	China China	Jan10-Jan26 Jan-Feb	62 50	36 29	26 21	8/9 6/9	(1)
32		8.	Yao et al	China	Jan01-Feb07	195	115	80	8/9	(3
33		9.	Young et al	China	Jan22-Jan31	18	9	9	6/9	(3 (3
34		10.	Zhang J et al	China	Jan16-Feb03	140	71	69	8/9	(3)
34 35		11.	Zhang M et al	China	Jan18-Feb03	9	5	4	7/9	(3
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36		12. 13.	Zhao et al Zhu et al	China China	Jan16-Feb03 Dec01-Feb15	101 12	56 8	45 4	8/9 7/9	(3 (3

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3	420	20. 21.	Kaiyuan S et al AL Giwa et al	China China	February, 2020 March, 2020	507 78771	281 57482	201 21289	6/9 9/9	(4 S) (4 S)
4		21. 22.	Qian G et al	China	March, 2020	91	37482	54	9/9 8/9	(44 4) (4 9)
5	421	23.	Livingston E et al	Italy	March, 2020	22512	13462	9050	7/9	(48)
6		24.	Wang Y et al	China	March, 2020	110	48	62	6/9	(42)
7	422	25.	KSID,2020	Korea	February, 2020	4212	1591	2621	9/9	(48)
8	422	26.	Su YJ et al	China	March, 2020	10	7	3	6/9	(48)
9		27.	Jennifer B et al	China	March, 2020	59600	30000	29600	8/9	(5 0)
10	423	28. 29.	Kui et al Deng L et al	China China	March, 2020 March, 2020	137 33	61 17	76 16	8/9 8/9	() []
11	425	29. 30.	Dong X et al	China	March, 2020	135	72	63	8/9 6/9	(52)
12		31.	Xiaobo et al	China	March, 2020	52	35	17	8/9	
	424	32.	Zhou F et al	China	March, 2020	191	119	72	6/9	(14)
13		33.	Wu Y et al	China	March, 2020	297	147	150	8/9	(59)
14	425	34.	Gao Q et al	China	January to February ,2020	213	108	105	7/9	(5 <u>5</u>
15	-	35.	Chen X et al	China	February 2020	291	145	146	8/9	(58
16	176	36.	Zhang G et al	China	December 2019	221	108	113	7/9	(5 8)
17	426	37.	Wu W et al	China	March, 2020	21	10	11	8/9	(58)
18		38. 20	Cao M et al	China	February, 2020	128	60	68 7	7/9 7/9	(SQ)
19	427	39. 40.	Chung et al Xiao F et al	China China	March, 2020 March, 2020	20 73	13 41	32	7/9 7/9	
20		40.	Qi D et al	China	January to February ,2020	267	149	118	6/9	(6 2)
21	428	42.	Liang et al	China	China	1590	911	679	7/9	(69)
22	.20	43.	Wang Y et al	China	February, 2020	55	22	23	6/9	(64)
	420	44.	Nicholas E et al	UK	April 2020	68	32	36	9/9	(69)
23	429	45.	Mizumoto K et al	Japan	March, 2020	634	321	313	8/9	(39)
24		46.	Chen X et al	China	March, 2020	48	37	11	7/9	(6ଞ୍ଚି
25	430	47.	Cheng J et al	China	March, 2020	1079	573	505	6/9	(67)
26		48.	Li J et al	China	March, 2020	47	28	19	9/9	(29)
27	431	49. 50.	Tian S et al Li et al	China China	April 2020 March, 2020	262 425	127 240	135 185	8/9 7/9	(68) - (4 Q
28	431	50. 51.	Liu Y et al	China	February, 2020	109	240 59	50	6/9	
29		51. 52.	Cao W et al	China	February, 2020	198	101	97	9/9	
30	432	53.	Chaolin et al	China	February, 2020	41	30	11	6/9	(71)
31		54.	Yang X et al	China	February, 2020	52	35	17	8/9	(13)
32	433	55.	Liu L et al	China	February, 2020	51	32	19	8/9	(72)
		56.	Huang C et al	China	February, 2020	41	30	11	8/9	4 1)
33	121 -	57.	Wang D et al	China	February, 2020	138	75	63	6/9	
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438	Table 2

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

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456 Table 3

Variable	Event	Total	Male	Studies	Male (%)	Female (%)	P value
Smoking Comorbidities	2863	11590	8693	19	75	25	0.002
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	20120	1,500,70	105200	40	(())	22.7	0.002
Sever / critical illness Death	38128 699028	158870 158870	105322 125322	49 46	66.3 78.8	33.7 21.2	0.003 0.001

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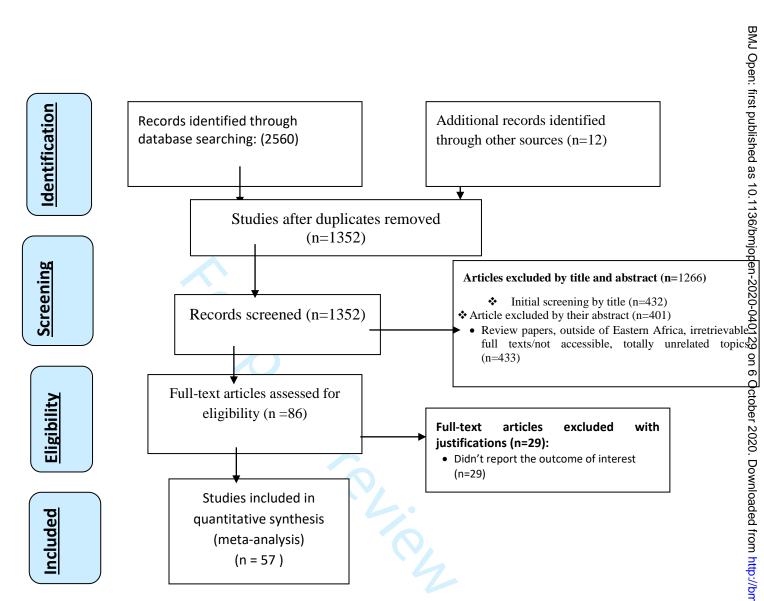


Figure 1: PRISMA flow diagram showed the results of the search and reasons for exclusion



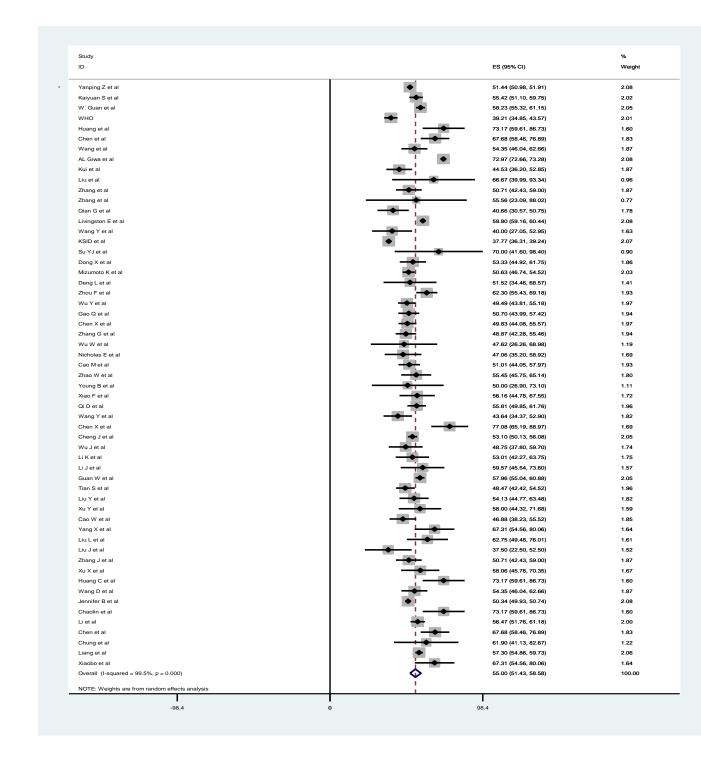


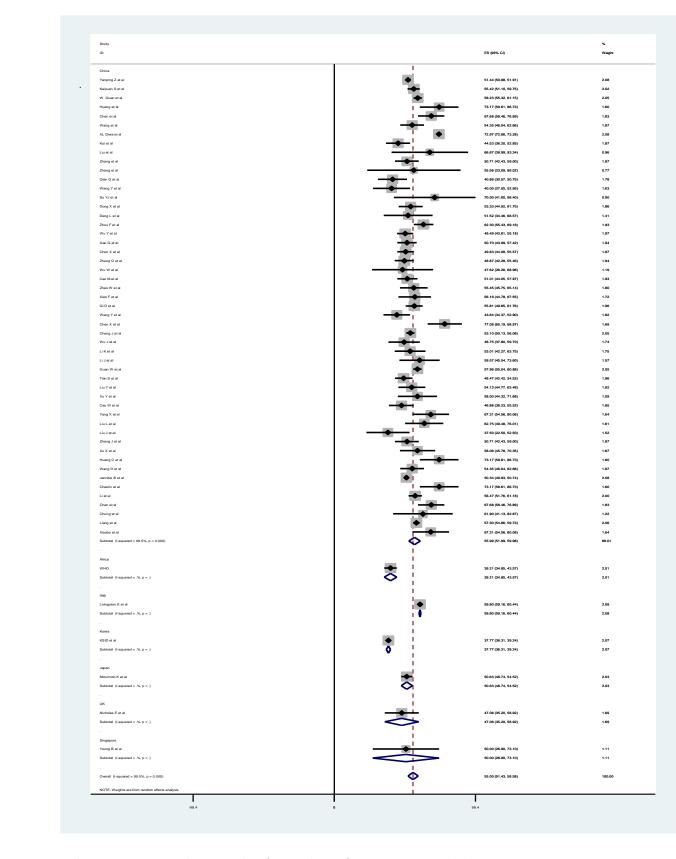
Figure 2: Forest plot showing the pooled prevalence of COVID-19 confirmed cases among male

