

## Supplementary Material

## Accumulating Impact of Smoking and Co-morbidities on Severity and Mortality of COVID-19 Infection: A Systematic Review and Meta-analysis

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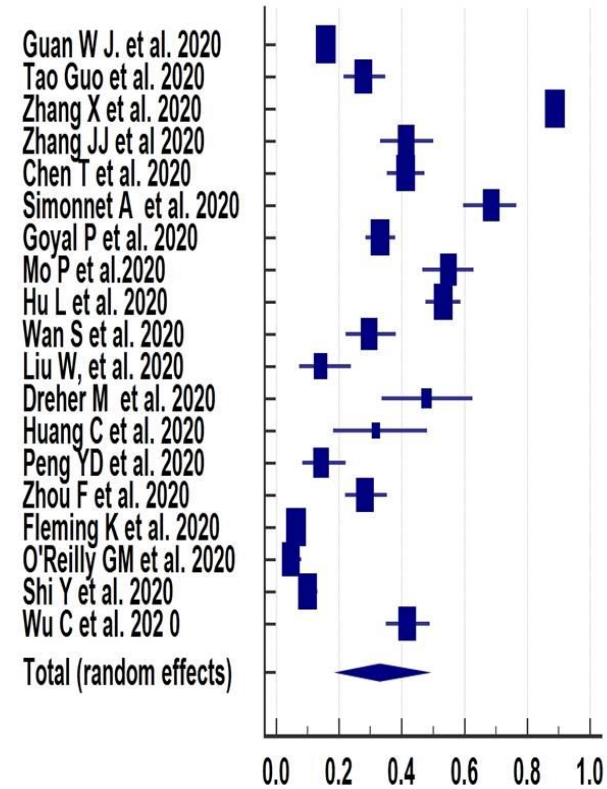
**Supplementary Table 1.** Descriptive clinical symptoms and treatments of patients.

	Guan W J et al. 2020 [1]	Tao Guo et al. 2020 [19]	Zhang JJ et al. 2020 [20]	Zhang X et al. 2020 [21]	Chen T et al. 2020 [22]	Simonnet A et al. 2020 [23]	Goyal P et al. 2020 [24]	Mo P et al. 2020 [25]	Hu L et al. 2020 [26]	Wan S et al. 2020 [27]	Liu W et al. 2020 [28]	Dreher M et al. 2020 [29]	Huang C et al. 2020 [30]	Zhou F et al. 2020 [32]	Fleming K et al. 2020 [33]	O'Reilly GM et al. 2020 [34]	Shi Y et al. 2020 [35]	Wu C et al. 2020 [36]	Prevalence (%)
<b>Signs and symptoms at admission</b>	<b>No. of Patients N (%)</b>																		
<b>Fever</b>	-	-	96.2	85.9	92.0	-	34.6	71.4	82.9	85.0	-	92.0	100	94.0	-	44.0	-	92.9	47.57
<b>Cough</b>	70.5	-	84.9	68.4	70.0	-	-	63.5	52.7	87.5	36.4	44.0	85.0	72.0	-	67.0	-	81.0	44.67
<b>Shortness of breath</b>	37.6	-		4.5	-	-	-	41.2	-	7.5	-	-	-	-	-	80.0	-	-	6.51
<b>Headache</b>	15.0	-		11.3	10.0	-	-	13.2	0	27.5	-	0	0	-	-	-	-	-	5.60
<b>Diarrhea</b>	5.8	-	15.8	7.9	24.0	-	-	5.9	-	-	-	24.0	0	4.0	-	70.0	-	-	5.89
<b>Nausea and vomiting</b>	6.9	-	8.8	3.8	12	-	-	5.3	0	0	-	4.0	54.0	6.0	-	100	-	3192.1	4.80
<b>Treatment</b>	<b>No. of Patients N (%)</b>																		
<b>Antibiotics</b>	80.3	100	-	-	93.0	-	-	-	93.8	100	-	83.0	100	98.0	-	-	-	98.8	30.65

<b>Antiviral treatment</b>	-	88.5	-	85.2	79.0	-	-	31.8	66.4	87.5	18.2	-	92.0	22.0	-	-	-	76.2	41.34
<b>Corticosteroids</b>	44.5	71.2	-	13.4	88.0	-	-	64.7	58.9	52.5	48.0	-	23.0	48.0	-	-	-	-	22.86
<b>Intravenous immunoglobulin</b>	-	13.5	-	-	39.0	-	-	8.2	-	-	-	-	-	67.0	-	-	-	-	4.46
<b>oxygen therapy</b>	71.1	-	--	43.6	100	-	-	84.7	-	80.0	-	-	-	33.0	-	-	-	20.2	30.41
<b>Non-invasive mechanical ventilation</b>	32.4	-	-	1.6	67.0	-	14.6	-	41.1	67.5	18.2	-	62.0	44.0	-	-	-	72.6	16.15

