

SYSTEMATIC REVIEW

Prevalence of Comorbidities in COVID-19 Patients: A Systematic Review and Meta-Analysis

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The paper was accepted without peer review process

Received: 10 April 2020

Accepted: 10 April 2020

Abstract

Background: In this study, we aimed to assess the prevalence of comorbidities in the confirmed COVID-19 patients. This might help showing which comorbidity might pose the patients at risk of more severe symptoms.

Methods: We searched all relevant databases on April 7th, 2020 using the keywords (“novel coronavirus” OR COVID-19 OR SARS-CoV-2 OR Coronavirus) AND (comorbidities OR clinical characteristics OR epidemiologic). We reviewed 33 papers’ full text out of 1053 papers. There were 32 papers from China and 1 from Taiwan. There was no language or study level limit. Prevalence of comorbidities including hypertension, diabetes mellitus, cardiovascular disease, chronic lung disease, chronic kidney disease, malignancies, cerebrovascular diseases, chronic liver disease and smoking were extracted to measure the pooled estimates. We used OpenMeta and used random-effect model to do a single arm meta-analysis.

Results: The mean age of the diagnosed patients was 51 years. The male to female ratio was 55 to 45. The most prevalent finding in the confirmed COVID-19 patients was hypertension, which was found in 1/5 of the patients (21%). Other most prevalent finding was diabetes mellitus (DM) in 11%, cerebrovascular disease in 2.4%, cardiovascular disease in 5.8%, chronic kidney disease in 3.6%, chronic liver disease in 2.9%, chronic pulmonary disease in 2.0%, malignancy in 2.7%, and smoking in 8.7% of the patients.

Conclusion: COVID-19 infection seems to be affecting every race, sex, age, irrespective of health status. The risk of symptomatic and severe disease might be higher due to the higher age which is usually accompanied with comorbidities. However, comorbidities do not seem to be the prerequisite for symptomatic and severe COVID-19 infection, except hypertension.

Level of evidence: IV

Keywords: Comorbidities, Coronavirus, COVID-19, Systematic review

Introduction

We are still unaware of many facts about the new coronavirus that is called COVID-19. In the beginning of its spread in Wuhan, China, the transmission and infectivity rate was reported very

low, leading everyone to believe that the mortality rate was even lower than a seasonal flu, and taking it even less seriously. The first reports were noting that it only affects older people with comorbidities and only they die

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because of inefficient immune system following multiple comorbidities. The threat was not considered seriously and later after it spread to other countries, doctors were seeing even younger patients that were dying despite having no past medical history, and the patient's status was aggravating so fast in hours that no one could help save the lives. Further studies showed cytokine storm as a reason which is an exaggerated immune response to the infection regardless of having comorbidities. Thus, simply having chronic conditions does not determine the prognosis.

In this study, we aimed to assess the prevalence of comorbidities in the confirmed COVID-19 patients. This might help showing which comorbidity might pose the patients at risk of more severe symptoms.

Materials and Methods

Search strategy

In order to identify all relevant studies, databases including EMBASE, PubMed, and google scholar were searched and papers published in the past year were screened carefully until April 7th, 2020 using title and abstract. Records were imported to EndNote X9 citation

manager and duplicates were excluded. The following search terms were employed to ensure inclusion of all relevant studies: ("novel coronavirus" OR COVID-19 OR SARS-CoV-2 OR Coronavirus) AND (comorbidities OR clinical characteristics OR epidemiologic*)

Inclusion and Exclusion Criteria

All articles with any design and study level (levels 1-4) that reported the prevalence of comorbidities among the confirmed COVID-19 patients were included. There was no language limit. We used the translated abstract of non-English articles. We excluded papers concerning children and papers without epidemiological information.

Data extraction and statistical analysis

All stages of the meta-analysis were done by the two authors (AK and AB) independently. Prevalence of comorbidities including hypertension, diabetes mellitus, cardiovascular disease, chronic lung disease, chronic kidney disease, malignancies, cerebrovascular diseases, chronic liver disease and smoking were extracted to measure the pooled estimates [Table 1]. The latest version of the statistical software OpenMeta

Table 1. Data extracted using 33 papers

First Author	Publication Date	Country	Number of patients	Sex (M/F)	Age (mean or median)	Age (SD or range)	HTN	DM	Malignancy	Chronic Lung Disease	Cardiovascular Disease	Chronic Liver Disease	Cerebrovascular Disease	Chronic Kidney Disease	Smoking
Yingzhen Du, et al.	4/4/2020	China	85	62/23	66	14	32	19	6	2	10	5		3	
Lang Wang, et al.	4/3/2020	China	339	166/173	69	65-76	138	54	15	21	53	2	21	13	
ChaominWu, et al.	3/14/2020	China	201	128/73	51	43-60	32	22	1	5	8	7		2	
Xiao Tang, et al.	4/1/2020	China	148	105/43	62	47-69	70	35			31			9	43
Qingxian Cai, et al.	4/3/2020	China	298	149/149	47	33-61	38	19	4		11	8			
Wei Liu, et al.	3/3/2020	China	78	39/39	38	33-57	8	5	4	2					5
Xiao-Wei Xu, et al.	2/23/2020	China	62	35/27	41	32-52	5	1		1		7	1	1	
Tao Chen, et al.	3/29/2020	China	274	171/103	62	44-70	93	47	7	18	23	11	4	4	12
Jiangshan Lian, et al.	3/27/2020	China	652	349/303	41	11.38	73	33	3	0	5	25		5	46
Jianlei Cao, et al.	4/3/2020	China	102	53/49	54	37-67	28	11	4	10	5	2	6	4	
Zhongliang Wang, et al.	3/17/2020	China	69	32/37	42	35-62	9	7	4	4	8	1			
Hansheng Xie, et al.	4/3/2020	China	79	44/35	60	48-66	14	8			7				
Yan Deng, et al.	3/27/2020	China	109 death 116 recovered	73/36 51/65	69 40	62-74 33-57	40 18	17 9	6 2	22 3	13 4				
Weina Guo, et al.	4/2/2020	China	174	76/98	59	49-67	43	37	17	14	32	8			
Wei-jie Guan, et al.	3/29/2020	China	1590	904/674	49	16	269	130	130	24	59	24	30	269	
Xi Jin, et al.	3/28/2020	China	74 GI symptoms 577 no GI symptoms	37/37 294/283	46 45	14 14	12 88	7 41	0 6	0 1	1 4	8 17		0 6	
Wen-Hsin Hsieh, et al.	3/30/2020	Taiwan	43	17/26	34	3-68	2	4	2	4	1	1			
Nanshan Chen, et al.	2/3/2020	China	99	67/32	56	13			1						3
Rui Wang, et al.	4/3/2020	China	5	3 to 2	58	47-67	4	1						5	
L. Zhang, et al.	4/1/2020	China	28	17/11	65	56-70			4	1		2			
Xiaoli Zhang, et al.	3/25/2020	China	72 normal imaging 573 abnormal imaging	33/39 295/278	35 47	14 14	4 96	4 44	0 6	0 1	0 5	2 23		0 6	
Jin-jin Zhang, et al.	2/23/2020	China	140	71/69	57	25-87	42	17		2	7		3	2	9

Table 1. Continued														
W. Guan, et al.	2/29/2020	China	1099	640/459	47	35-58	165	81	10	12	27	15	8	137
Chaolin Huang, et al.	1/28/2020	China	41	30/11	49	41-58	6	8	1	1	6	1		3
Yingxia Liu, et al.	2/13/2020	China	12	8 to 4	54	10-72	3	2	0	1	4	0	2	
Dawei Wang, et al.	2/8/2020	China	138	75/63	56	42-68	43	14	10	4	20	4	7	4
Jie Li, et al.	1/1/2020	China	17	9 to 8	45	13	1					1		3
Jian Wu, et al.	2/29/2020	China	80	39/41	46	15.42			1	0		1		
Kui Liu, et al.	2/12/2020	China	137	61/76	57	20-83	13	14	2	2	10			
Wenhua Liang, et al.	2/19/2020	China	1590							18				111
Yichun Cheng, et al.	4/6/2020	China	701	367/334	63	50-71	233	100	32	13			14	
Xiaobing Wang, et al.	4/7/2020	China	1012	524/488	50	39-58	46	27		20	15			
Ya-nan Han, et al.	4/7/2020	China	25	12 to 13	44	22-70	7	9						

GI: gastrointestinal; HTN: hypertension; DM: diabetes mellitus

[Analyst] (1) was used to do a single arm Meta-analysis. This analysis took study effects into account, and the results were calculated by a binary random-effect method (Dersimonian-Laird). A confidence interval of 95% was selected and the I² statistic and Cochran's Q test were measured to assess statistical heterogeneity. Forest plots were used to illustrate the prevalence with 95% confidence interval.

