

A systematic review and meta-analysis of geographic differences in comorbidities and associated severity and mortality among individuals with COVID-19

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Comorbidities

We collected status of the comorbidities (number of subjects without any comorbidity, number of subjects with one comorbidity, number of subjects with multiple comorbidities), the type of comorbidity that included hypertension (HTN), diabetes mellitus (DM), cardiovascular disease (CVD), obesity (OB), cerebrovascular accident (CVA), lung disease, cancer/malignancy, either of chronic or acute kidney disease (CKD) and liver related disease.

In our study, the HTN includes isolated hypertension, pulmonary hypertension, and high blood pressure. The CVD includes heart failure, atrial fibrillation, coronary heart disease, congestive heart failure, cardiac insufficiency, subvalvular aortic stenosis, myocardial infarction and other ischemic heart diseases. Cerebrovascular disease includes a history of all types of strokes and cerebrovascular accident. Chronic lung diseases involves chronic lung disease , asthma, chronic obstructive pulmonary disease , chronic respiratory disease, small airway obstruction syndrome, chronic lower respiratory disease, environmental lung disease, interstitial lung disease, chronic respiratory failure, diaphragm palsy, pulmonary vascular disease, tuberculosis, bronchitis, emphysema, and other chronic lung diseases. Cancer/malignancy contains solid malignant tumors, hematological malignant disease, and any other form of cancers or malignancies. CKD/ other renal disease consists of acute kidney injury, chronic kidney disease, end stage renal disease, and other renal diseases.

Primary outcomes

The primary outcomes in this study were COVID-19 severity and mortality. Any COVID-19 patients who had one of the following criteria: (a) admitted to the intensive care unit (ICU), (b) required mechanical ventilation support, (c) required mechanical shock/life support, (d) developed sepsis or septic shock, or (e) poor prognosis or labeled as critically ill by the attending physicians, were classified as severe COVID-19. Any study who reported death as the outcome for COVID-19 patients regardless of any underlying comorbidities was considered as mortality event due to COVID-19.

Comparing variables

The primary variables of interest for comparing outcomes were geographic location, age groups, and gender. The geographic location was grouped into Asia (China, India, Iran, Oman, South Korea), Europe (Denmark, France, Germany, Italy, Netherlands, Poland, Spain, Switzerland, Turkey, UK, and Italy), Latin America (Brazil and Mexico), South Africa, and USA. Based on the distribution of average age, the age was categorized into ≤ 50 years, 51 – 65 years, and > 65 years. Similarly, the percentage of the female population was divided into two groups as $\leq 50\%$: male dominant and $> 50\%$: female dominant.

Quality Assessment

Only seven out of the first eight items (criteria to assess the non-randomized and non-comparative studies) of MINORS were used in this study. Item number five (unbiased assessment of the study endpoint) was not used as the study endpoints were straight forward and the blind evaluation was not needed. Since the majority of the included studies were cross-sectional conducted on hospitalization of COVID-19 patients, we did not report any loss to follow up. A score from 0 to 2 was given for all the seven items according to whether the item related attributes were reported or not as well as adequate or not [0 (unreported), 1 (reported but inadequate) or 2 (reported and adequate)]. The total score assigned to each study was categorized for the quality assessment which follows: 0–2, very low quality; 3–6, low quality; 7–10, fair quality; and 11–14, high quality. In addition, we also evaluated publication bias for the primary outcomes within each comorbidity using Egger's test.