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4	Study ommited	Coef.	[95% Conf.	Interval]
5	Cheng J et al	20.732838	20.445127	21.020546
6	xu x et al	17.418531	17.156216	17.680845
7	Liu L et al	17.381458	17.119438	17.643478
8	Yao et al	17.516275	17.25304	17.77951
9	Wang Yet al	17.346966	17.085199	17.608732
	Wu J et al		17.100435	17.624273
10	Xia W et al Xiao F et al	17.317913 17.338419	17.056414 17.076689	17.579412 17.600149
11	Cao M	17.330419	17.078194	17.60206
12	Qian G et al	17.322186	17.060547	17.583824
13	Liu C et al	17.311192	17.049721	17.57266
14	zhao et al	17.313881	17.052284	17.57548
15	Yang et al	17.312496	17.050829	17.574163
16	Gao Q et al	17.313957	17.052176	17.575737
	Guan W		17.068779	17.595478
17	Cao W et al Chen X	17.310188	17.048569 17.04727	17.571806 17.571028
18	Tian et al	17.307884	17.046061	17.569708
19	Tian S et al	17.307884	17.046061	17.569708
20	Yanping Z et al	16.002106	15.621832	16.382381
21	Qi D et al	17.304249	17.042439	17.566059
22	W. Guan et_al	17.256212	16.993301	17.519123
23	Liu K et al	17.298866	17.037294	17.56044
23	Liu W et al Li Y et al	17.30262 17.304375	17.041122 17.042908	17.564116 17.565842
	Xu Y et al	17.304575	17.042908	17.56613
25	Wang D et al	17.297497	17.035929	17.559065
26	Wang D et al	17.297497	17.035929	17.559065
27	Wu Y et al	17.280704	17.018961	17.54245
28	Livingston E et al	14.335077	14.044443	14.625712
29	Li K et al	17.299694	17.0382	17.561188
30	Li K et al Chen W et al	17.299694 17.301987	17.0382 17.040525	17.561188 17.56345
31	Huang C et al	17.303835	17.040323	17.565281
32	Wu W et al	17.305992	17.044569	17.567415
	Young et al	17.306377	17.044958	17.567799
33	Wang Y et al	17.293758	17.032244	17.555273
34	zhang J et al	17.283909	17.022371	17.545444
35	Zhang J et al		17.022371	17.545444
36	Wu W et al Chen L et al	17.30135 17.302288	17.039911 17.040859	17.56279 17.563717
37	Liu Y et al	17.284363	17.02286	17.545866
38	Chen X et al	17.295172	17.033726	17.556618
39	zhou F et al	17.243504	16.981913	17.505095
	Liu Y et al	17.302118	17.040703	17.563536
40	Li J et al	17.256153	16.994654	17.517653
41	Yang X et al	17.308687	17.047285	17.570087
42	Combined	17.308687	17.047285	17.570088
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Figure 3: sensitivity analysis for pooled prevalence of COVID-19 confirmed cases among males



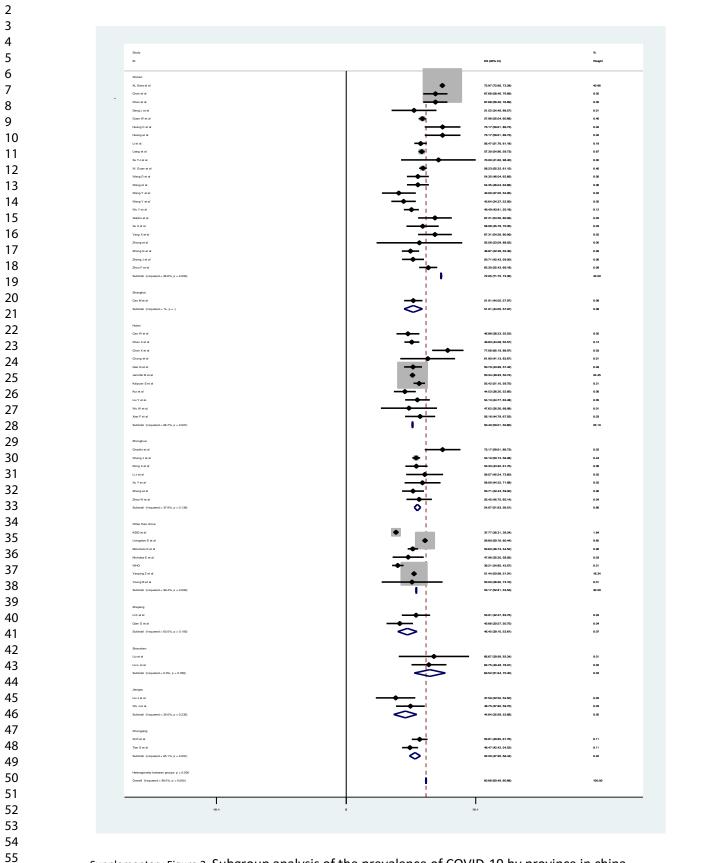
Supplementary Figure 1: Subgroup analysis for prevalence of COVID-19 among males by countries

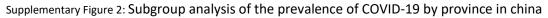
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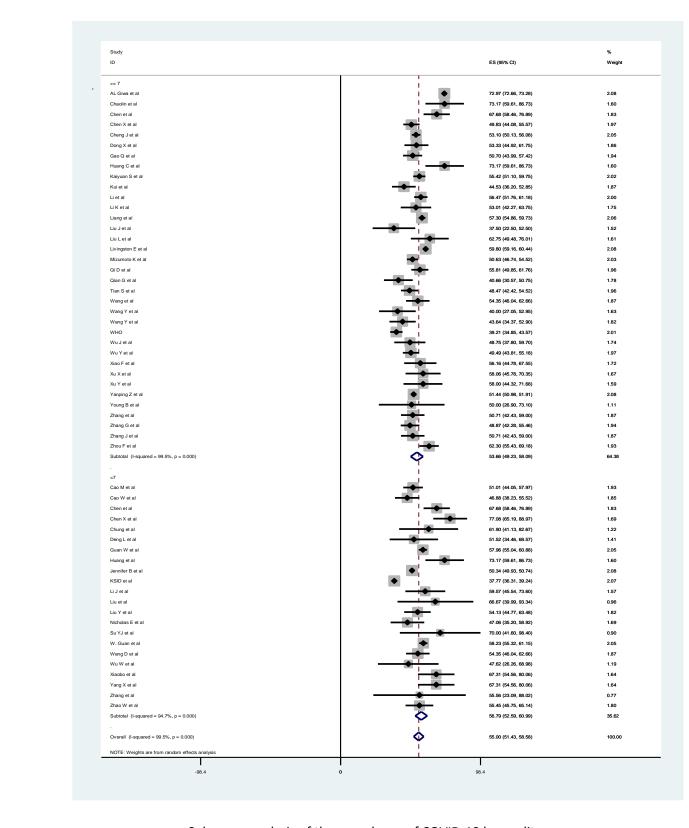
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Supplementary Figure 3: Subgroup analysis of the prevalence of COVID-19 by quality score

