Prevalence of severe illness and mortality among coronavirus disease (COVID-19) confirmed patients: A systematic review and meta-analysis.

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Abstract

Aim: The coronavirus disease (COVID-19) first identified in Wuhan, China in late 2019 as the cause of an outbreak of respiratory illness. It has rapidly spread around the world, and been declared a pandemic and Public Health Emergency of International Concern by the World Health Organization (WHO). As of 15 April 2020, this epidemic had spread to 210 countries with 2008 164 confirmed cases, including 127,152 deaths and 486,247 recovery.

Objective: To assess the pooled prevalence of severe illness and mortality among COVID-19 confirmed cases.

Methods: Using PRISMA guideline, we systematically reviewed and meta-analyzed studies that assessed the prevalence of severe illness and mortality among COVID-19 confirmed cases from PubMed, Cochrane library, and Google Scholar. Heterogeneity across the studies was evaluated using the Q and the I2 test. A weighted inverse variance random-effects model was applied to estimate the global magnitude of severe illness cases and mortality among COVID-19 confirmed cases. The subgroup analysis was done through stratification by sample size and by country. A funnel plot and Egger's regression test were used to see publication bias. Sensitivity analysis was also done to identify the impact of studies on the pooled prevalence.

Result: A total of 62 studies with 158870 participants were used for analysis. The pooled prevalence of severe illness was found to be 24.24(20.51-27.97; I2=99.2%; p<0.001). The pooled prevalence of mortality among COVID-19 confirmed cases was 4.41(3.59-5.24; I2=97.7%; p<0.001). In both outcomes the results of sensitivity analysis showed the findings were not dependent on a single study. Moreover a funnel plot showed symmetrical distribution. Egger's regression test p-value was not significant, which indicates the absence of publication bias in both outcomes.

Conclusions: Infection with COVID-19 is associated with significant severe illness and mortality. Nearly one 4th of COVID-19 cases in the world are severe and nearly one 25th of COVID-19 cases in the world end up with death. Additional studies regarding risk factors which determine severity and mortality due to COVID-19 is recommended. Everyone should take actions, such as hand washing with sanitizer, social distancing, avoid crowding (2m apart if coming together is a must), to help slow the spread of COVID-19 and protect older adults from severe illness.

Keywords: COVID-19, Severe illness, Mortality, Systematic review, Meta-analysis.

Abbreviations

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

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Introduction

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 World Health Organization (WHO) used the term 2019 novel coronavirus to refer to a coronavirus that affected the lower respiratory tract of patients with pneumonia in Wuhan, China on 29 December 2019. The WHO also announced that the official name of the 2019 novel coronavirus is coronavirus disease (COVID-19) [5,6]. The virus has now been named Sever Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee of Taxonomy of Viruses (ICTV) [7]. COVID-19 has now been declared as a Public Health Emergency of International Concern by the WHO on 30th January 2020 [8].

Most COVID-19 infected patients have developed mild symptoms and spontaneously resolved. However, some have developed various deadly complications [9]. Particularly, patients with critical illness were aged and are with medical comorbidities such as chronic respiratory, cardiovascular, cerebrovascular, endocrine, and digestive disease developed

severs and critical conditions including death [10]. WHO stated that the spread of COVID-19 can be interrupted by early detection, isolation, prompt treatment, and the implementation of a robust system to trace contacts [11]. COVID-19 likely emerged from an animal source but now is spreading from person to person [12]. Centers for Disease Control and Human coronaviruses most commonly spread from an infected person to others through a variety of means, such as airborne droplets from coughing and sneezing; close personal contact, including touching and shaking hands; and touching one's nose, mouth, or eyes before washing one's hands. It is currently unknown if the virus can be spread through semen or sexual intercourse.

Susceptibility to COVID-19 seems to be associated with age, biological sex, and comorbidities [13]. Although the COVID-19 causes a mild illness in a majority of cases, severe illness requiring hospital admission is not uncommon [14]. 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 [15,16].