Results

Study characteristics

We included 33 studies for data extraction out of 1053 papers found on COVID-19 on April 7th, 2020 [Figure 1].

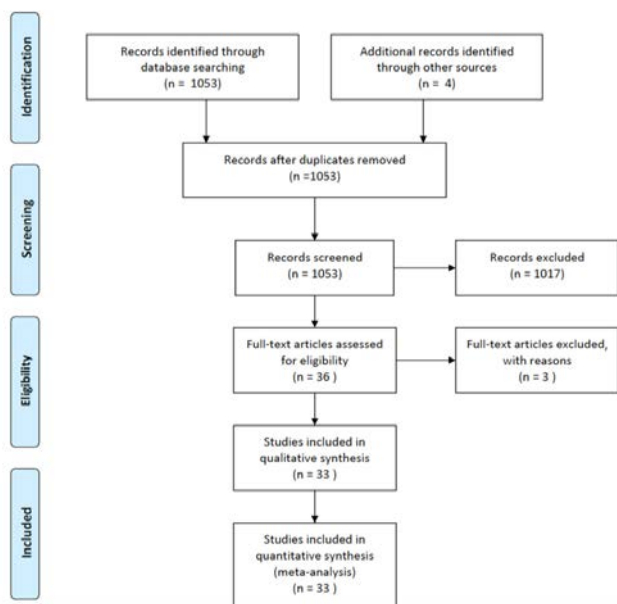


Figure 1. PRISMA flow diagram. [From Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group [2009]. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 6[7]:e1000097. <https://doi.org/10.1371/journal.pmed.1000097>.]

There were 32 papers from China and 1 paper from Taiwan (2). All 33 papers were in English language. In total, these studies included 9,249 patients comprising of 5,036 men and 4,191 women with confirmed COVID-19 since December 2019. (2-34)

Test of heterogeneity

We performed statistical testing for heterogeneity to determine if the prevalence of comorbidities was the same in all studies. Cochran Q result rejected the null hypothesis that there is no heterogeneity between studies if *P* value was <0.05. Moreover, I² revealed that how much percent of the variation across the studies was because of heterogeneity rather than sampling error and chance. Following rule of thumb, we considered I² greater than 40% as substantial heterogeneity. Considering the presence of heterogeneity in all fields, we used random-effects model to conduct the meta-analysis.

Age distribution

Based on the random effect model after inclusion of 33 studies, the mean age of the confirmed COVID-19 patients was 51 years (95% CI, 49-54 years old). Cochran Q statistics showed 95% heterogeneity among studies which was high and significant (Q=655, *P*<0.001, I²=95) [Figure 2].

Sex distribution

Based on the random effect model after inclusion of 32 studies, 55% (95% CI, 53%-57%) of the patients were men while 45% (95% CI, 43%-47%) were women. Cochran Q statistics showed 74% heterogeneity among studies which was high and significant (Q=120, *P*<0.001, I²=74) [Figures 3; 4].

Prevalence of cerebrovascular disease

Based on the random effect model after inclusion of 8 studies, the prevalence of cerebrovascular disease among the confirmed COVID-19 patients was 2.4% (95% CI, 1.5%-3.4%). Cochran Q statistics showed 64% heterogeneity among studies which was high and significant (Q=19, *P*=0.007, I²=64) [Figure 5].

Studies	Estimate (95% C.I.)
Yingzhen Du, et al. 2020	65.800 (62.781, 68.819)
Lang Wang, et al. 2020	69.000 (65.000, 73.000)
ChaominWu, et al. 2020	51.000 (43.000, 59.000)
Xiao Tang, et al. 2020	62.000 (47.000, 77.000)
Qingxian Cai, et al. 2020	47.000 (33.000, 61.000)
Wei Liu, et al. 2020	38.000 (19.000, 57.000)
Xiao-Wei Xu, et al. 2020	41.000 (30.000, 52.000)
Tao Chen, et al. 2020	62.000 (44.000, 80.000)
Jiangshan Lian, et al. 2020	41.150 (40.276, 42.024)
Jianlei Cao, et al. 2020	54.000 (37.000, 71.000)
Zhongliang Wang, et al. 2020	42.000 (35.000, 49.000)
Hansheng Xie, et al. 2020	60.000 (48.000, 72.000)
Yan Deng, et al.death 2020	69.000 (62.000, 76.000)
Yan Deng, et al.recovered 2020	40.000 (33.000, 47.000)
Weina Guo, et al. 2020	59.000 (49.000, 69.000)
Wei-jie Guan, et al. 2020	48.900 (48.099, 49.701)
Xi Jin, et al.GI 2020	46.140 (42.907, 49.373)
Xi Jin, et al.nonGI 2020	45.090 (43.911, 46.269)
Wen-Hsin Hsih, et al. 2020	34.000 (3.000, 65.000)
Nanshan Chen, et al. 2020	55.500 (52.920, 58.080)
Rui Wang, et al. 2020	57.600 (47.000, 68.200)
L. Zhang, et al. 2020	65.000 (56.000, 74.000)
Xiaoli Zhang, et al. normal imaging 2020	34.900 (31.620, 38.180)
Xiaoli Zhang, et al. abnormal imaging 2020	46.650 (45.518, 47.782)
Jin-Jin Zhang, et al. 2020	57.000 (25.000, 89.000)
W. Guan, et al. 2020	47.000 (35.000, 59.000)
Chaolin Huang, et al. 2020	49.000 (41.000, 57.000)
Yingxia Liu, et al. 2020	53.600 (35.200, 72.000)
DaweiWang, et al. 2020	56.000 (42.000, 70.000)
Jie Li, et al. 2020	45.000 (38.915, 51.085)
Jian Wu, et al. 2020	46.100 (42.721, 49.479)
Kui Liu, et al. 2020	57.000 (31.000, 83.000)
Yichun Cheng, et al. 2020	63.000 (50.000, 76.000)
Xiaobing Wang, et al. 2020	50.000 (39.000, 61.000)
Ya-nan Han, et al. 2020	44.000 (22.000, 66.000)
Overall (I²=9481 % , P<0.001)	51.212 (48.585, 53.839)

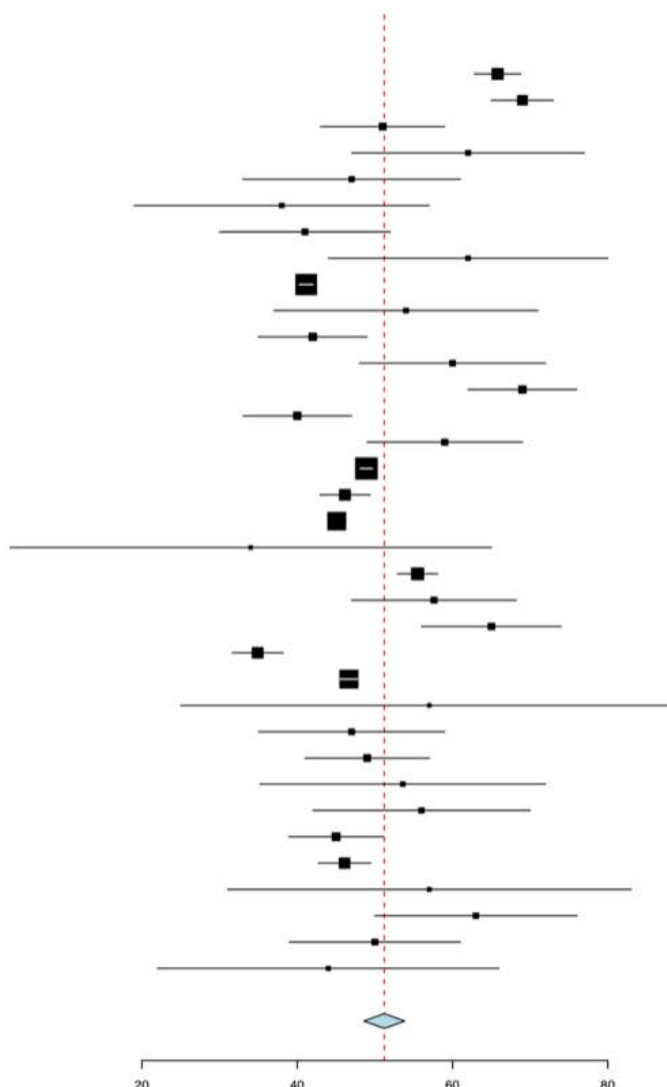


Figure 2. Forest plot of the age distribution using random effect model.