Critical/Severe Cases			
Study	Sample size	Proportion (%) 95% CI	Weight (%)
Guan W J <i>et al.</i> 2020	1099	15.74 (13.63- 18.03)	5.37
Tao Guo <i>et al.</i> 2020	187	27.80 (21.51-34.81)	5.32
Zhang X <i>et al.</i> 2020	645	88.83 (86.15-91.16)	5.36
Zhang JJ <i>et al.</i> 2020	140	41.42 (33.17- 50.05)	5.30
Chen T <i>et al.</i> 2020	274	41.24 (35.35- 47.32)	5.34
Simonnet A <i>et al.</i> 2020	124	68.54 (59.59-76.58)	5.29
Goyal P <i>et al.</i> 2020	393	33.07 (28.44- 37.97)	5.35
Mo P <i>et al.</i> 2020	155	54.83 (46.65- 62.83)	5.31
Hu L <i>et al.</i> 2020	323	53.25 (47.64- 58.79)	5.35
Wan S <i>et al.</i> 2020	135	29.63 (22.08- 38.09)	5.30
Liu W <i>et al.</i> 2020	78	14.10 (7.25- 23.83)	5.24
Dreher M <i>et al.</i> 2020	50	48.00(33.66- 62.58)	5.16
Huang C <i>et al.</i> 2020	41	31.70 (18.08- 48.08)	5.11
Peng YD <i>et al.</i> 2020	112	14.28 (8.39- 22.16)	5.28
Zhou F <i>et al.</i> 2020	191	28.27 (22.00- 35.22)	5.32
Fleming K <i>et al.</i> 2020	7162	6.38 (5.82- 6.97)	5.38
O'Reilly GM <i>et al.</i> 2020	240	4.58 (2.31- 8.05)	5.29
Shi Y <i>et al.</i> 2020	487	10.06 (7.53- 13.08)	5.36
Wu C <i>et al.</i> 2020	201	41.79 (34.89- 48.93)	5.32
<b>Total (random effects)</b>	12037	32.96 [19.90- 47.52]	100.00

**Test for heterogeneity**  
 Q-3322.5932, DF-18, Significance level-P < 0.0001  
 I<sup>2</sup>(inconsistency)-99.46%, 95% CI for I<sup>2</sup>- 99.38-99.53



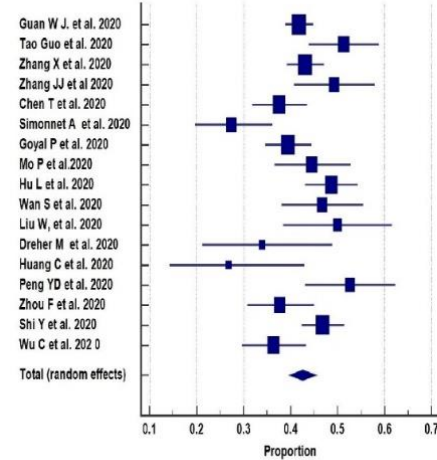
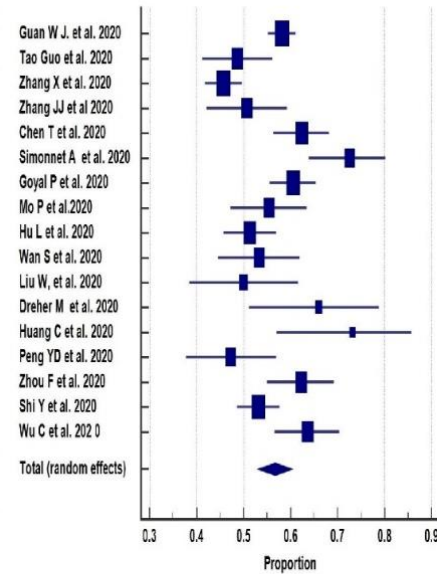
SUPPLEMENTARY FIG 1. Pooled prevalence of critical/ Sever patients in COVID-19.