Since the occurrence of COVID-19 infection in Wuhan, China, in December 2019, it has quickly spread across China and numerous other countries [17-22]. So far, 2019-nCoV has affected more than 210 countries with 2008 164 confirmed cases, including 127,152 deaths and 486,247 recoveries [23].Given the rapid spread of COVID-19 and its health related impacts, many research articles have been done already been published about this epidemic [24]. However, inconsistency in prevalence of severe illness and mortality has been observed across different studies in different settings. Moreover, there is lack of systematic review and meta-analysis which indicated the worldwide clear picture of the disease clinical spectrum regarding prevalence of severity and fatality. Hence, this systematic review and meta-analysis was conducted to assess the pooled prevalence of severe illness and death due to COVID-19.

Review question

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

What is the prevalence of severe illness among COVID-19 confirmed cases?

What is the prevalence of death among COVID-19 confirmed cases?

Methods

Search strategy

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

Study selection and screening

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

Inclusion and exclusion criteria

Those studies had reported the prevalence of severe illness and/or mortality among COVID-19 confirmed patients and published in the English language. Studies which didn't report the prevalence of severe illness and/or mortality 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 severe illness was considered as the prevalence of both severe and critical illness; while the prevalence of mortality was considered prevalence of death among COVID-19 confirmed cases within a specific population and multiply by 100 to be prevalence report in both case.

Quality assessment

Using the Joanna Briggs Institute (JBI) quality appraisal checklist the authors appraised the quality of included studies. 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, whereas the studies scored 3 and below were considered as high risk or poor quality (Table S2)[25].

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 of severe illness, and the number of mortality. The data extraction sheet was piloted using 4 papers randomly, and it was adjusted after piloted the template. Two of the authors extracted the data using the extraction form in collaboration. The third and fourth authors checked the correctness of the data independently. Any disagreements between reviewers were resolved through discussions with third and fourth reviewers when required. The mistyping of data was resolved through crosschecking with the included papers.

Synthesis of results

The authors transformed the data to STATA 14 for analysis after it was extracted in an excel sheet considering prevalence of severe illness and mortality reported. We pooled the overall prevalence estimates of severe illness and mortality 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 I2statistic 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.

Results

Study selection

A total of 2572 studies were identified using electronic searches (through Database searching (n=6867)) and other sources (n=12)). After duplication removal, a total of 1850 articles remained (722 duplicated). Finally, 86 studies were screened for full-text review and, 62 articles (n=158870 patients) were selected for the analysis (Figure 1).