Prevalence of cardiovascular disease

Based on the random effect model after inclusion of 23 studies, the prevalence of cardiovascular disease among the confirmed COVID-19 patients was 5.8% (95% CI, 4.5%-7.1%). Cochran Q statistics showed 91% heterogeneity among studies which was high and significant (Q=250, P<0.001, I²=91) [Figure 6].

Prevalence of chronic kidney disease

Based on the random effect model after inclusion of 17 studies, the prevalence of chronic kidney disease among the confirmed COVID-19 patients was 3.6% (95% CI, 2.0%-5.1%). Cochran Q statistics showed 96% heterogeneity among studies which was high and significant (Q=368, P<0.001, I²=96) [Figure 7].

Prevalence of diabetes mellitus

Based on the random effect model after inclusion of 29 studies, the prevalence of diabetes mellitus among the confirmed COVID-19 patients was 11% (95% CI, 8.9%-12.7%). Cochran Q statistics showed 89% heterogeneity among studies which was high and significant (Q=252, P<0.001, I²=89) [Figure 8].

Prevalence of hypertension

Based on the random effect model after inclusion of 29 studies, the prevalence of hypertension among the confirmed COVID-19 patients was 21% (95% CI, 17%-24.6%). Cochran Q statistics showed 96% heterogeneity among studies which was high and significant (Q=687, P<0.001, I²=96) [Figure 9].

Studies	Estimate (95% C.I.)	Ev/Trt
Yingzhen Du, et al. 2020	0.729 (0.635, 0.824)	62/85
Lang Wang, et al. 2020	0.490 (0.436, 0.543)	166/339
ChaominWu, et al. 2020	0.637 (0.570, 0.703)	128/201
Xiao Tang, et al. 2020	0.709 (0.636, 0.783)	105/148
Qingxian Cai, et al. 2020	0.500 (0.443, 0.557)	149/298
Wei Liu, et al. 2020	0.500 (0.389, 0.611)	39/78
Xiao-Wei Xu, et al. 2020	0.565 (0.441, 0.688)	35/62
Tao Chen, et al. 2020	0.624 (0.567, 0.681)	171/274
Jiangshan Lian, et al. 2020	0.535 (0.497, 0.574)	349/652
Jianlei Cao, et al. 2020	0.520 (0.423, 0.617)	53/102
Zhongliang Wang, et al. 2020	0.464 (0.346, 0.581)	32/69
Hansheng Xie, et al. 2020	0.557 (0.447, 0.667)	44/79
Yan Deng, et al. 2020	0.551 (0.486, 0.616)	124/225
Weina Guo, et al. 2020	0.437 (0.363, 0.510)	76/174
Wei-jie Guan, et al. 2020	0.569 (0.544, 0.593)	904/1590
Xi Jin, et al. 2020	0.508 (0.470, 0.547)	331/651
Wen-Hsin Hsieh, et al. 2020	0.395 (0.249, 0.541)	17/43
Nanshan Chen, et al. 2020	0.677 (0.585, 0.769)	67/99
Rui Wang, et al. 2020	0.600 (0.171, 1.000)	3/5
L. Zhang, et al. 2020	0.607 (0.426, 0.788)	17/28
Xiaoli Zhang, et al. 2020	0.509 (0.470, 0.547)	328/645
Jin-Jin Zhang, et al. 2020	0.507 (0.424, 0.590)	71/140
W. Guan, et al. 2020	0.582 (0.553, 0.612)	640/1099
Chaolin Huang, et al. 2020	0.732 (0.596, 0.867)	30/41
Yingxia Liu, et al. 2020	0.667 (0.400, 0.933)	8/12
DaweiWang, et al. 2020	0.543 (0.460, 0.627)	75/138
Jie Li, et al. 2020	0.529 (0.292, 0.767)	9/17
Jian Wu, et al. 2020	0.487 (0.378, 0.597)	39/80
Kui Liu, et al. 2020	0.445 (0.362, 0.528)	61/137
Yichun Cheng, et al. 2020	0.524 (0.487, 0.561)	367/701
Xiaobing Wang, et al. 2020	0.518 (0.487, 0.549)	524/1012
Ya-nan Han, et al. 2020	0.480 (0.284, 0.676)	12/25
Overall (I²=7328 % , P<0.001)	0.549 (0.526, 0.572)	5036/9249

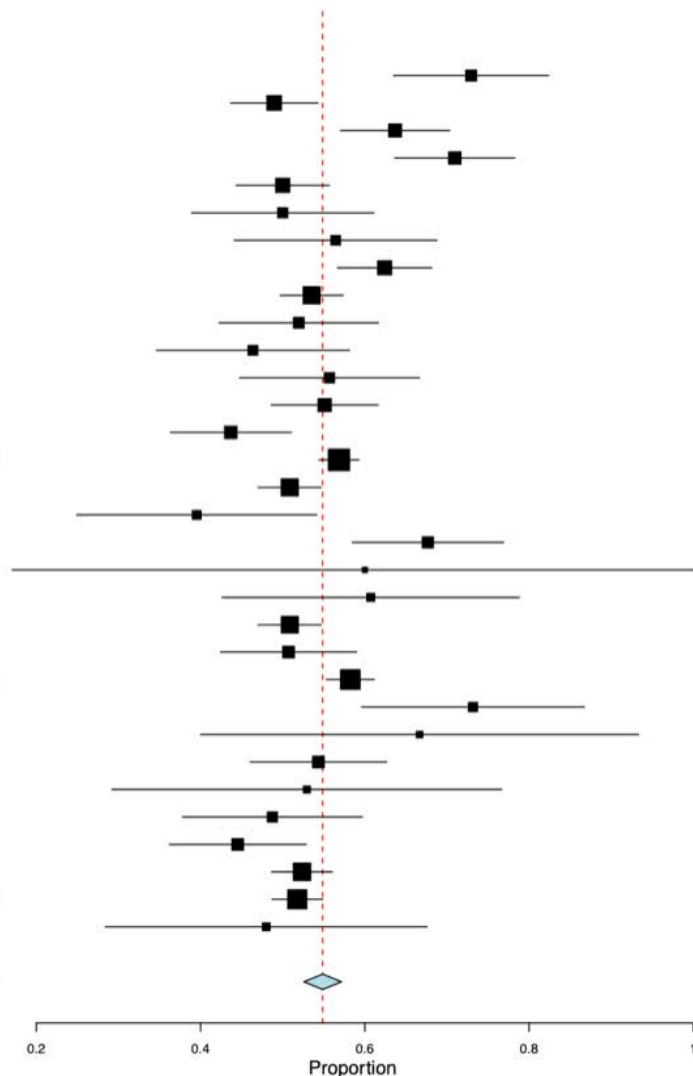


Figure 3. Forest plot of the Sex (male) ratio using random effect model.

Prevalence of liver disease

Based on the random effect model after inclusion of 20 studies, the prevalence of liver disease among the confirmed COVID-19 patients was 2.9% (95% CI, 2.0%-3.7%). Cochran Q statistics showed 62% heterogeneity among studies which was high and significant (Q=50, P<0.001, I²=62) [Figure 10].

Prevalence of pulmonary disease

Based on the random effect model after inclusion of 25 studies, the prevalence of chronic pulmonary disease among the confirmed COVID-19 patients was 2.0% (95% CI, 1.4%-2.5%). Cochran Q statistics showed 85% heterogeneity among studies which was high and significant (Q=162, P<0.001, I²=85) [Figure 11].

Prevalence of malignancy

Based on the random effect model after inclusion of 24 studies, the prevalence of malignancy among the confirmed COVID-19 patients was 2.7% (95% CI, 1.9%-3.5%). Cochran Q statistics showed 87% heterogeneity among studies which was high and significant (Q=181, P<0.001, I²=87) [Figure 12].