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Study ID		ES (95% CI)	% Weight
>384	•		
AL Giwa et al Cheng J et al	· · · ·	72.97 (72.66, 73.28) 53.10 (50.13, 56.08)	2.08
Guan W et al	•	57.96 (55.04, 60.88)	2.05
Jennifer B et al	•	50.34 (49.93, 50.74)	2.08
Kaiyuan S et al	+	55.42 (51.10, 59.75)	2.02
KSID et al	• •	37.77 (36.31, 39.24)	2.07
Lietal LiKetal		56.47 (51.76, 61.18) 53.01 (42.27, 63.75)	2.00 1.75
Lincetal		53.01 (42.27, 63.75) 57.30 (54.86, 59.73)	1.75
Livingston E et al	•	59.80 (59.16, 60.44)	2.08
Mizumoto K et al	•	50.63 (46.74, 54.52)	2.03
W. Guan et al	•	58.23 (55.32, 61.15)	2.05
WHO KING THE REPORT	• •	39.21 (34.85, 43.57)	2.01
Yanping Z et al Subtotal (I-squared = 99.9%, p = 0.000)		51.44 (50.98, 51.91) 53.86 (47.09, 60.63)	2.08 28.39
-		00.00 (47.00, 00.00)	20.00
<384	1		
Cao M et al		51.01 (44.05, 57.97)	1.93
Cao W et al		46.88 (38.23, 55.52)	1.85
Chaolin et al Chen et al		73.17 (59.61, 86.73) 67.68 (58.46, 76.89)	1.60
Chen et al		67.68 (58.46, 76.89) 67.68 (58.46, 76.89)	1.83 1.83
Chen X et al		49.83 (44.08, 55.57)	1.97
Chen X et al		77.08 (65.19, 88.97)	1.69
Chung et al		61.90 (41.13, 82.67)	1.22
Deng L et al		51.52 (34.46, 68.57)	1.41
Dong X et al Gao Q et al		53.33 (44.92, 61.75) 50.70 (43.99, 57.42)	1.86 1.94
Huang C et al		73.17 (59.61, 86.73)	1.60
Huang et al	·	73.17 (59.61, 86.73)	1.60
Kui et al		44.53 (36.20, 52.85)	1.87
Li J et al		59.57 (45.54, 73.60)	1.57
Liu et al		66.67 (39.99, 93.34) 37.50 (22.50, 52.50)	0.96
Liu L et al		62.75 (49.48, 76.01)	1.61
Liu Y et al		54.13 (44.77, 63.48)	1.82
Nicholas E et al		47.06 (35.20, 58.92)	1.69
Qi D et al	*	55.81 (49.85, 61.76)	1.96
Qian G et al Su YJ et al		40.66 (30.57, 50.75) 70.00 (41.60, 98.40)	1.78
Tian S et al		48.47 (42.42, 54.52)	1.96
Wang D et al		54.35 (46.04, 62.66)	1.87
Wang et al		54.35 (46.04, 62.66)	1.87
Wang Y et al		40.00 (27.05, 52.95)	1.63
Wang Yetal Wu Jetal		43.64 (34.37, 52.90) 48.75 (37.80, 59.70)	1.82
Wu Jetal		48.75 (37.80, 59.70) 47.62 (26.26, 68.98)	1.74
Wu Y et al		49.49 (43.81, 55.18)	1.97
Xiao F et al		56.16 (44.78, 67.55)	1.72
Xiaobo et al		67.31 (54.56, 80.06)	1.64
Xu X et al		58.06 (45.78, 70.35)	1.67
Xu Yetal Yang Xetal		58.00 (44.32, 71.68) 67.31 (54.56, 80.06)	1.59
Young B et al		50.00 (26.90, 73.10)	1.11
Zhang et al		50.71 (42.43, 59.00)	1.87
Zhang et al		55.56 (23.09, 88.02)	0.77
Zhang G et al		48.87 (42.28, 55.46)	1.94
Zhang J et al Zhao W et al		50.71 (42.43, 59.00) 55.45 (45.75, 65.14)	1.87
Zhao w et al Zhou F et al		55.45 (45.75, 65.14) 62.30 (55.43, 69.18)	1.80
Subtotal (I-squared = 64.5%, p = 0.000)	o	54.96 (52.35, 57.57)	71.61
Overall (I-squared = 99.5%, p = 0.000)	▲	55.00 (51.43, 58.58)	100.00
NOTE: Weights are from random effects analysis			
-98.4	0	98.4	

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Table S1. Search strategy used for one of the databases

Medline/PubMed			
	Search terms		
<u>Group</u>	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	
щл			
#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

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Table S2: Quality appraisal result of included studies in East Africa, from 2002-2019. Using

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BMJ Open: first Joanna Briggs Institute (JBI) quality appraisal checklist 5 6 published Author Quality assessment questions 7 Overall appraisal Yes Quality status 8 Q10 Total Q11 62 63 Q5 Q6 5 Q8 69 9 5 9 as 10 **Cross-sectional studies** 10.1136/bmjopen-2020-0401 11 Ν Y Ν Y Y Ν Y Y Y 6/9 Low risk Included Li K et al 1. 12 Y Y Y Y Y Y Y 9/9 Y Y Low risk Included Liu Y et al 2. 13 Y Y UC Y Y Ν Y Y Ν 6/9 Low risk Included 3. Liu Y et al 14 Y Y Y Y Y UC Y Y Y 8/9 Low risk Included 4. Liu J et al 15 Y Y Y Y Ν Y Y Y 8/9 Y Included 16 Low risk 5. Wu J et al 17 Y UC 8/9 Y Y Y Ν Υ Υ Υ Low risk Included 6. Xu X et al 18 UC Y Y Y Y Ν Y Y Ν 6/9 Low risk Included 7. Xu Y et al 19 Y Y Y Y Y Ν Y Y Y 8/9 Low risk Included Yao et al 8. 20 129 Ν Ν Y Y Y Ν Y Y 6/9 Low risk Included 9. Young et al Υ 21 on Y Y Y Y Y Y Y Y Ν 8/9 Low risk Included 10. Zhang J et al 22 <u>б</u> Y Y UC Y Y Ν Y Y Y 7/9 Low risk Included 23 October 2020 11. Zhang M et al 24 Y Y Y Y UC Y Y Y 8/9 Low risk Included 12. Zhao et al Y 25 Y Y Y Y Y Y Y UC Ν 7/9 Low risk Included 13. Zhu et al 26 Ν Y Y Y Y Y 8/9 Y Y Y Low risk Included 14. Yanping Z et al 27 Y UC Y Y Y Ν Y Y Y 7/9 Low risk Included 15. W. Guan et al 28 Downloaded Y UC Y Y Y Y 7/9Y Y Ν 16. WHO ,2020 Low risk Included 29 Y UC Y Y Y Y Y Y 7/9 Ν Low risk Included 30 17. Huang et al 31 UC Y Y Y Y Ν Y Y Y 6/9 Low risk Included 18. Chen et al 32 Y Y Y Y Y Ν Y Y Ν 7/9 Low risk Included 19. Wang et al trom 33 Y Ν Y Y Y Y Y Ν N 6/9 Included Low risk 20. Kaiyuan S et al 34 Υ Υ Υ Y Υ Υ Υ Υ Y 9/9 Low risk Included 21. AL Giwa et al 35 Y Y UC Y Y Ν Y Y Y 8/9 Low risk Included 22. Qian G et al 36 UC 7/9 Y Υ Y Υ Υ Ν 37 23. Livingston E et al Y Y Low risk Included pen Y Ν Y Y Y Y Y 38 Ν Ν 6/9 Low risk Included 24. Wang Y et al 39 Υ Υ Υ Y Y Υ Υ Υ Υ 9/9 Low risk Included B 25. KSID,2020 40 Y UC Y Y Y Ν Y Y Ν 6/9 Low risk Included 26. Su YJ et al 41 Y Y Y Y UC Y Y 8/9 Y Y Low risk Included 27. Jennifer B et al 42 on Y Y Y Y Y Ν Y Y Y 8/9 Low risk Included 28. Kui et al 43 April Y UC Y Y Y Ν Y Y Y 8/9 Low risk Included 29. Deng L et al 44 UC Y Y Y Y Ν Y Y Ν 6/9 Low risk Included 45 30. Dong X et al 19 46 Y Y Y Y Y Y Y Y Ν 8/9 Low risk Included 31. Xiaobo et al 2024 47 Ν Y Ν Y Y Ν Y Y Y 6/9 Low risk Included 32. Zhou F et al 48 by Y Y Y Y Y Y Y Y N 8/9 Low risk Included 33. Wu Y et al 49 ' guest UC 7/9 Y Y Y Y Y Y Y Included Ν Low risk 34. Gao Q et al 50 Y Y Y Y Y UC Y Y Y 8/9 Low risk Included 35. Chen X et al 51 Protected by copyright. Y UC Y Y Y Ν Y Y Y 7/9 Low risk Included 52 36. Zhang G et al 53 Y Ν Y Y 8/9 Low risk Included Y Y Y Y Y 37. Wu W et al 54 Y Y Y Y Y UC Y Y 7/9 Ν Low risk Included 38. Cao M et al 55 Y UC Y Y Y Ν Y Y Y 7/9 Low risk Included 39. Chung et al 56 57