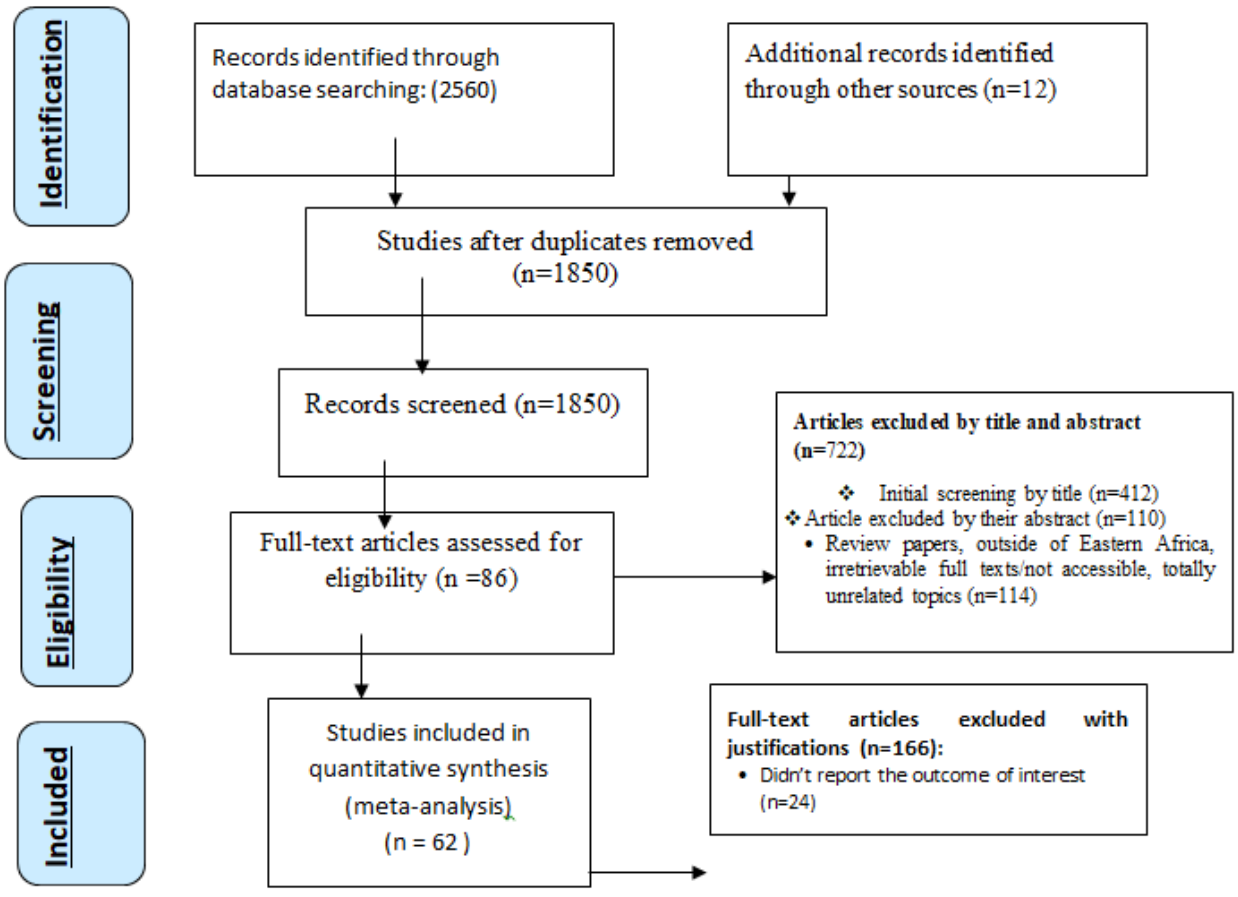

Figure 1. *PRISMA flow diagram showed the results of the search and reasons for exclusion.*

Characteristics of included studies

A total of 62 studies included in the systematic review and meta-analysis (1, 15, 16, 18, 22, 26-79). All studies published in 2020 G.C The studies included participants ranging from 9 (28)to 78771 (57) (Table1).

Table 1. *Characteristics of included studies for severe illness and mortality among COVID-19 confirmed cases.*

Sr no	Author	Country	Study Period	Sample Size	Severe illness	Death
1.	Cai et al. [26]	China	Jan19-Feb03	10		0
2.	Chen C et al. [27]	China	Jan-Feb	150	24	11
3.	Chen H et al. [28]	China	Jan20-Jan31	9		0
4.	Chen L et al. [29]	China	Jan14-Jan29	29	19	2
5.	Chen N et al. [18]	China	Jan01-Jan20	0	56	11
6.	Chen W et al. [30]	China	NA	57	18	NA
7.	Feng et al. [31]	China	Jan16-Feb06	15		0
8.	Li K et al. [32]	China	Jan-Feb	83	25	N/A
9.	Li Y et al. [33]	China	Jan-Feb	54	14	0
10.	Liu C et al. [34]	China	Jan23-Feb08	32	4	0
11.	Liu K et al. [35]	China	Dec30-Jan24	137	60	16
12.	Liu W et al. [36]	China	Dec30-Jan24	78	28	2
13.	Liu Y et al. [37]	China	Jan11-Jan20	12	12	0
14.	Tian et al. [38]	China	Jan20-Feb10	262	46	3
15.	Wang D et al. [39]	China	Jan25-Feb21	31		0
16.	Wang D et al. [40]	China	Jan01-Jan28	138	72	6
17.	Wang L et al. [41]	China	Jan21-Feb05	18	2	0
18.	Wu J et al. [42]	China	Jan22-Feb14	80	6	0
19.	Wu W et al. [43]	China	Jan19-Jan25	40	21	2
20.	Xia W et al. [44]	China	Jan23-Feb8	20	1	0
21.	Xu X et al. [45]	China	Jan10-Jan26	62	2	0
22.	Xu Y et al. [46]	China	Jan-Feb	50	16	0
23.	Yang et al. [15]	China	Jan17-Feb10	149	23	0
24.	Yao et al. [47]	China	Jan01-Feb07	195	10	0
25.	Young et al. [48]	China	Jan22-Jan31	18	8	0
26.	Zhang J et al. [49]	China	Jan16-Feb03	140	58	NA
27.	Zhang M et al. [50]	China	Jan18-Feb03	9		0
28.	Zhao et al. [51]	China	Jan16-Feb03	101	14	NA
29.	Zhu et al. [52]	China	Dec01-Feb15	12		0
30.	Yanping Z et al. [53]	China	Feb-20	44672	10342	1023
31.	W. Guan et al. [54]	China	Feb-20	1099	307	15
32.	WHO ,2020 [55]	Africa	Mar-20	414179		18440
33.	Huang et al. [1]	China	Jan, 2020	41		6
34.	Chen et al. [56]	China	Dec-20	99		11
35.	Wang et al. [22]	China	Mar-20	138		6
36.	AL Giwa et al. [57]	China	March, 2020	78771		2461