Prevalence of smoking

Based on the random effect model after inclusion of 10 studies, the prevalence of smoking among the confirmed COVID-19 patients was 8.6% (95% CI, 5.8%-11.4%). Cochran Q statistics showed 88% heterogeneity among studies which was high and significant (Q=74, P<0.001, I²=88) [Figure 13].

Studies	Estimate (95% C.I.)	Ev/Trt
Yingzhen Du, et al. 2020	0.271 (0.176, 0.365)	23/85
Lang Wang, et al. 2020	0.510 (0.457, 0.564)	173/339
ChaominWu, et al. 2020	0.363 (0.297, 0.430)	73/201
Xiao Tang, et al. 2020	0.291 (0.217, 0.364)	43/148
Qingxian Cai, et al. 2020	0.500 (0.443, 0.557)	149/298
Wei Liu, et al. 2020	0.500 (0.389, 0.611)	39/78
Xiao-Wei Xu, et al. 2020	0.435 (0.312, 0.559)	27/62
Tao Chen, et al. 2020	0.376 (0.319, 0.433)	103/274
Jiangshan Lian, et al. 2020	0.465 (0.426, 0.503)	303/652
Jianlei Cao, et al. 2020	0.480 (0.383, 0.577)	49/102
Zhongliang Wang, et al. 2020	0.536 (0.419, 0.654)	37/69
Hansheng Xie, et al. 2020	0.443 (0.333, 0.553)	35/79
Yan Deng, et al. 2020	0.404 (0.340, 0.469)	91/225
Weina Guo, et al. 2020	0.563 (0.490, 0.637)	98/174
Wei-jie Guan, et al. 2020	0.424 (0.400, 0.448)	674/1590
Xi Jin, et al. 2020	0.492 (0.453, 0.530)	320/651
Wen-Hsin Hsieh, et al. 2020	0.605 (0.459, 0.751)	26/43
Nanshan Chen, et al. 2020	0.323 (0.231, 0.415)	32/99
Rui Wang, et al. 2020	0.400 (0.000, 0.829)	2/5
L. Zhang, et al. 2020	0.393 (0.212, 0.574)	11/28
Xiaoli Zhang, et al. 2020	0.491 (0.453, 0.530)	317/645
Jin-Jin Zhang, et al. 2020	0.493 (0.410, 0.576)	69/140
W. Guan, et al. 2020	0.418 (0.388, 0.447)	459/1099
Chaolin Huang, et al. 2020	0.268 (0.133, 0.404)	11/41
Yingxia Liu, et al. 2020	0.333 (0.067, 0.600)	4/12
DaweiWang, et al. 2020	0.457 (0.373, 0.540)	63/138
Jie Li, et al. 2020	0.471 (0.233, 0.708)	8/17
Jian Wu, et al. 2020	0.512 (0.403, 0.622)	41/80
Kui Liu, et al. 2020	0.555 (0.472, 0.638)	76/137
Yichun Cheng, et al. 2020	0.476 (0.439, 0.513)	334/701
Xiaobing Wang, et al. 2020	0.482 (0.451, 0.513)	488/1012
Ya-nan Han, et al. 2020	0.520 (0.324, 0.716)	13/25
Overall (I²=7430 % , P<0.001)	0.449 (0.426, 0.472)	4191/9249

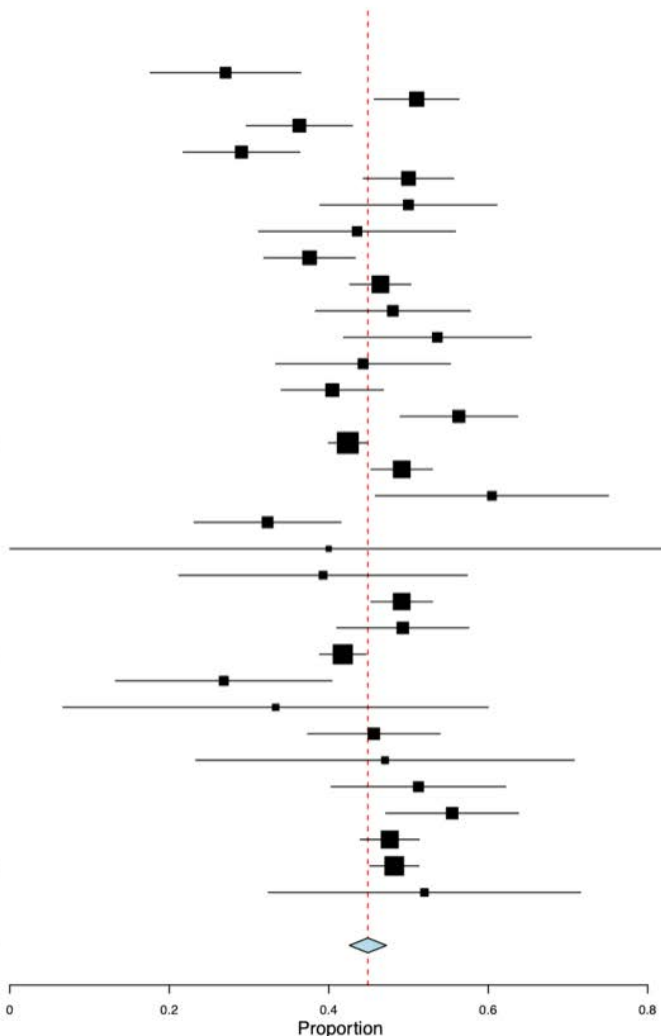


Figure 4. Forest plot of the Sex (Female) ratio using random effect model.

Studies	Estimate (95% C.I.)	Ev/Trt
Lang Wang, et al. 2020	0.062 (0.036, 0.088)	21/339
Xiao-Wei Xu, et al. 2020	0.016 (0.000, 0.047)	1/62
Tao Chen, et al. 2020	0.015 (0.000, 0.029)	4/274
Jianlei Cao, et al. 2020	0.059 (0.013, 0.104)	6/102
Wei-jie Guan, et al. 2020	0.019 (0.012, 0.026)	30/1590
Jin-Jin Zhang, et al. 2020	0.021 (0.000, 0.045)	3/140
W. Guan, et al. 2020	0.014 (0.007, 0.021)	15/1099
DaweiWang, et al. 2020	0.051 (0.014, 0.087)	7/138
Overall (I²=6370 % , P=0.007)	0.024 (0.015, 0.034)	87/3744

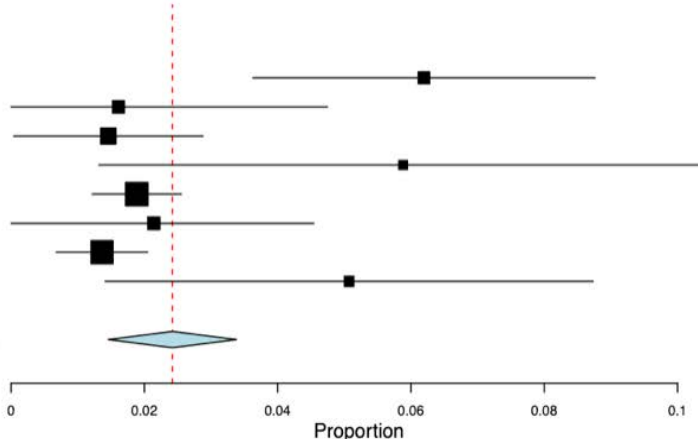


Figure 5. Forest plot of the cerebrovascular disease prevalence among COVID-19 patients using random effect model.