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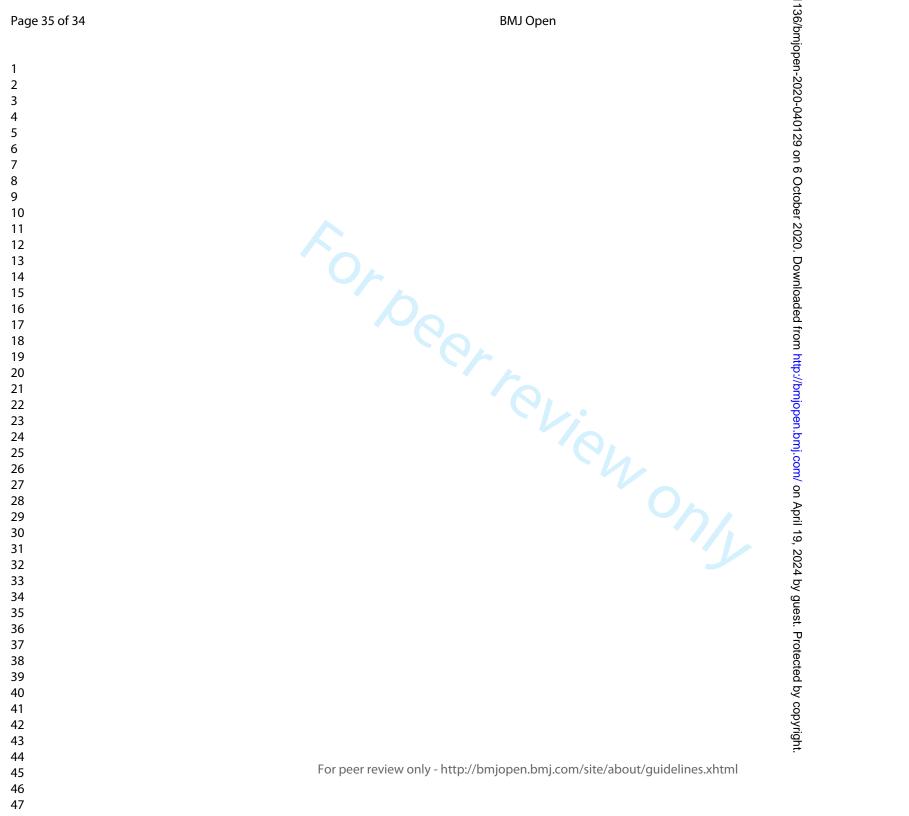
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33 67. Yang X et al Y UC Y Y Y Y Y N 7/9 Low risk Included
35 68. Liu L et al UC Y Y Y Y N Y Y Y A 6/9 Low risk Included
36 69. Zhang J et al Y Y Y Y N Y Y N/9 Low risk Included
 Key: Y=yes, N=no, UC=unclear, Q=Question Key: Y=yes, N=no, UC=unclear, Q=Question Key: Y=yes, N=no, UC=unclear, Q=Question
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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?				
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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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	0-040
2	Biruk Beletew Abate ^{1*} , Ayelign Mengesha Kassie ¹ , Mesfin Wudu Kassaw ¹ , Teshome Gebremeskel A	
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15	*Corresponding Author: Biruk Beletew Abate; E-mail: <u>birukkelemb@gmail.com</u>	April 1
16	Running title: Sex difference in coronavirus disease (COVID-19)	19, 20
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19	Design: Systematic review and meta-analysis.	Protected by copyright
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2 3	20	Setting: PubMed, Cochrane library, and Google Scholar were searched for related information. The authors developed a data
4 5	21	extraction form on the excel sheet and the following data were extracted for eligible studies: author, country, gample size, number
6 7	22	female patients, and the number of male patients. Using STATA 14 for analysis authors pooled the overall prevalence male and/or
8 9	23	female by a random effect meta-analysis model. We examined the heterogeneity of effect size using the Q statistic and the I ² statistics.
10 11	24	Subgroup and sensitivity analysis was done Publication bias was also checked.
12 13 14	25	Participants: Studies with COVID-19 confirmed cases were included. ⁸ ⁸ ⁹
15 16 17	26	Intervention: sex (male/female) of COVID-19 confirmed cases were considered
18 19	27	Primary and secondary outcome measures: Primary outcomes were prevalence of COVID-19 among males and females.
20 21	28	Result: A total of 57 studies with 221195 participants were used for analysis. The pooled prevalence of COV
22 23	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
24	30	study. Moreover a funnel plot showed symmetrical distribution. Egger's regression test p-value was not significant, which indicates
25 26	31	the absence of publication bias in both outcomes.
27 28	32	Conclusions: The prevalence of symptomatic COVID-19 found to be higher among males than females. The high prevalence of
29 30	33	smoking and alcohol consumption has contributed for high prevalence of COVID-19 among males. Additional studies regarding
31	34	discrepancy severity and mortality rate due to COVID-19 among males and females and associated factors is gecommended.
32 33	35	Keywords: COVID-19; sex difference; Systematic review; Meta-analysis
34 35	36	Article summary Strength and limitations
36 37	37	Strength and limitations
38 39	38	We used a pre-specified protocol for search strategy and data abstraction and
40 41 42	39	• We used internationally accepted tools for a critical appraisal system for quality assessment of individual studies.
43 44 45 46		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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 Because of the inclusion of studies which are published in English only, language bias is likely.
 Point of the inclusion of studies which are published in English only language bias is likely.

 In addition most included are from China due to lack of literatures from other countries in the point of the inclusion of the inclusion of studies which reported the inclusion of the inclusicenter of the inclusion of the inclusion of the inclus • on 6 October 2 outcome of interest. Background A COVID-19, first identified in Wuhan, China in late 2019, has rapidly evolved resulted in a pandemic by the first quarter of 2020, as indicated by the substantial rise in the number of cases and the fast geographical spread of the disease (1-4). The WHO announced that the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19) (5, 6). The virus has nove been named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) (7). COVID-19 has now been declared as a Public Health Emergency of International Concern by the WHO on 3th/₂th January 2020(8). COVID-19 affects people differently, in terms of infection with the virus SARS-CoV-2 and mortality rates(9)10). Susceptibility to symptomatic COVID-19 seems to be associated with age, biological sex, and comorbidities (11). Although the COVID-19 causes a mild illness in a majority of cases, severe illness requiring hospital admission is not uncommon (12). Besides, it has the potential to precipitate a life-threatening critical illness, characterized by respiratory failure, circulatory shock, sepsis or other organ failure, requiring intensive care(13, 14). According to Global Health 5050 data gathering, the number of COVID-19 confirmed cases and the death rate due to COVID-19 is high among males in different countries (15-17). The report in the lancet and Global Health 5050 summarize, sex-disaggregated data are essential for understanding the distributions of risk, infection, and disease in the population, and the extent to which sex and gender affect clinical outcomes [18]. Besides, knowing the degree to which outbreaks upsets women and men in different way is an important step for generating effective, equitable policies and interventions. Since the occurrence of COVID-19 infection in Wuhan, China, in December 2019 (19), it as quickly spread across China and numerous other countries(20-24). So far, 2019-nCoV has affected more than 193 countries with 2,²⁶733,591 confirmed cases, including 191185 deaths and 751,404 recovery (25). Even though, some previously published papers haven showed the sex right.

BMJ Open variation, those findings are not conclusive due to inconsistency in prevalence of COVID-19 among males and females. Moreover, there is lack of systematic review and meta-analysis which indicated the worldwide clear picture of sex variation on the risk of COVID-19. Hence, this systematic review and meta-analysis was conducted to assess the pooled prevalence eff COVID-19 among males and females. October 2020. Downloaded from ht

Review question

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

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

Methods

Search strategy

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

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136/bmjopen-202 COVID-19 confirmed patients on PubMed database (Table S1). Thus, the PubMed search combines #1 ABD #2 AND #3 AND #4 0129 on 6 Oc (Table S1). The searching date was January 2000 to December 2019.

Study selection and screening

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

Inclusion and exclusion criteria

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

Patient and Public Involvement: Patients or the public WERE NOT involved in the design, or conduct, or reporting, or 024 by gues dissemination plans of our research

Quality assessment

Using the Joanna Briggs Institute (JBI) quality appraisal checklist the authors appraised the quality of included studies (28). There was a team of four reviewers and the papers were split amongst the team. Each paper was then assessed by two reviewers and any disagreements were discussed with the third and the fourth reviewers. Studies were considered as low risk or good quality when it

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BMJ Open scored 4 and above (28), whereas the studies scored 3 and below were considered as high risk or poor quality as described in detail previously (26, 27) (Table S2). 129 on 6

Data extraction

The authors developed a data extraction form on the excel sheet and the following data were extracted for eligible studies: author, country, sample size, number female patients, and the number of male patients as described in detail pregiously (26, 27). The data extraction sheet was piloted using 4 papers randomly, and it was adjusted after piloted the template as described in detail previously (26, 27). Two of the authors extracted the data using the extraction form in collaboration. The third and fourth authors checked the correctness of the data independently. Any disagreements between reviewers were resolved through discussions with third and fourth reviewers when required as described in detail previously (26, 27). The mistyping of data was resolved through crosschecking with the included papers. The case definition considered was as follows: confirmed case: detection of SARS-CoV-2 nucleic acid in a clinical specimen; possible case: any person with at least one of the following symptoms: cough, fever, short ness of breath, sudden onset of anosmia, ageusia or dysgeusia; probable case: any person with at least one of the following symptoms : cough, fever. shortness of breath, sudden onset of anosmia, ageusia or dysgeusia, with close contact with a confirmed \mathcal{E} OVID-19 case in the 14 days prior to onset of symptom or having been a resident or a staff member, in the 14 days prior to onset of symptoms, in a residential institution for vulnerable people where ongoing COVID-19 transmission has been confirmed. April 19