37.	Qian G et al. [58]	China	March, 2020	91	9	0
38.	Livingston E et al. [59]	Italy	March, 2020	22512	6731	1625
39.	Wang Y et al. [60]	China	March, 2020	55	2	
40.	KSID,2020 [61]	Korea	February, 2020	4212	22	22
41.	Dong X et al. [62]	China	March, 2020	135		3
42.	Zhou F et al. [16]	China	March, 2020	191	119	54
43.	Wu Y et al. [63]	China	March, 2020	297	83	17
44.	Gao Q et al. [64]	China	January to February ,2020	213	33	
45.	Chen X et al. [65]	China	Feb-20	291	50	
46.	Zhang G et al. [66]	China	Dec-19	221		6
47.	Wu W et al. [67]	China	March, 2020	21	7	
48.	Cao M et al. [68]	China	February, 2020	198	19	1
49.	Xiao F et al. [69]	China	March, 2020	73	4	9
50.	Qi D et al. [70]	China	January to February ,2020	267	50	53
51.	Wang Y et al. [71]	China	February, 2020	110	38	0
52.	Chen X et al. [72]	China	March, 2020	48	27	3
53.	Cheng J et al. [73]	China	March, 2020	1079	12	11
54.	Li J et al. [74]	China	March, 2020	47	41	1
55.	Guan W et al. [75]	China	February, 2020	1099	173	15
56.	Tian S et al. [76]	China	Apr-20	262	46	3
57.	Liu Y et al. [1]	China	February, 2020	109	53	31
58.	Cao W et al. [77]	China	February, 2020	128	21	0
59.	Yang X et al. [15]	China	February, 2020	52	52	32
60.	Liu L et al. [78]	China	February, 2020	51	1	1
61.	Huang C et al. [1]	China	February, 2020	41	13	3
62.	Wang D et al. [79]	China	February, 2020	138	36	6

Meta-analysis

Prevalence of severe illness among COVID-19 confirmed patients

Most of the studies (n=46) had reported the prevalence severe illness [1, 15, 16, 18, 27, 29, 30, 32-49, 51, 53, 54, 58-61, 63-65, 67-79].

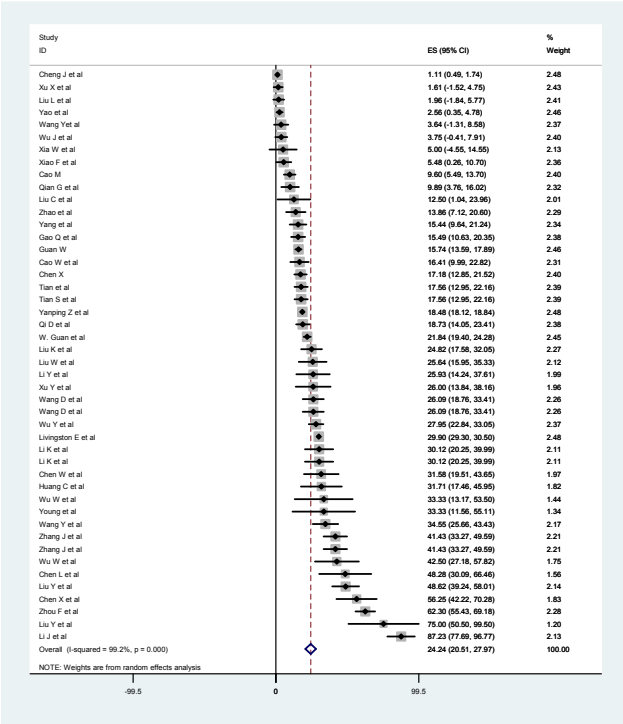

Figure 2. *Forest plot showing the pooled prevalence of severe illness among COVID-19 confirmed cases.*

The prevalence of severe illness ranges from 1.11 (73)to 87.23(74) random-effects model analysis from those studies revealed that, the pooled prevalence of severe illness is 24.24(20.51-27.97; I2=99.2%; p<0.001) (Figure 2).