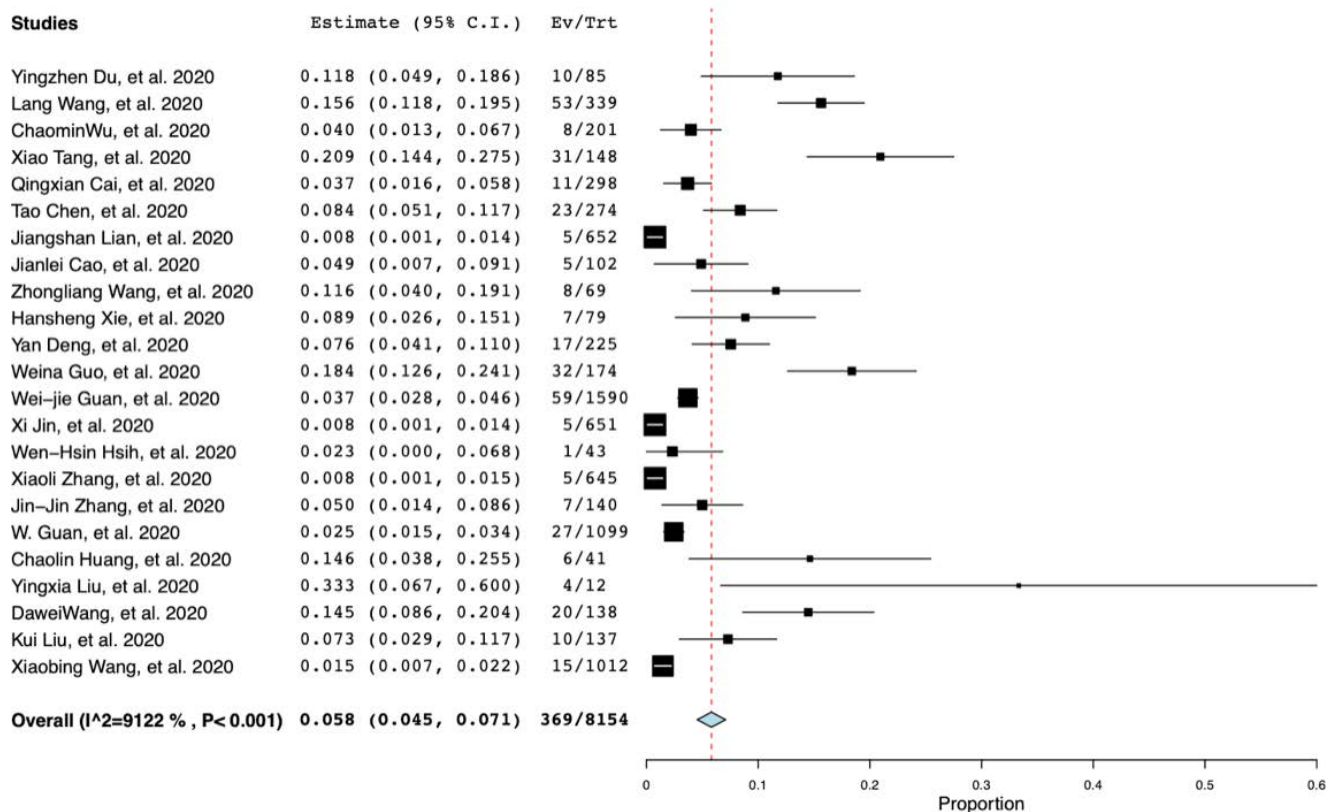


Figure 6. Forest plot of the cardiovascular disease prevalence among COVID-19 patients using random effect model.

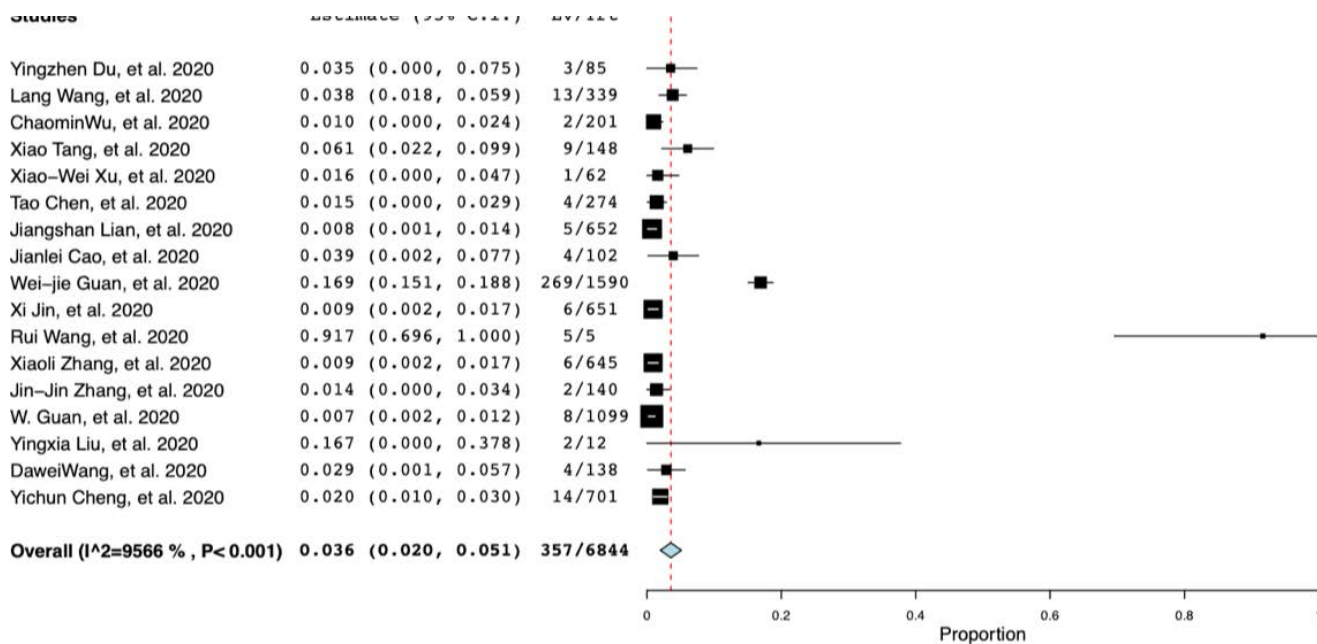


Figure 7. Forest plot of the chronic kidney disease prevalence among COVID-19 patients using random effect model.