Synthesis of results

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

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2 3 4	121	was done by the study country and sample size. Sensitivity analysis was employed to examine the effect of a single study on the
4 5	122	overall estimation. Publication bias was checked by the funnel plot and more objectively through Egger's regression test.
6 7	123	Result
, 8 9	124	Study selection
10	125	A total of 2574 studies were identified using electronic searches (through Database searching (n = 2560)) and other sources (n = 12)).
11 12	126	After duplication removal, a total of 1352 articles remained (1222 duplicated). Finally, 86 studies were screeked for full-text review
13 14	127	and, 57 articles (n=221195 patients) were selected for the analysis (Figure 1). This citation manager automatigally identifies duplicates
15 16	128	creates a separate group among imported references, which can be deleted. For those different citation for the same paper we screened
17	129	and de-duplicated the citations by hand, which were recorded on a Microsoft Excel spreadsheet after assessing if they have the same
18 19 20	130	author, title, publication date, volume, issue, sample size, etc we removed the duplicated one.
21 22	131	Characteristics of included studies
23	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
24 25	133	The studies included participants ranging from 9 (76) to 78771 (46) (Table 1).
26 27	134	Meta-analysis
28	135	Prevalence of COVID-19 among male
29 30	136	All studies (n=57) with a total of 2,21195 patients had reported the sex proportion of COVID-19 (1, $1\frac{1}{6}$ 13, 14, 24, 29-75). The
31 32	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
33 34	138	from those studies revealed that, the pooled prevalence of COVID-19 confirmed cases is 55.00(51.43-55.58; I ² =99.5%; p<0.001)
35	139	(Figure 2).
36 37 38 39 40 41 42	140	(Figure 2). Subgroup analysis of COVID-19 confirmed cases among male
43		right.
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136/bmjopen-202 The subgroup analysis was done through stratification by country, providences, sample size and quality Ecore. Based on this, the 1 prevalence of COVID-19 was found to be 55.99(51.99-59.99), 39.21(34.85-43.84), 59.80(59.16-60744), 37.77(36.31-39.24), 2 50.00(26.90-73.10) in China, Africa, Italy, Korea, and Singapore respectively (Table 2 and Supplementary Fig 1). 3 The pooled prevalence of COVID-19 among male in Wuhan, Shanghai, Hubei, Zhonghua, outside china, Zhi ang, Shenzhen, Jiangsu, 4 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); $I^2 = 66.7$; 5 $P = 0.001, 54.07 (95\% CI:51.63-56.51); I^2 = 37.9; P = 0.139, 53.17(95\% CI:52.81-53.53); I^2 = 99.4, P = 0.000, 46.45(95\% CI:39.10-10.000); I^2 = 99.4, P = 0.000; I^2 = 99.4, P = 0.000;$ 6 53.81) ; $I^2 = 99.4$, P = 0.00, 63.52(95% CI:51.64-75.40) ; $I^2 = 0.0$, P = 0.796, 44.84(95% CI:35.99-53.68) ; $I^2 = 29$, P = 0.235, and 52.20(95% CI:47.95-56.44); I² =65.1, P= 0.09) respectively (Table 2 and Supplementary Fig 2). 8 Regarding quality score the pooled prevalence of COVID-19 among male in studies which scored greater than or equal to seven was 9 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 n seven from JBI quality appraisal checklist(Table 2 and Supplementary Fig 3). Regarding sample size the pooled prevalence of COVID-19 among male in studies which have sample size greater than or equal to 2 384 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 3 than seven from JBI quality appraisal checklist(Table 2 and Supplementary figure 4). April 19, 2024 Sensitivity analysis 5 We employed a leave-one-out sensitivity analysis to identify the impact of individual research on the posted prevalence of severe 6 illness among COVID-19confirmed cases. The results of this sensitivity analysis showed that our findings were not dependent on a 7 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) 8 Yanping Z ET al after the deletion of a single study (Figure 3). ted by copyright. 9 **Publication Bias** 0 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open BMJ Open We have also checked publication bias and, a funnel plot showed symmetrical distribution. Egger's regression test p-value was 0.599. Both the symmetric funnel plot and the insignificant p-value (<0.05) indicates the absence of publication bias **Meta-regression** റ Univariate meta-regression analyses revealed that the prevalence of smoking was found to be high in males . This contributed for high prevalence of COVID-19 among males (P=0.002). Comorbidities like hypertension (0.042), diabetic mellitus (0.012, chronic respiratory disease (0.021), and cardio vascular disease (0.001) were also found to be higher in males and these significantly increases the prevalence of COVID-19. Besides, higher proportion of sever/critical illness (0.003) and death (0.001) were also observed among males (Table 3). ded from ht Discussion This systematic review and meta-analysis were conducted to assess the sex difference in getting COVID -19 diseases. Fifty seven studies were included in the final analysis. The result of this systematic review and meta-analysis revealed that the pooled prevalence of COVID -19 confirmed cases among males and females was found to be 55.00(51.43-56.58; I2=99.5%; p< 0.001) and 45.00(41.42-48.57) respectively. This indicates COVID -19 is prevalent in males than females. This finding was also reported by other studies (77, 78). A study in Ontario, Canada showed that men were fore likely to test positive(79, 80). In Pakistan 72% of COVID-19 cases were male(81). According to Global Health 5050 data gathering, the number of COVID-19 confirmed cases and the death rate due to COVID-19 is high among males in different countries \$5-17). This might be due to behavioral factors and roles which increase the risk of acquiring COVID-19 tend to occ Male are more involved in different risky behaviors like alcohol consumption (82-84), key activities in burialprites; as employees in basic sectors and occupations that continue being active and require them to work outside the home and interact with other people during the containment phase (e.g., food or pharmacy manufacturing and sales, agriculture or food production and distribution, opyright. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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BMJ Open transportation, and security). Because of such behaviors males mostly don't stay at home, sit together, and remove their mask while they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease. In China 50% of men in smoke, but because it is not considered acceptable for women to smoke, only 2% of them do so. Smoking is associated with adverse outcomes of COVID-19: for instance, the combined results of five studies showed that smokers wered 4 times more likely than non-smokers to have severe symptoms of COVID-19 (85). Besides, smoking is related to higher expression of ACE2 (the receptor for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), which might be the reason for the higher prevalence of COVID-19 in this subgroup of patients than in women (86).

Men tended to develop more symptomatic and serious cases than women, according to the clinical classification of severity. Similar occasions occurred during previous coronavirus epidemics: men had worse outcomes of illness from severe æute respiratory syndrome (SARS), (87)and a higher risk of dying from Middle East respiratory syndrome (MERS)(88). Biolatical sex variation is said to be one of the reason for the sex discrepancy of COVID-19 cases, severity and mortality(89). Women are in general able to mount a more vigorous immune response to infections and vaccinations(90). Some previous studies on coronaviruses in mice have suggested that the hormone estrogen may have a protective role. Estrogens suppress the escalation phase of the immune response that leads to increased cytokine release(91). The authors showed that female mice treated with an estrogen receptor antagenist died at close to the same rate as the male mice(92). April

The X chromosome is known to contain the largest number of immune-related genes in the whole genome(8). With their XX chromosome, women have a double copy of key immune genes compared to the single copy in XY men. This boost extends to both the general reaction to infection (the innate response) and also to the more specific response to microbes incleding antibody formation (adaptive immunity)(88). Thus women's immune systems are generally more responsive to infections. This might mean women are able to tackle the novel coronavirus more effectively but this has not yet been proven. tected by copyright.

BMJ Open Besides, the above listed behavioral factors like smoking and alcohol consumption tend to occur more among men, those behaviors predisposes males for cardiac and respiratory diseases. This may also explain the overall higher mortality rates among men (86, 93, 94). A systematic review and meta-analysis revealed that comorbid disease, such as respiratory system disease, hypertension, and October 2020 cardiovascular disease as risk a risk factors for death compared with patients without comorbidity(95).