Subgroup analysis of the severe illness

The subgroup analysis was done through stratification by sample size. Based on this, the prevalence of severe illness was found to be 17.82(5.92-29.73) from those studies that have sample size greater than 384 and 25.27(20.74-29.80) from studies having sample size less than 384(Supplementary Fig 1). Based on the study country, the prevalence of severe illness was found to be 24.01 in china and 29.9 in Italy (Supplementary Fig 2).

Sensitivity analysis

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

Study ommited	Coef.	[95% Conf.	Interval]
Cheng J et al	20.732838	20.445127	21.020546
Xu X et al	17.418531	17.156216	17.680845
Liu L et al	17.381458	17.119438	17.643478
Yao et al	17.516275	17.25304	17.77951
Wang Yet al	17.346966	17.085199	17.608732
Wu J et al	17.362354	17.100435	17.624273
Xia W et al	17.317913	17.056414	17.579412
Xiao F et al	17.338419	17.076689	17.600149
Cao M	17.340126	17.078194	17.60206
Qian G et al	17.322186	17.060547	17.583824
Liu C et al	17.311192	17.049721	17.57266
Zhao et al	17.313881	17.052284	17.57548
Yang et al	17.312496	17.050829	17.574163
Gao Q et al	17.313957	17.052176	17.575737
Guan W	17.332129	17.068779	17.595478
Cao W et al	17.310188	17.048569	17.571806
Chen X	17.309149	17.04727	17.571028
Tian et al	17.307884	17.046061	17.569708
Tian S et al	17.307884	17.046061	17.569708
Yanping Z et al	16.002106	15.621832	16.382381
Qi D et al	17.304249	17.042439	17.566059
W. Guan et al	17.256212	16.993301	17.519123
Liu K et al	17.298866	17.037294	17.56044
Liu W et al	17.30262	17.041122	17.564116
Li Y et al	17.304375	17.042908	17.565842
Xu Y et al	17.304667	17.043205	17.56613
Wang D et al	17.297497	17.035929	17.559065
Wang D et al	17.297497	17.035929	17.559065
Wu Y et al	17.280704	17.018961	17.54245
Livingston E et al	14.335077	14.044443	14.625712
Li K et al	17.299694	17.0382	17.561188
Li K et al	17.299694	17.0382	17.561188
Chen W et al	17.301987	17.040525	17.56345
Huang C et al	17.303835	17.042391	17.565281
Wu W et al	17.305992	17.044569	17.567415
Young et al	17.306377	17.044958	17.567799
Wang Y et al	17.293758	17.032244	17.555273
Zhang J et al	17.283909	17.022371	17.545444
Zhang J et al	17.283909	17.022371	17.545444
Wu W et al	17.30135	17.039811	17.56279
Chen L et al	17.302288	17.040859	17.563717
Liu Y et al	17.284363	17.02286	17.545866
Chen X et al	17.295172	17.033726	17.556618
Zhou F et al	17.243504	16.981913	17.505095
Liu Y et al	17.302118	17.040703	17.563536
Li J et al	17.256153	16.994654	17.517653
Yang X et al	17.308687	17.047285	17.570087
Combined	17.308687	17.047285	17.570088

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

Publication Bias

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

Tests for Publication Bias

Begg's Test

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

Egger's test

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

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

Prevalence of mortality among COVID-19 confirmed patients

Most of the studies (n=36) had reported prevalence of mortality (1, 15, 16, 18, 22, 27, 29, 35, 36, 38, 40, 43, 53-57, 59, 61-63, 66, 68-79). The prevalence of mortality ranges from 0.51(0.48-1.49) (68) to 61.54 (15). The random-effects model analysis from those studies revealed that, the pooled

Subgroup analysis of the prevalence of mortality

The subgroup analysis was done through stratification by sample size. Based on this, the prevalence of mortality was found to be 2.66(2.58-2.74) from those studies that have sample size greater than 384 and 2.05(1.67-2.43) from studies having sample size less than 384(Supplementary Fig 3). Based on the study country, the prevalence of mortality was found to be 3.63 in china and 7.22 in Italy (Supplementary Fig 4).prevalence of mortalityis 4.41(3.59-5.24; I2=97.7%; p<0.001) (Figure 5).