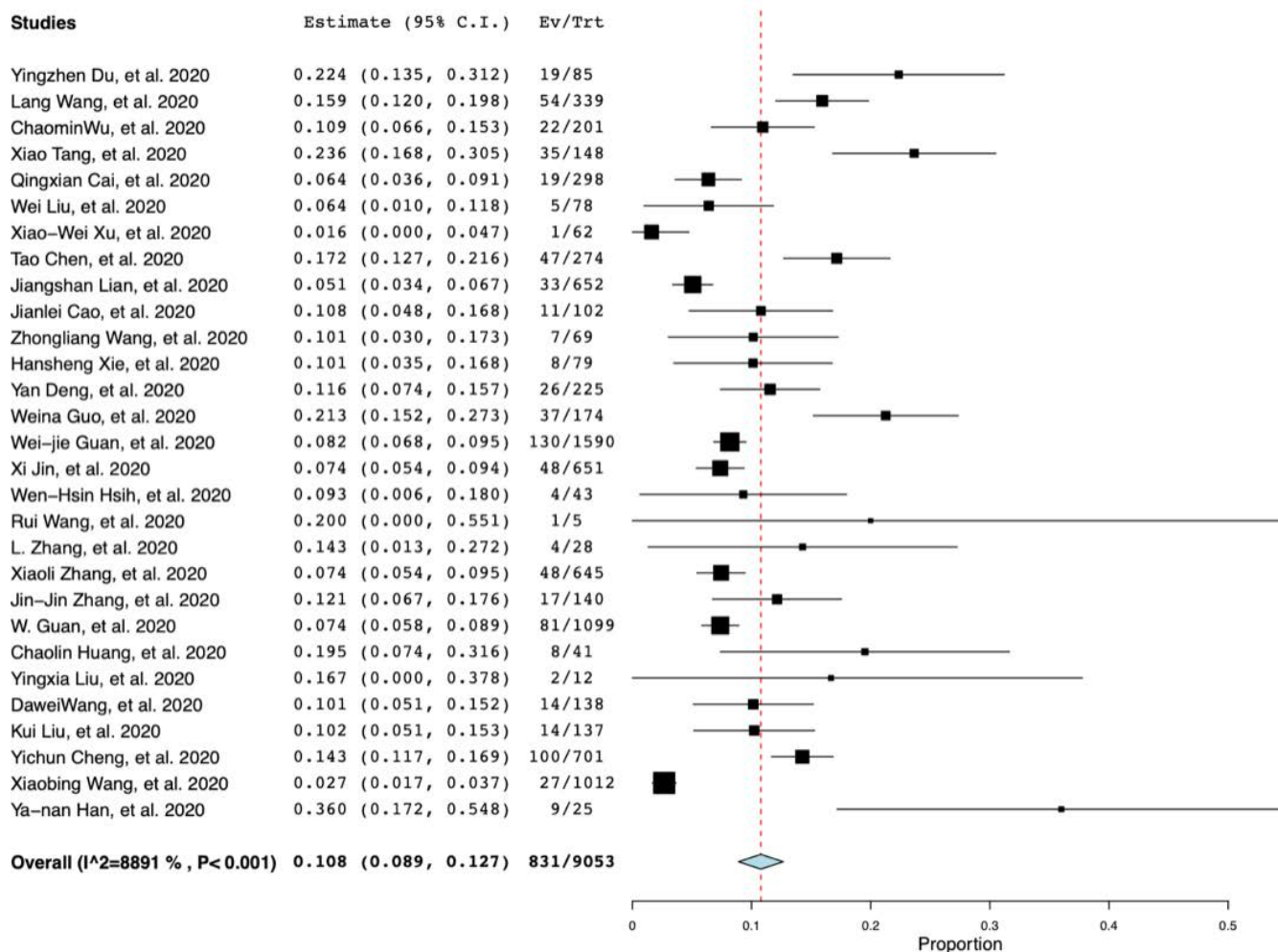


Figure 8. Forest plot of the diabetes mellitus prevalence among COVID-19 patients using random effect model.

Discussion

In this study, we aimed to assess the prevalence of accompanying comorbidities in patients tested positive for COVID-19. It seems that the most prevalent comorbidity was hypertension while other comorbidities are counting for less than 10% among the patients.

One main limitation of our study was that most of the studies were from the Chinese population which differences in race and ethnicity may play a role particularly when we see differences in mortality rates around the world. We assume that the prevalence and rates might differ in future papers that consider other populations. Another limitation of our study is that we are not sure if the prevalence reporting were complete because most of these papers emerged at the time that papers were published too fast with no peer review. We are only trusting the current literature so far from China and we have to be vigilant about the accuracy of data.

Thus, we did not perform quality assessment because we were to include all published papers.

The mean age of the diagnosed patients was 51 years. It is intuitive that younger age groups are not showing too severe symptoms to make them refer to the hospitals and thus they remain undiagnosed. The male to female ratio was 55/45 showing slightly higher infection rate or probably slightly more severe presentation to refer the patients to the hospitals. This might be due to the fact that men are spending more time out of house at work, which causes men contracting the disease first and slightly more severe.

The most prevalent finding in the confirmed COVID-19 patients was hypertension, which was found in 1/5 of the patients and is consistent with the tendency of the virus binding with ACE2 receptor. Other most prevalent finding was diabetes mellitus (DM) in almost 10% of the patients. Other comorbidities were less than 10%.

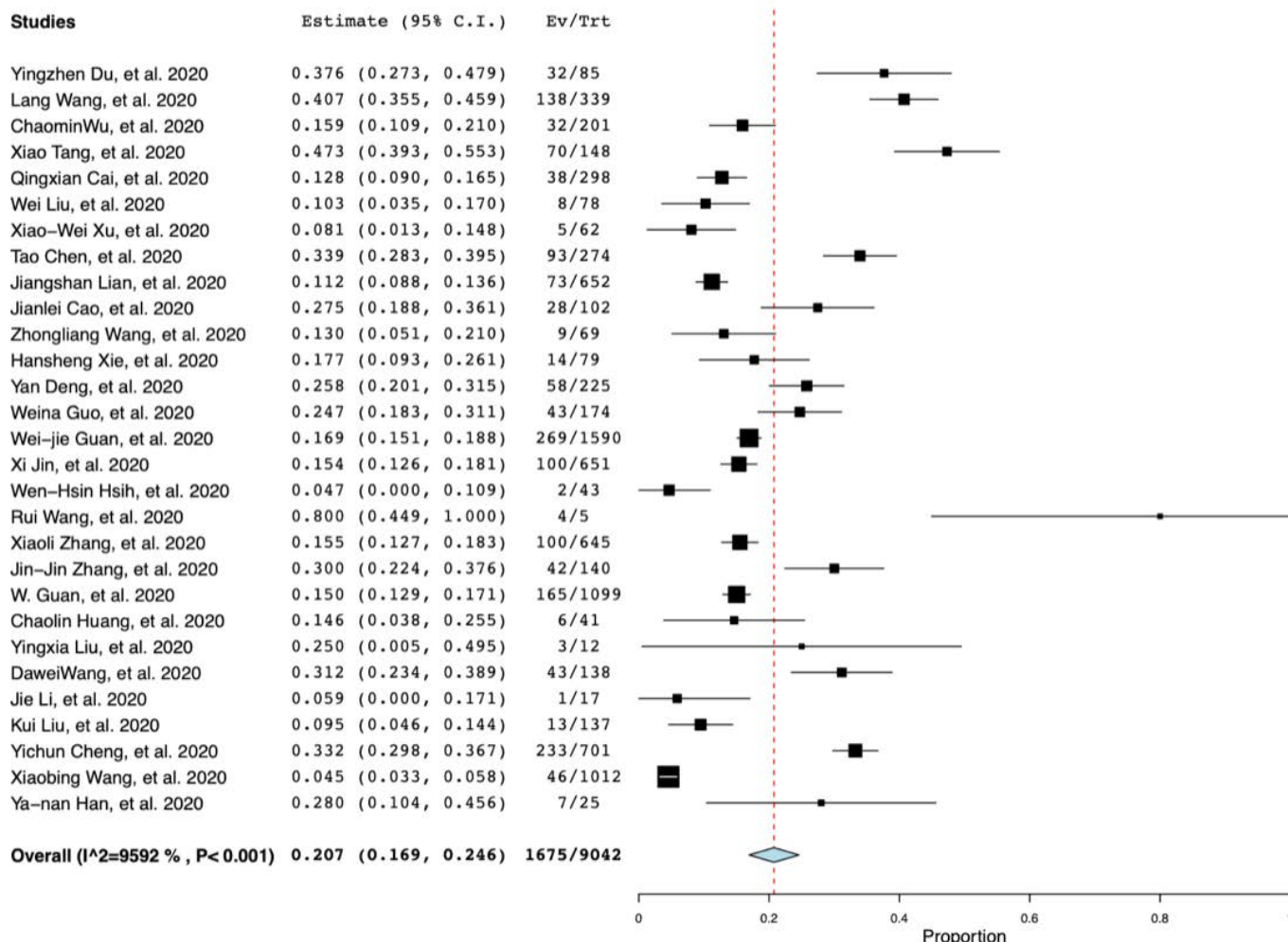


Figure 9. Forest plot of the hypertension prevalence among COVID-19 patients using random effect model.

It seems that these rates are also found with other common conditions and is not supporting the idea that more comorbidities increase the risk of symptomatic COVID-19 unless hypertension is present.

Other systematic reviews that included limited studies in the beginning of this outbreak reported the same finding about accompanying hypertension as the most prevalent risk to symptomatic COVID-19 infection. Although other reports have noted accompanying of different comorbidities such chronic liver, kidney, heart and even lung diseases, we presume that the comorbidities only cause the patients refer more to the hospital, but the comorbidities do not seem to be the cause of disease severity or even mortality. There is limited data about smoking as an influencing factor on the severity of the disease. Thus so far, we cannot make any conclusion, but obviously smoking recession improves airway clearance.

COVID-19 infection seems to be affecting every race, sex, age, irrespective of health status. The risk of symptomatic and severe disease might be higher due to the higher age which is usually accompanied with comorbidities. However, comorbidities do not seem to be the prerequisite for symptomatic and severe COVID-19 infection, except hypertension.