Male			
Study	Sample size	Proportion (%) 95% CI	Weight (%)
Guan W J <i>et al.</i> 2020	1099	58.23 (55.25-61.17)	7.67
Tao Guo <i>et al.</i> 2020	187	48.66 (41.30- 56.06)	6.08
Zhang X <i>et al.</i> 2020	645	45.73 (41.84- 49.67)	7.39
Zhang JJ <i>et al.</i> 2020	140	50.71 (42.13- 59.25)	5.61
Chen T <i>et al.</i> 2020	274	62.40(56.38- 68.16)	6.60
Simonnet A <i>et al.</i> 2020	124	72.58(63.84- 80.20)	5.40
Goyal P <i>et al.</i> 2020	393	60.56(55.53- 65.42)	6.99
Mo P <i>et al.</i> 2020	155	55.48(47.29- 63.45)	5.79
Hu L <i>et al.</i> 2020	323	51.39 (45.79-56.96)	6.79
Wan S <i>et al.</i> 2020	135	53.33(44.55- 61.96)	5.55
Liu W <i>et al.</i> 2020	78	50.00 (38.45- 61.54)	4.52
Dreher M <i>et al.</i> 2020	50	66.00(51.23- 78.79)	3.64
Huang C <i>et al.</i> 2020	41	73.17(57.05-85.77)	3.26
Peng YD <i>et al.</i> 2020	112	47.32 (37.81-56.97)	5.22
Zhou F <i>et al.</i> 2020	191	62.30(55.02- 69.19)	6.11
Shi Y <i>et al.</i> 2020	487	53.18(48.64-57.68)	7.18
Wu C <i>et al.</i> 202 0	201	63.68 (56.62- 70.33)	6.19
<b>Total (random effects)</b>	<b>4635</b>	<b>56.71(53.20- 60.19)</b>	<b>100.00</b>

**Test for heterogeneity**  
 Q- 82.2014, DF-16, Significance level-P < 0.0001  
 I<sup>2</sup> (inconsistency)-80.54%, 95% CI for I<sup>2</sup>-69.71 to 87.49

Female			
Study	Sample size	Proportion (%) 95% CI	Weight (%)
Guan W J <i>et al.</i> 2020	1099	41.76 (38.82 - 44.74)	8.74
Tao Guo <i>et al.</i> 2020	187	51.33 (43.93-58.69)	6.01
Zhang X <i>et al.</i> 2020	645	43.10 (39.24- 47.02)	8.20
Zhang JJ <i>et al.</i> 2020	140	49.28(40.74-57.86)	5.34
Chen T <i>et al.</i> 2020	274	37.59(31.83- 43.61)	6.82
Simonnet A <i>et al.</i> 2020	124	27.41(19.79-36.15)	5.05
Goyal P <i>et al.</i> 2020	393	39.44(34.57-44.46)	7.49
Mo P <i>et al.</i> 2020	155	44.51(36.54- 52.70)	5.58
Hu L <i>et al.</i> 2020	323	48.60(43.03- 54.20)	7.14
Wan S <i>et al.</i> 2020	135	46.66(38.03- 55.44)	5.25
Liu W <i>et al.</i> 2020	78	50.00 (38.45- 61.54)	3.95
Dreher M <i>et al.</i> 2020	50	34.00(21.20-48.76)	2.98
Huang C <i>et al.</i> 2020	41	26.82(14.22- 42.94)	2.60
Peng YD <i>et al.</i> 2020	112	52.67(43.02- 62.18)	4.80
Zhou F <i>et al.</i> 2020	191	37.69(30.80-44.97)	6.06
Shi Y <i>et al.</i> 2020	487	46.81(42.31-51.35)	7.82
Wu C <i>et al.</i> 202 0	201	36.31(29.66-43.37)	6.17
<b>Total (random effects)</b>	<b>4635</b>	<b>42.57 (39.77- 45.40)</b>	<b>100.00</b>

**Test for heterogeneity**  
 Q- 52.2645, DF-16- Significance level, P < 0.0001  
 I<sup>2</sup> (inconsistency)-69.39%, 95% CI for I<sup>2</sup>-49.61 to 81.40



SUPPLEMENTARY FIG 2. Pool prevalence of gender in COVID-19.

**Fig. 3 PRISMA 2009 Checklist:** "Accumulating impact of smoking and co-morbidities on severity and mortality of COVID-19 infection: A systematic review and meta-analysis.

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

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6 Fig 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6-7 Table 1 S1 Table 1
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).	n/a
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	7-8 Fig 2-6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Fig 2-6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
<b>DISCUSSION</b>			
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).	8-12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	8-11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	13

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