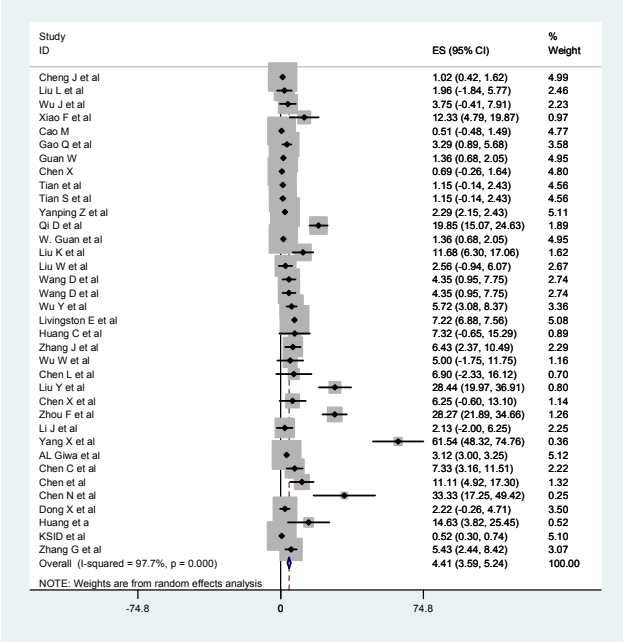

Figure 5. *Forest plot showing the pooled prevalence of mortality among COVID-19 confirmed cases.*

Sensitivity analysis

We employed a leave-one-out sensitivity analysis to identify the impact of individual research on the pooled prevalence of mortality among COVID-19 confirmed cases. The results of this sensitivity analysis showed that our findings were not dependent on a single study. Our pooled estimated prevalence of severe illness varied between 3.63 (2.94-4.33) Livingston et al. and 5.16 (4.11-6.20) Yanping Z et al. after the deletion of a single study (Figure 6).

Study omitted	Coef.	[95% Conf.	Interval]
Cheng J et al	4.6060462	3.752996	5.4590964
Xu X et al	4.4131703	3.5858574	5.2404833
Liu L et al	4.4764647	3.638365	5.3145647
Yao et al	4.4131703	3.5858574	5.2404833
Wang Yet al	4.4131703	3.5858574	5.2404833
Wu J et al	4.4295168	3.5924692	5.2665644
Xia W et al	4.4131703	3.5858574	5.2404833
Xiao F et al	4.3319082	3.5015624	5.1622539
Cao M	4.6096416	3.761678	5.4576054
Qian G et al	4.4131703	3.5858574	5.2404833
Liu C et al	4.4131703	3.5858574	5.2404833
Zhao et al	4.4131703	3.5858574	5.2404833
Yang et al	4.4131703	3.5858574	5.2404833
Gao Q et al	4.4577389	3.6144211	5.3010569
Guan W	4.5891881	3.7355742	5.442802
Cao W et al	4.4131703	3.5858574	5.2404833
Chen X	4.6037507	3.7550282	5.4524732
Tian et al	4.5736351	3.7255149	5.4217548
Tian S et al	4.5736351	3.7255149	5.4217548
Yanping Z et al	5.1571832	4.1105399	6.2038264
Qi D et al	4.0855241	3.2602186	4.9108295
W. Guan et al	4.5891881	3.7355742	5.442802
Liu K et al	4.2874351	3.4552445	5.1196251
Liu W et al	4.4655504	3.626487	5.3046145
Li Y et al	4.4131703	3.5858574	5.2404833
Xu Y et al	4.4131703	3.5858574	5.2404833
Wang D et al	4.4160953	3.5768785	5.2553124
Wang D et al	4.4160953	3.5768785	5.2553124
Wu Y et al	4.3662734	3.5250475	5.207499
Livingston E et al	3.6344378	2.9425719	4.326304
Li K et al	4.4131703	3.5858574	5.2404833
Li K et al	4.4131703	3.5858574	5.2404833
Chen W et al	4.4131703	3.5858574	5.2404833
Huang C et al	4.3870573	3.5560491	5.2180657
Wu W et al	4.4131703	3.5858574	5.2404833
Young et al	4.4131703	3.5858574	5.2404833
Combined	4.4131704	3.5858574	5.2404834