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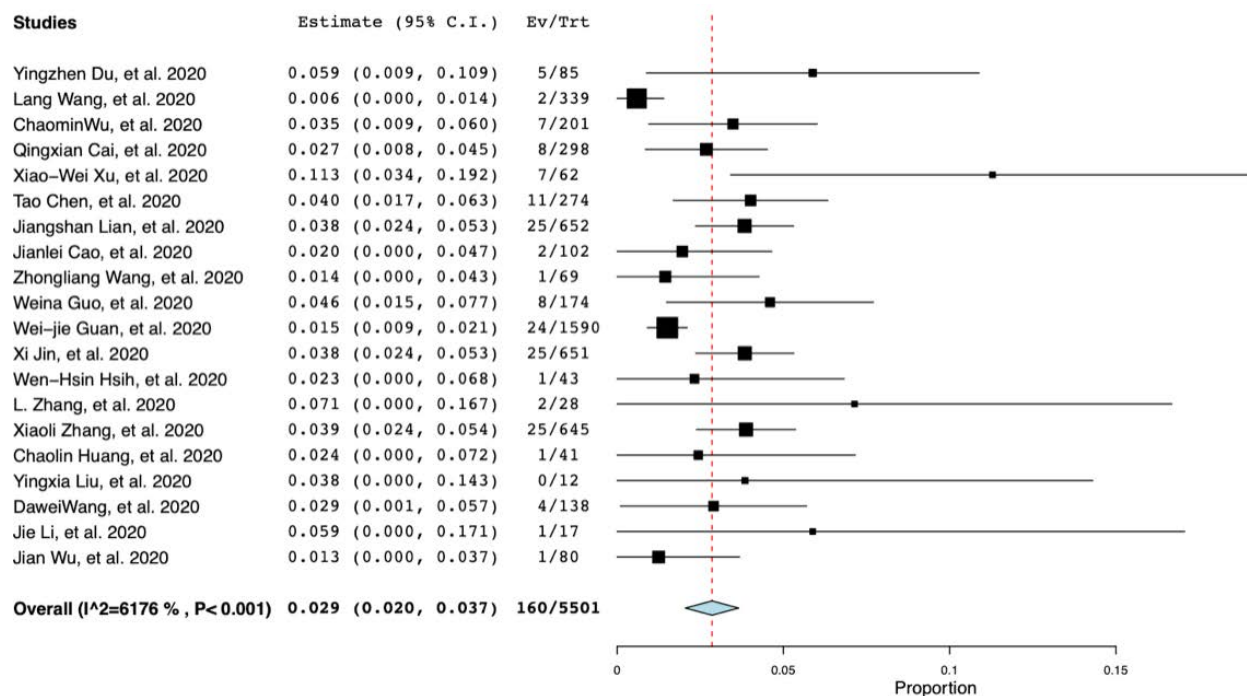


Figure 10. Forest plot of the chronic liver disease prevalence among COVID-19 patients using random effect model.

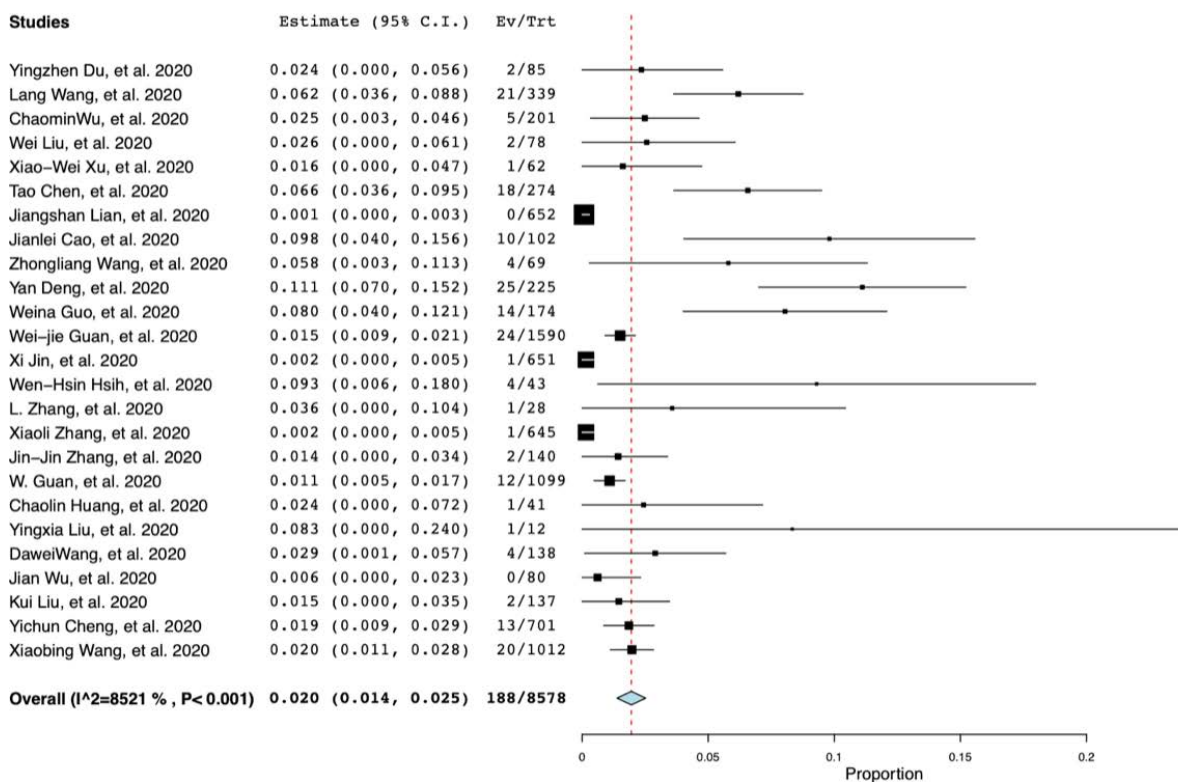


Figure 11. Forest plot of the chronic pulmonary disease prevalence among COVID-19 patients using random effect model.

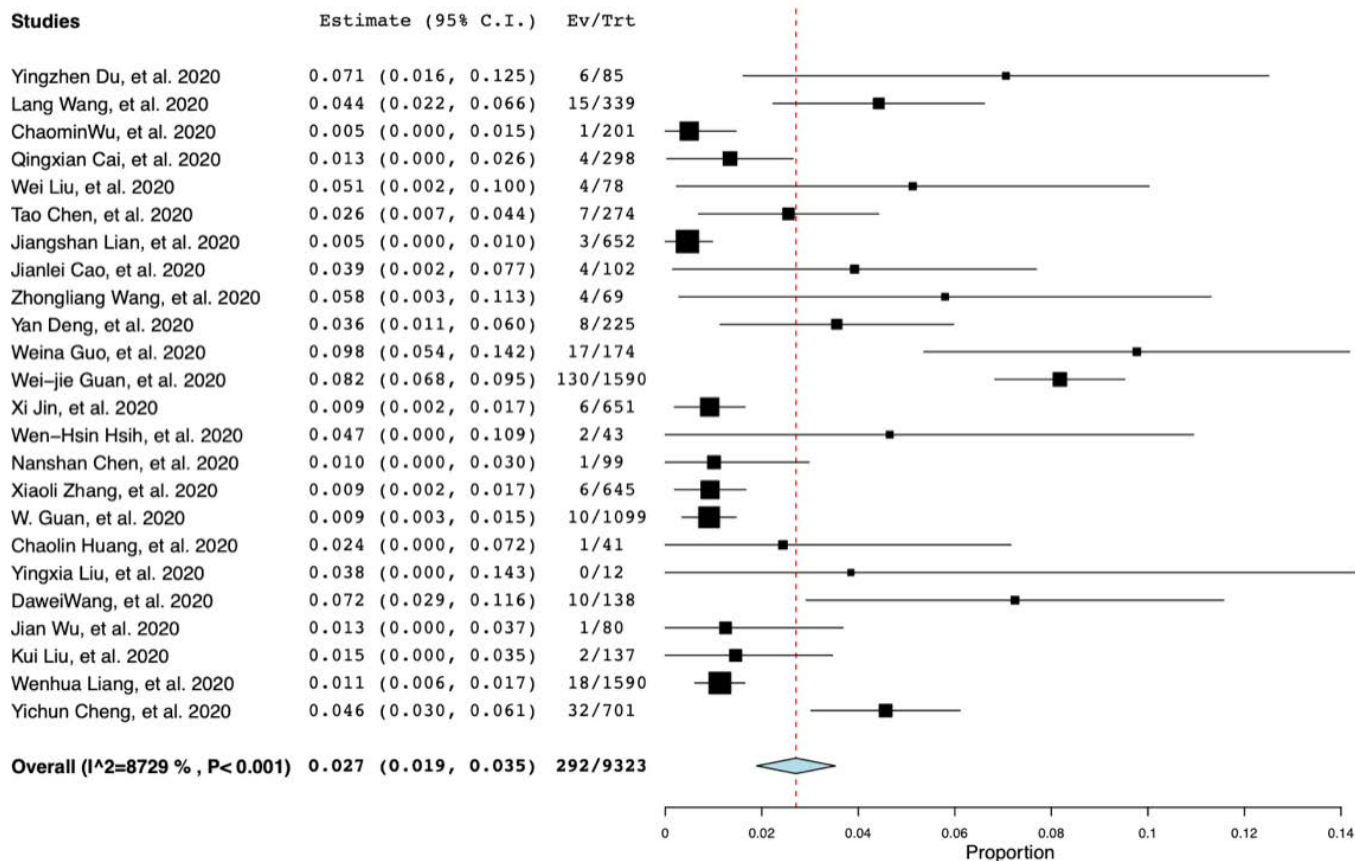


Figure 12. Forest plot of the malignancy prevalence among COVID-19 patients using random effect model.