Conclusions

The prevalence of symptomatic COVID-19 found to be higher among males than females. The high prevalence of smoking and alcohol consumption has contributed for high prevalence of COVID-19 among males (3-5), and occupationa exposures because of which males mostly don't stay at home, sit together, remove their mask while they drink and smoke. These increased levels of exposure makes males at high risk of acquiring COVID-19 disease; that is why it is more prevalent in male. Smoking and drinking alcohol reduce your overall health and therefore make you more susceptible to symptomatic COVID-19 infection. Although there has been a rapid surge in research in response to the outbreak of COVID-19, additional studies regarding discrepancy in severe illness and mortality due to COVID-19 among males and females and factors which determine the exposure, severity and mortality due to COVID-19 is recommended. Abbreviations COVID-19: coronavirus disease 2019; WHO: World Health Organization; ICTV: International Committee of Taxonomy of Viruses;

SARS-CoV-2: Sever Acute Respiratory Syndrome Coronavirus 2; CI: Confidence Interval; AOR: Adjuster Sodds ratio; ARTI: Acute **Respiratory Tract Infections** by guest. Protected by copyright. **Declarations**

Ethics approval and consent to participate

Not applicable

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10 11 12	224	The datasets analyzed during the current study are available from the corresponding author upon reasonable i	ů,
13 14 15	225	Competing interests	. Downloaded
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23 24 25	229	Authors' contributions	en.bmi.
26 27	230	BB, AM, MW, TG and SA: developed the study design and protocol, literature review, selection of studies	X
28	231	extraction, statistical analysis, interpretation of the data and developing the initial drafts of the manuscript and	gd prepared the final draft
29 30 31	232	of the manuscript. All authors read and approved the final manuscript.	oril 19,
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11 12 409) F	Figure 2	: Forest plot s	howing the p	ooled prevalence of	COVID-19 con	nfirmed c	ases amo	ng male	October 2020.	
13 14 410 15) F	Figure 3	: Sensitivity a	inalysis for po	oled prevalence of	COVID-19 con	firmed ca	ases amor	ng males	Downloaded	
16 411 17	L]	Fable L	egends								
18 412	2]	Table 1:	Characteristi	cs of included	studies for male/fe	male among CO	OVID-19	confirme	d cases	from	
19 20 413	3 1	Table 2:	Subgroup and	alysis of the p	ooled prevalence of	f COVID-19 by	country,	province	, quality score	, and sample size	
21 22 414	1 J	Fable 3:	a meta-regr	ession analys	is showing factors	which have eff	fect on th	e sex diff	ference of CO	WID-	
23 24 415	- 1	Table 1								en.	
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27		Sr no	Author	Country	Study Period	Sample Size	Male	Female	Quality score	Reference	
28		1.	Li K et al	China	Jan-Feb	83	44	39	6/9		
29		2.	Liu Y et al	China	Jan11-Jan20	12	8	4	9/9	(3 4	

Sr no	Author	Country	Study Period	Sample Size	Male	Female	Quality score	Referenc
1.	Li K et al	China	Jan-Feb	83	44	39	6/9	(2) 1
2.	Liu Y et al	China	Jan11-Jan20	12	8	4	9/9	(30)
3.	Liu Y et al	China	Jan23-Feb8	109	59	50	6/9	(31)
4.	Liu J et al	China	Jan-Feb	40	15	25	8/9	(3 29
5.	Wu J et al	China	Jan22-Feb14	80	39	41	8/9	
6.	Xu X et al	China	Jan10-Jan26	62	36	26	8/9	(10)
7.	Xu Y et al	China	Jan-Feb	50	29	21	6/9	(34)
8.	Yao et al	China	Jan01-Feb07	195	115	80	8/9	(35)
9.	Young et al	China	Jan22-Jan31	18	9	9	6/9	(3 6
10.	Zhang J et al	China	Jan16-Feb03	140	71	69	8/9	(38)
11.	Zhang M et al	China	Jan18-Feb03	9	5	4	7/9	(32)244057 (32) (1343057 (33)38585 (33)38555 (33)38555 (33)38555 (33)385555 (33)385555 (33)3855555 (33)38555555 (33)385555555555555555555555555555555555
12.	Zhao et al	China	Jan16-Feb03	101	56	45	8/9	(395
13.	Zhu et al	China	Dec01-Feb15	12	8	4	7/9	(465)
14.	Yanping Z et al	China	February 2020	44672	22981	21691	8/9	386000000000000000000000000000000000000
15.	W. Guan et al	China	February 2020	1099	640	459	7/9	(42)
16.	WHO ,2020	Africa	March 2020	482	189	177	7/9	(435)
17.	Huang et al	China	Jan, 2020	41	30	11	7/9	egpyright.

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2 3	416	18.	Chen et al	China	December 2020	99	67	32	6/9	<u> </u>
4	410	19.	Wang et al	China	March 2020	138	75	63	7/9	(2 4
5	417	20.	Kaiyuan S et al	China	February, 2020	507	281	201	6/9	(45
6	71/	21.	AL Giwa et al	China	March, 2020	78771	57482	21289	9/9	(48)
		22.	Qian G et al	China	March, 2020	91	37	54	8/9 7/0	
7	418	23. 24.	Livingston E et al Wang Y et al	Italy China	March, 2020 March, 2020	22512 110	13462 48	9050 62	7/9 6/9	(48)
8	410	24. 25.	KSID,2020	Korea	February, 2020	4212	1591	2621	0/9 9/9	(49)
9		23. 26.	Su YJ et al	China	March, 2020	10	7	3	6/9	(5 9
10	419	20. 27.	Jennifer B et al	China	March, 2020	59600	30000	29600	8/9	(59)
11	415	28.	Kui et al	China	March, 2020	137	61	76	8/9	(51)
12		29.	Deng L et al	China	March, 2020	33	17	16	8/9	(5 1 2)
	420	30.	Dong X et al	China	March, 2020	135	72	63	6/9	(55)
13		31.	Xiaobo et al	China	March, 2020	52	35	17	8/9	
14	421	32.	Zhou F et al	China	March, 2020	191	119	72	6/9	(14)
15	421	33.	Wu Y et al	China	March, 2020	297	147	150	8/9	(5 0
16		34.	Gao Q et al	China	January to February ,2020	213	108	105	7/9	(52)
17	422	35.	Chen X et al	China	February 2020	291	145	146	8/9	(58)
		36.	Zhang G et al	China	December 2019	221	108	113	7/9	(58)
18	422	37.	Wu W et al	China	March, 2020	21	10	11	8/9	(68)
19	423	38.	Cao M et al	China	February, 2020	128	60	68	7/9	(6 <u>म</u> (6 <u>म</u>
20		39.	Chung et al	China	March, 2020	20	13	7	7/9	(62)
21	424	40.	Xiao F et al	China	March, 2020	73	41	32	7/9	(6)
22		41.	Qi D et al	China	January to February ,2020	267	149	118	6/9	(64).
	405	42.	Liang et al	China	China	1590	911	679	7/9	(6급) (66) (66) (61) (41)
23	425	43.	Wang Y et al	China	February, 2020	55	22	23	6/9	(66)
24		44.	Nicholas E et al	UK	April 2020	68	32	36	9/9	(6 <u>평</u>
25	426	45.	Mizumoto K et al	Japan	March, 2020	634	321	313	8/9	(4 1)
26	.20	46.	Chen X et al	China	March, 2020	48	37	11	7/9	(68)
27		47.	Cheng J et al	China	March, 2020	1079	573	505	6/9	(69)
28	427	48.	Li J et al	China	March, 2020	47	28	19	9/9	(39
		49.	Tian S et al	China	April 2020	262	127	135	8/9	(76)
29	428	50.	Li et al	China	March, 2020	425	240	185	7/9	
30	120	51.	Liu Y et al	China	February, 2020	109	59	50	6/9	(3 9) (7 9) (14) (729) (729) (729) (729) (729) (729)
31		52.	Cao W et al	China	February, 2020	198	101	97	9/9 6/9	(72)
32	429	53. 54.	Chaolin et al	China China	February, 2020	41 52	30 35	11 17	8/9 8/9	
33		54. 55.	Yang X et al Liu L et al	China	February, 2020 February, 2020	52 51	35 32	17	8/9 8/9	
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Variables	Characteristics	Pooled prevalence (95% CI)	I ² (P-value)
By province in	Wuhan	72.05 (71.71-72.35)	96.6 (0.00)
china	Shanghai	51.01 (44.05-57.97)	-
	Hubei	50.40 (50.1-50.80)	66.7 (0.001)
	Zhonghua	54.07 (95% CI:51.63-56.51)	37.9 (0.139)
	Zhejiang	46.45 (39.10-53.81)	99.4 (0.00)
	Shenzhen	63.52 (51.64-75.40)	0.0 (0.796)
	Jiangsu	44.84 (35.99-53.68)	29 (0.235)
	Chongqing	52.20 (47.95-56.44)	65.1 (0.09)
	outside china	53.17 (52.81-53.53)	99.4 (0.00)
By country	China	55.99(51.99-59.99)	99.5 (0.00)
	Africa	39.21(34.85-43.84)	-
	Italy	59.80(59.16-60.44)	-
	Korea	37.77(36.31-39.24)	-
	Singapore	50.00(26.90-73.10)	-
By JBI quality	>=7	53.66 (95% CI:49.23-58.09)	99.5 (0.00)
score	<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)
			C

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Table 3

Variable	Event	Total	Male	Studies	Male (%)	Female (%)	P value
Smoking Comorbidities	2863	11590	8693	19	75	25	0.002
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	20120	1 500 70	105200	40	(())	22.7	0.002
Sever / critical illness Death	38128 699028	158870 158870	105322 125322	49 46	66.3 78.8	33.7 21.2	0.003 0.001