Figure 6. *Sensitivity analysis pooled prevalence of mortality among COVID-19 confirmed cases.*

Publication Bias

We have also checked publication bias and, a funnel plot showed symmetrical distribution. Egger's regression test p-value was 0.218, which indicates the absence of publication bias (Figure 7)

Tests for Publication Bias

Begg's Test

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adj. Kendall's Score (P-Q) =      291
      Std. Dev. of Score =    73.42 (corrected for ties)
      Number of Studies  =       36
                       z =     3.96
                 Pr > |z| =    0.000
                       z =     3.95 (continuity corrected)
                 Pr > |z| =    0.000 (continuity corrected)
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Egger's test

Std_Eff	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
slope	2.450718	.3014306	8.13	0.000	1.838137	3.063298
bias	1.569554	1.25073	1.25	0.218	-.9722357	4.111343

Figure 7. *Publication bias pooled prevalence of mortality among COVID-19 confirmed cases.*

Discussion

Recently, following the COVID-19 outbreak, numerous questions have been raised; comprising what is the range of disease severity and case fatality? [80]. This systematic review and meta-analysis were conducted to assess the magnitude of severe illness and mortality among COVID -19 confirmed cases. Sixty two studies were included in the final analysis. Forty six studies reported the prevalence of severe illness and the pooled prevalence of severe illness among COVID -19 confirmed cases was found to be 24.24 with 95% CI of (20.51-27.97). This result is in line with a previous review which indicated 24% of the cases were severe illness (39). On the other hand the finding was higher than another studies 19%(14), and 19% while it was lower than another study, 32.6% [81,82]. The discrepancy might due to in most countries, there is lack of extensive; systematic testing globally. Besides, preferably testing those severe diseases can result in selection bias, which resulted in variation in the proportion of severe cases. The subgroup analysis result revealed that the prevalence of severe illness was found to be 17.82(5.92-29.73) from those studies that have sample size greater than 384 and 25.27(20.74-29.80) from studies having sample size less than 384. Based on the study country, the prevalence of severe illness was found to be 24.01 in china and 29.9 in Italy.

In this review the pooled prevalence of mortality is 4.41(3.59-5.24; I2=97.7%; p<0.001)which is consistent with a study in in another two studies 10% to 27%, and 4% [82,83].However, this result is higher than a previous review, 0.8% (39), 2.3% (14), 3.67%, and 1.4 % [84]. On the other hand the finding is lower than death rate in Italy, 11%, and 11.1% [9,85]. This might be due to some countries only test patients severe illness to go to hospital and don't test the mild ill (or even asymptomatic) Covid-19 patients who don't get to hospital the death rate can appear higher than in countries where testing is widespread. The subgroup analysis result revealed that the prevalence of mortality was found to be 2.66(2.58-2.74) from those studies that have sample size greater than 384 and 2.05(1.67-2.43) from studies having sample size less than 384(Supplementary Fig 1). Based on the study country, the prevalence of mortality was found to be 3.63 in china and 7.22 in Italy. The possible justification for the increased death rates in Italy might be due to patient

demographics (i.e., older patients might be more prevalent in countries such as Italy)[86].

This study result implies that COVID-19 can result in severe illness and death throughout the World. Everyone can take actions, such as hand washing with sanitizer, social distancing, avoid crowding (2m apart if coming together is must), to help slow the spread of COVID-19 and protect older adults from severe illness. Additional studies regarding risk factors which determine severity and mortality due to COVID-19 is recommended.

Strength and Limitations

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

Conclusions

Infection with COVID-19 is associated with significant severe illness and mortality. Nearly one 4th of COVID-19 cases in the world are severe and nearly one 25th of COVID-19 cases in the world end up with death. Although there has been a rapid surge in research in response to the outbreak of COVID-19, additional studies regarding risk factors which determine severity and mortality due to COVID-19 is recommended. Everyone should take actions, such as hand washing with sanitizer, social distancing, avoid crowding (2m apart if coming together is must), to help slow the spread of COVID-19 and protect older adults from severe illness.

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Availability of Data and Material

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

Competing Interests

We have confirmed that we have no competing interests.

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Authors' Contributions

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

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