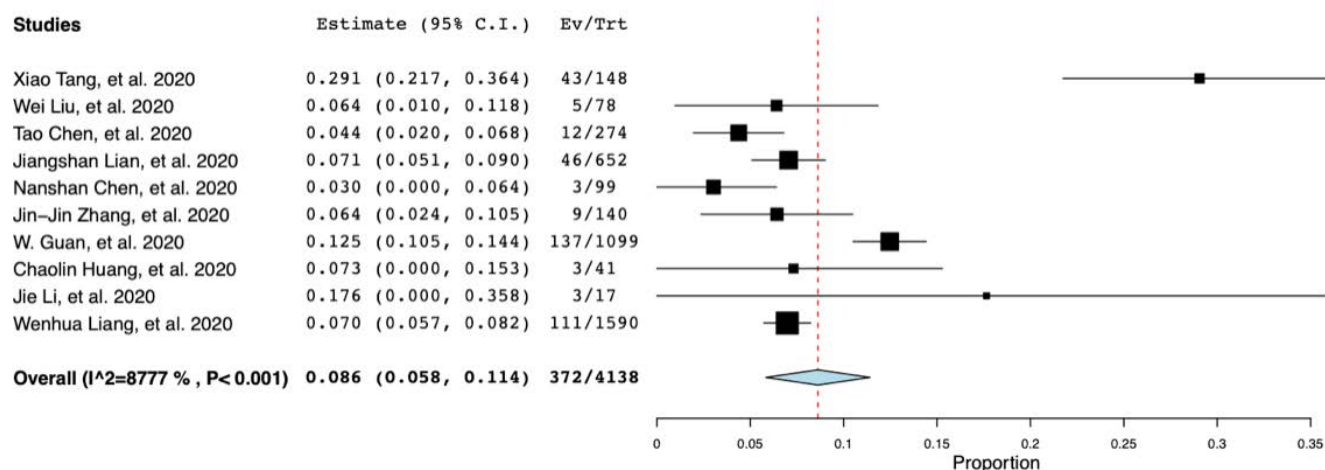


Figure 13. Forest plot of the smoking prevalence among COVID-19 patients using random effect model.

References

1. Wallace BC, Dahabreh IJ, Trikalinos TA, Lau J, Trow P, Schmid CH. Closing the gap between methodologists and end-users: R as a computational back-end. *J Stat Softw.* 2012; 49(5):1-15.
2. Hsieh WH, Cheng MY, Ho MW, Chou CH, Lin PC, Chi CY, et al. Featuring COVID-19 cases via screening symptomatic patients with epidemiologic link during flu season in a medical center of central Taiwan. *J Microbiol Immunol Infect.* 2020; In Press.
3. Cai Q, Huang D, Ou P, Yu H, Zhu Z, Xia Z, et al. COVID-19 in a designated infectious diseases hospital outside Hubei province, China. *Allergy.* 2020; In Press.
4. Cao J, Tu WJ, Cheng W, Yu L, Liu YK, Hu X, et al. Clinical features and short-term outcomes of 102 patients with corona virus disease 2019 in Wuhan, China. *Clin Infect Dis.* 2020; 2:ciaa243.
5. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet.* 2020; 395(10223):507-13.
6. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ.* 2020; 368(1):m1091.
7. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int.* 2020; 2538(20):30255-6.
8. Deng Y, Liu W, Liu K, Fang YY, Shang J, Zhou L, et al. Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 (COVID-19) in Wuhan, China: a retrospective study. *Chin Med J (Engl).* 2020; In Press.
9. Du Y, Tu L, Zhu P, Mu M, Wang R, Yang P, et al. Clinical features of 85 fatal cases of COVID-19 from Wuhan: a retrospective observational study. *Am J Respir Crit Care Med.* 2020; In Press.
10. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: a nationwide analysis. *Eur Respir J.* 2020; 26:2000547.
11. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* 2020; In Press.
12. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. *Diabetes Metab Res Rev.* 2020; 31(1):e3319.
13. Han YN, Feng ZW, Sun LN, Ren XX, Wang H, Xue YM, et al. A comparative-descriptive analysis of clinical characteristics in 2019-Coronavirus-infected children and adults. *J Med Virol.* 2020; In Press.
14. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020; 395(10223):497-506.
15. Jin X, Lian JS, Hu JH, Gao J, Zheng L, Zhang YM, et al. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. *Gut.* 2020; In Press.
16. Li J, Li S, Cai Y, Liu Q, Li X, Zeng Z, et al. Epidemiological and clinical characteristics of 17 hospitalized patients with 2019 novel coronavirus infections outside Wuhan, China. *MedRxiv.* 2020; In Press.
17. Lian J, Jin X, Hao S, Cai H, Zhang S, Zheng L, et al. Analysis of epidemiological and clinical features in older patients with corona virus disease 2019 (COVID-19) out of Wuhan. *Clin Infect Dis.* 2020; 25:ciaa242.
18. Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol.* 2020; 21(3):335-7.
19. Liu K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chin Med J (Engl).* 2020; In Press.
20. Liu W, Tao ZW, Lei W, Ming-Li Y, Kui L, Ling Z, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. *Chin Med J (Engl).* 2020; In Press.
21. Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. *Sci China Life Sci.* 2020; 63(3):364-74.
22. Tang X, Du R, Wang R, Cao T, Guan L, Yang C, et al. Comparison of hospitalized patients with acute respiratory distress syndrome caused by COVID-19 and H1N1. *Chest.* 2020; In Press.
23. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA.* 2020; In Press.
24. Wang L, He W, Yu X, Hu D, Bao M, Liu H, et al. Coronavirus disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up. *J Infect.* 2020; In Press.
25. Wang R, Liao C, He H, Hu C, Wei Z, Hong Z, et al. COVID-19 in hemodialysis patients: a report of 5 cases. *Am J Kidney Dis.* 2020; In Press.
26. Wang X, Fang J, Zhu Y, Chen L, Ding F, Zhou R, et al. Clinical characteristics of non-critically ill patients with novel coronavirus infection (COVID-19) in a Fangcang Hospital. *Clin Microbiol Infect.* 2020; In Press.
27. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical features of 69 cases with coronavirus disease 2019 in Wuhan, China. *Clin Infect Dis.* 2020; 16:ciaa272.
28. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019

- pneumonia in Wuhan, China. *JAMA Intern Med.* 2020; In Press.
29. Wu J, Liu J, Zhao X, Liu C, Wang W, Wang D, et al. Clinical characteristics of imported cases of COVID-19 in Jiangsu province: a multicenter descriptive study. *Clin Infect Dis.* 2020; 29:ciaa199.
30. Xie H, Zhao J, Lian N, Lin S, Xie Q, Zhuo H. Clinical characteristics of Non-ICU hospitalized patients with coronavirus disease 2019 and liver injury: a retrospective study. *Liver Int.* 2020; In Press.
31. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-CoV-2) outside of Wuhan, China: retrospective case series. *BMJ.* 2020; 368:m606.
32. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy.* 2020; In Press.
33. Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Ann Oncol.* 2020; In Press.
34. Zhang X, Cai H, Hu J, Lian J, Gu J, Zhang S, et al. Epidemiological, clinical characteristics of cases of SARS-CoV-2 infection with abnormal imaging findings. *Int J Infect Dis.* 2020; In Press.