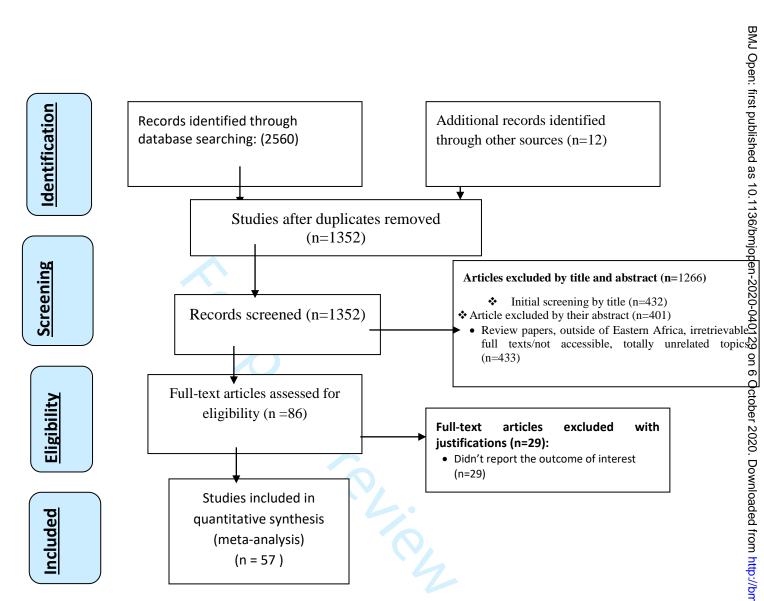


Figure 1: PRISMA flow diagram showed the results of the search and reasons for exclusion



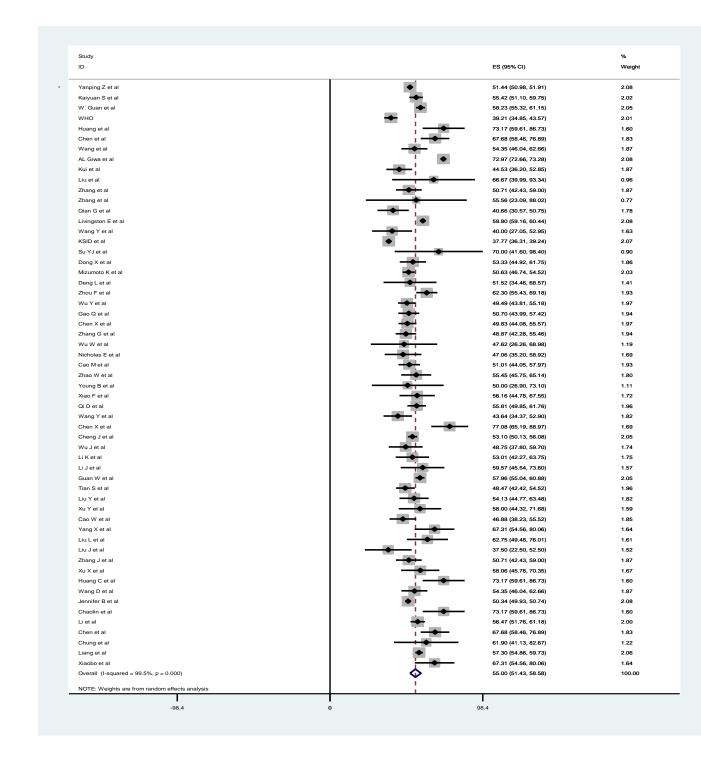
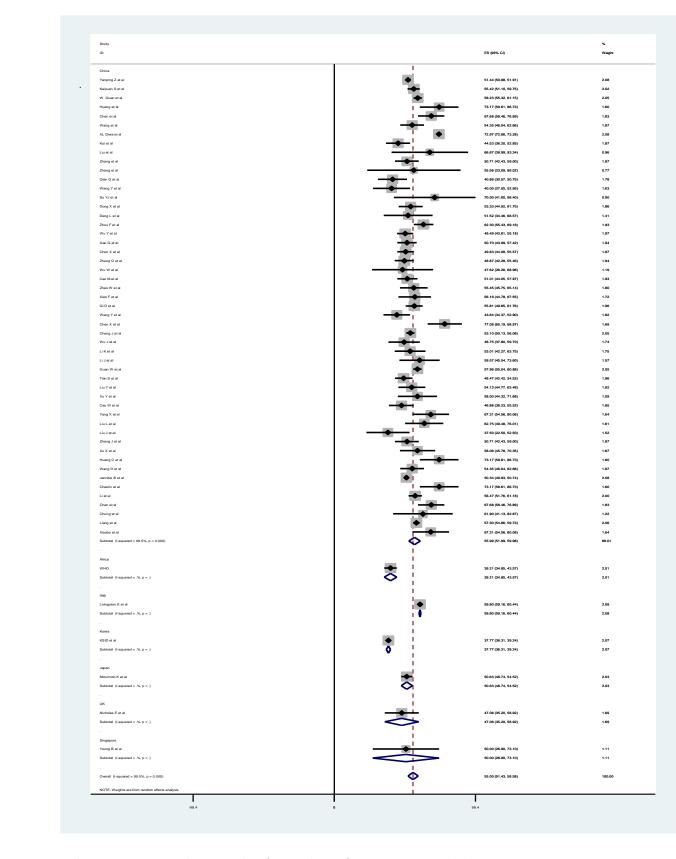


Figure 2: Forest plot showing the pooled prevalence of COVID-19 confirmed cases among male

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4	Study ommited	Coef.	[95% Conf.	Interval]
5	Cheng J et al	20.732838	20.445127	21.020546
6	xu x et al	17.418531	17.156216	17.680845
7	Liu L et al	17.381458	17.119438	17.643478
8	Yao et al	17.516275	17.25304	17.77951
9	Wang Yet al	17.346966	17.085199	17.608732
	Wu J et al		17.100435	17.624273
10	Xia W et al Xiao F et al	17.317913 17.338419	17.056414 17.076689	17.579412 17.600149
11	Cao M	17.330419	17.078194	17.60206
12	Qian G et al	17.322186	17.060547	17.583824
13	Liu C et al	17.311192	17.049721	17.57266
14	zhao et al	17.313881	17.052284	17.57548
15	Yang et al	17.312496	17.050829	17.574163
16	Gao Q et al	17.313957	17.052176	17.575737
	Guan W		17.068779	17.595478
17	Cao W et al Chen X	17.310188	17.048569 17.04727	17.571806 17.571028
18	Tian et al	17.307884	17.046061	17.569708
19	Tian S et al	17.307884	17.046061	17.569708
20	Yanping Z et al	16.002106	15.621832	16.382381
21	Qi D et al	17.304249	17.042439	17.566059
22	W. Guan et_al	17.256212	16.993301	17.519123
23	Liu K et al	17.298866	17.037294	17.56044
23	Liu W et al Li Y et al	17.30262 17.304375	17.041122 17.042908	17.564116 17.565842
	Xu Y et al	17.304575	17.042908	17.56613
25	Wang D et al	17.297497	17.035929	17.559065
26	Wang D et al	17.297497	17.035929	17.559065
27	Wu Y et al	17.280704	17.018961	17.54245
28	Livingston E et al	14.335077	14.044443	14.625712
29	Li K et al	17.299694	17.0382	17.561188
30	Li K et al Chen W et al	17.299694 17.301987	17.0382 17.040525	17.561188 17.56345
31	Huang C et al	17.303835	17.040323	17.565281
32	Wu W et al	17.305992	17.044569	17.567415
	Young et al	17.306377	17.044958	17.567799
33	Wang Y et al	17.293758	17.032244	17.555273
34	zhang J et al	17.283909	17.022371	17.545444
35	Zhang J et al		17.022371	17.545444
36	Wu W et al Chen L et al	17.30135 17.302288	17.039911 17.040859	17.56279 17.563717
37	Liu Y et al	17.284363	17.02286	17.545866
38	Chen X et al	17.295172	17.033726	17.556618
39	zhou F et al	17.243504	16.981913	17.505095
	Liu Y et al	17.302118	17.040703	17.563536
40	Li J et al	17.256153	16.994654	17.517653
41	Yang X et al	17.308687	17.047285	17.570087
42	Combined	17.308687	17.047285	17.570088
43				
44				

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



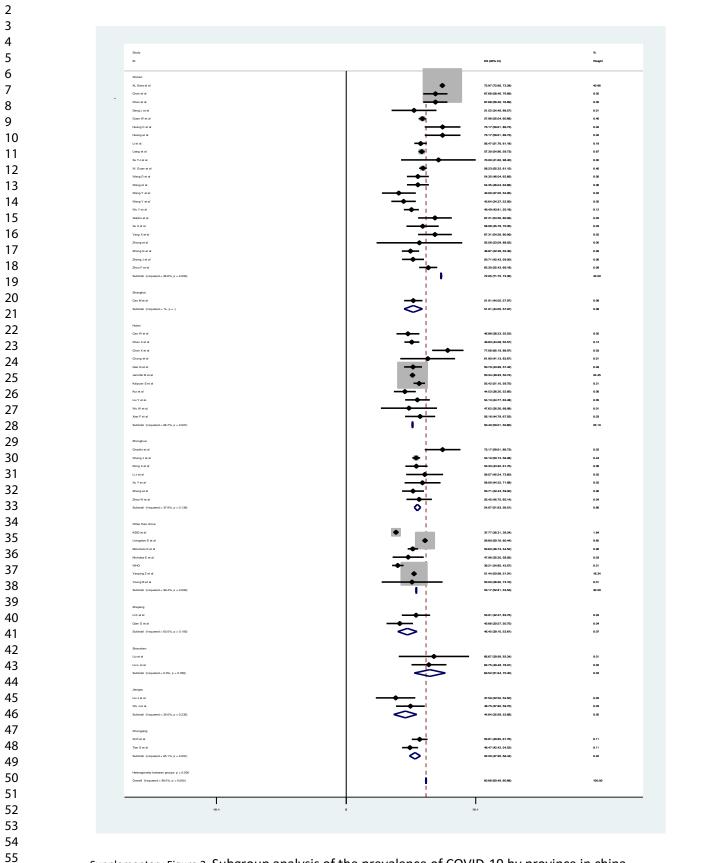
Supplementary Figure 1: Subgroup analysis for prevalence of COVID-19 among males by countries

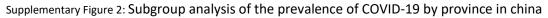
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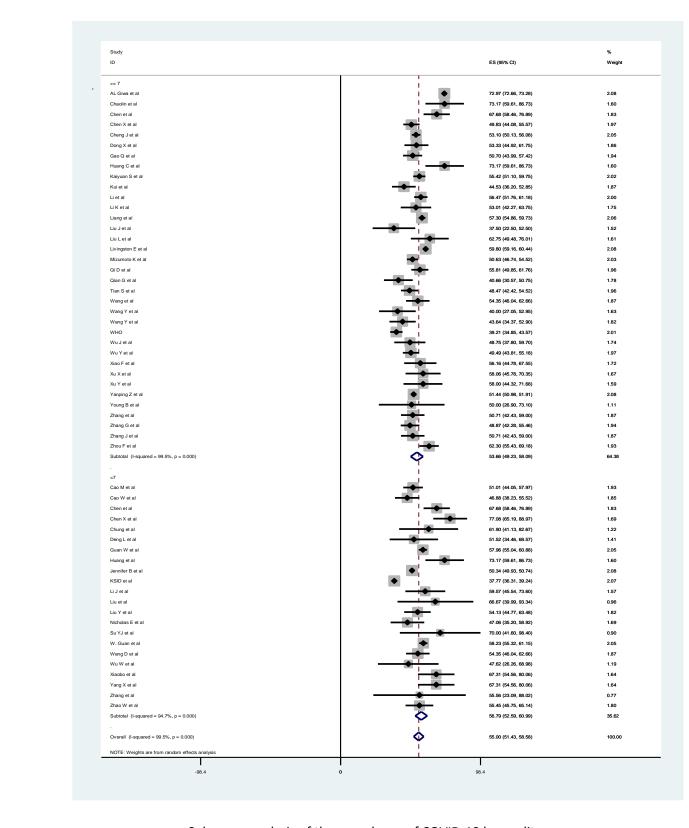
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Supplementary Figure 3: Subgroup analysis of the prevalence of COVID-19 by quality score

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Note	Jennifer B et al	•	50.34 (49.93, 50.74)	2.08
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Nonunii 2000000000000000000000000000000000000			59.80 (59.16, 60.44)	2.08
No 21 dbb.dbg) 20 Verget net 20 dbb.dbg) 20 dbb 20 dbb.dbg) 20 dbb 20 dbb.dbg) 20 dbb 10 mbb.dbg) 20		●	50.63 (46.74, 54.52)	2.03
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Nungeral Changeral <lichangeral< li=""> <lichangeral< li=""></lichangeral<></lichangeral<>	Chen X et al	• • · · · · · · · · · · · · · · · · · ·	49.83 (44.08, 55.57)	1.97
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Overall (I-squared = 99.5%, p = 0.000)				
Overall (I-squared = 99.5%, p = 0.000)				
Overall (I-squared = 99.5%, p = 0.000)				
Overall (I-squared = 99.5%, p = 0.000)	Zhou F et al	<u>_</u>	62.30 (55.43, 69.18)	1.93
	Subtotal (I-squared = 64.5%, p = 0.000)	♦	54.96 (52.35, 57.57)	71.61
	Overall (I-squared = 99.5%, p = 0.000)	6	55.00 (51.43, 58.58)	100.00
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Table S1. Search strategy used for one of the databases

Medline/PubMed			
	Search terms		
<u>Group</u>	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

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Table S2: Quality appraisal result of included studies in East Africa, from 2002-2019. Using

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BMJ Open: first Joanna Briggs Institute (JBI) quality appraisal checklist 5 6 published Author Quality assessment questions 7 Overall appraisal Yes Quality status 8 Q10 Total Q11 62 63 Q5 Q6 5 Q8 69 9 5 9 as 10 **Cross-sectional studies** 10.1136/bmjopen-2020-0401 11 Ν Y Ν Y Y Ν Y Y Y 6/9 Low risk Included Li K et al 1. 12 Y Y Y Y Y Y Y 9/9 Y Y Low risk Included Liu Y et al 2. 13 Y Y UC Y Y Ν Y Y Ν 6/9 Low risk Included 3. Liu Y et al 14 Y Y Y Y Y UC Y Y Y 8/9 Low risk Included 4. Liu J et al 15 Y Y Y Y Ν Y Y Y 8/9 Y Included 16 Low risk 5. Wu J et al 17 Y UC 8/9 Y Y Y Ν Υ Υ Υ Low risk Included 6. Xu X et al 18 UC Y Y Y Y Ν Y Y Ν 6/9 Low risk Included 7. Xu Y et al 19 Y Y Y Y Y Ν Y Y Y 8/9 Low risk Included Yao et al 8. 20 29 Ν Ν Y Y Y Ν Y Y 6/9 Low risk Included 9. Young et al Υ 21 on Y Y Y Y Y Y Y Y Ν 8/9 Low risk Included 10. Zhang J et al 22 <u>б</u> Y Y UC Y Y Ν Y Y Y 7/9 Low risk Included 23 October 2020 11. Zhang M et al 24 Y Y Y Y UC Y Y Y 8/9 Low risk Included 12. Zhao et al Y 25 Y Y Y Y Y Y Y UC Ν 7/9 Low risk Included 13. Zhu et al 26 Ν Y Y Y Y Y 8/9 Y Y Y Low risk Included 14. Yanping Z et al 27 Y UC Y Y Y Ν Y Y Y 7/9 Low risk Included 15. W. Guan et al 28 Downloaded Y UC Y Y Y Y 7/9Y Y Ν 16. WHO ,2020 Low risk Included 29 Y UC Y Y Y Y Y Y 7/9 Ν Low risk Included 30 17. Huang et al 31 UC Y Y Y Y Ν Y Y Y 6/9 Low risk Included 18. Chen et al 32 Y Y Y Y Y Ν Y Y Ν 7/9 Low risk Included 19. Wang et al trom 33 Y Ν Y Y Y Y Y Ν N 6/9 Included Low risk 20. Kaiyuan S et al 34 Υ Υ Υ Y Υ Υ Υ Υ Y 9/9 Low risk Included 21. AL Giwa et al 35 Y Y UC Y Y Ν Y Y Y 8/9 Low risk Included 22. Qian G et al 36 UC 7/9 Y Υ Y Υ Υ Ν 37 23. Livingston E et al Y Y Low risk Included pen Y Ν Y Y Y Y Y 38 Ν Ν 6/9 Low risk Included 24. Wang Y et al 39 Υ Υ Υ Y Y Υ Υ Υ Υ 9/9 Low risk Included B 25. KSID,2020 40 Y UC Y Y Y Ν Y Y Ν 6/9 Low risk Included 26. Su YJ et al 41 Y Y Y Y UC Y Y 8/9 Y Y Low risk Included 27. Jennifer B et al 42 on Y Y Y Y Y Ν Y Y Y 8/9 Low risk Included 28. Kui et al 43 April Y UC Y Y Y Ν Y Y Y 8/9 Low risk Included 29. Deng L et al 44 UC Y Y Y Y Ν Y Y Ν 6/9 Low risk Included 45 30. Dong X et al 19 46 Y Y Y Y Y Y Y Y Ν 8/9 Low risk Included 31. Xiaobo et al 2024 47 Ν Y Ν Y Y Ν Y Y Y 6/9 Low risk Included 32. Zhou F et al 48 by Y Y Y Y Y Y Y Y N 8/9 Low risk Included 33. Wu Y et al 49 ' guest UC 7/9 Y Y Y Y Y Y Y Included Ν Low risk 34. Gao Q et al 50 Y Y Y Y Y UC Y Y Y 8/9 Low risk Included 35. Chen X et al 51 Protected by copyright. Y UC Y Y Y Ν Y Y Y 7/9 Low risk Included 52 36. Zhang G et al 53 Y Ν Y Y 8/9 Low risk Included Y Y Y Y Y 37. Wu W et al 54 Y Y Y Y Y UC Y Y 7/9 Ν Low risk Included 38. Cao M et al 55 Y UC Y Y Y Ν Y Y Y 7/9 Low risk Included 39. Chung et al 56 57

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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			cicai	
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?				<u> </u>
response rate managed appropriately?				

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