Supplementary Table 1

Characteristics and quality assessment score of included studies

Study	Country	No. of patients	No. of Female (%)	Age, mean \pm SD /median (IQR)	Comorbidity	Multiple morbidities	Severity	Mortality	Hospitalization status	Quality assessment
Wang, L et al. ¹	China	339	173 (51)	71 \pm 8	206	NA	NA	NA	Hospitalized	12
Cao, J et al. ²	China	102	49 (48)	54 (37, 67)	47	NA	NA	17	Hospitalized	13
Chen, T et al. ³	China	274	103 (37.6)	62 (44, 70)	133	NA	NA	113	Hospitalized	12
Deng, Y et al. ⁴	China	225	101 (44.9)	69 (62, 74)	127	NA	NA	109	Hospitalized	12
Yuan, M et al. ⁵	China	27	15 (55.6)	60 (47, 69)	13	NA	NA	10	Hospitalized	10
Wu, C et al. ⁶	China	201	73 (36.3)	51 (43, 60)	66	NA	NA	NA	Hospitalized	12
Li, K et al. ⁷	China	83	39 (47)	45.5 \pm 12.3	15	NA	25	NA	Hospitalized	12
Yang, X et al. ⁸	China	52	17 (32.7)	59.7 \pm 13.3	21	NA	NA	32	Hospitalized	11
Zhang, JJ et al. ⁹	China	140	69 (49.3)	57 (25, 87)	90	NA	58	NA	Hospitalized	13
Wang, D et al. ¹⁰	China	138	63 (45.7)	56 (42, 68)	64	NA	36	NA	Hospitalized	13
Huang, C et al. ¹¹	China	41	11 (26.8)	49 (41, 58)	13	NA	13	NA	Hospitalized	12
Wang, Z et al. ¹²	China	69	37 (53.6)	42 (35, 62)	25	NA	NA	NA	Hospitalized	12
Guan, WJ et al. ¹³	China	1590	686 (43.1)	48.9 \pm 16.3	399	52	254	50	Hospitalized	13
Chen, T et al. ¹⁴	China	55	21 (38.2)	74 (65, 91)	35	NA	NA	19	Hospitalized	11

Chen, Q et al. ¹⁵	China	145	66 (45.5)	47.5 ± 14.6	75	NA	43	NA	Hospitalized	12
Zhang, G et al. ¹⁶	China	221	113 (51.1)	55 (39, 67)	78	NA	55	NA	Hospitalized	12
Zhang, R et al. ¹⁷	China	120	77 (64.2)	45.4 ± 15.6	32	NA	30	NA	Hospitalized	12
Nikpouraghdam, M et al. ¹⁸	Iran	2964	1009 (34)	56 (46, 65)	323	NA	NA	239	Hospitalized	9
Li, Y et al. ¹⁹	China	54	20 (37)	61.8 ± 14.5	30	NA	54	NA	Hospitalized	11
Zhou, F et al. ²⁰	China	191	73 (38.2)	56 (46, 67)	91	NA	NA	54	Hospitalized	12
He, R et al. ²¹	China	204	125 (61.3)	49 (34, 62)	57	NA	NA	NA	Hospitalized	12
Yang, AP et al. ²²	China	93	37 (39.8)	46.4 ± 17.6	50	NA	24	NA	Hospitalized	11
Borobia, AM et al. ²³	Spain	2226	1152 (51.8)	61 (46, 78)	1747	NA	NA	460	Hospitalized	13
Zhang, C et al. ²⁴	China	80	47 (58.8)	51.2 ± 17.5	56	NA	NA	NA	Hospitalized	11
Zhao, J et al. ²⁵	China	29	15 (51.7)	56 (32, 66)	19	8	21	1	Hospitalized	11
Yao, Q et al. ²⁶	China	108	65 (60.2)	52 (37, 58)	25	NA	25	12	Hospitalized	13
Kayem, G et al. ²⁷	France	617	100 (100)	NA	NA	NA	NA	NA	Hospitalized	9
Tambe, MP et al. ²⁸	India	197	107 (54.3)	45.8 ± 17.3	93	NA	NA	58	Hospitalized	13
Yang, Q et al. ²⁹	China	136	70 (51.5)	56 (44, 64)	NA	NA	NA	NA	Hospitalized	12
Şenkal, N et al. ³⁰	Turkey	611	248 (40.6)	57 ± 15	NA	NA	NA	NA	Hospitalized	13
Shi, S et al. ³¹	China	416	211 (50.7)	64 (21, 95)	NA	NA	NA	NA	Hospitalized	12
Mani, VR et al. ³²	USA	184	73 (39.7)	64.7 ± 14.9	NA	NA	NA	NA	Hospitalized	12
Li, M et al. ³³	China	83	49 (59)	43 (32, 62)	42	NA	18	6	Hospitalized	11
Salacup, G et al. ³⁴	USA	242	119 (49.2)	66 (58, 76)	NA	NA	NA	NA	Hospitalized	12

Shi, S et al. ³⁵	China	671	322 (48)	63 (50, 72)	NA	NA	NA	NA	Hospitalized	13
Kalyanaraman Marcello, R. et al. ³⁶	USA	6248	2396 (38.3)	61 (50, 73)	NA	NA	NA	NA	Hospitalized	13
Israelsen, SB et al. ³⁷	Denmark	175	90 (51.4)	71 (55, 81)	125	NA	NA	NA	Hospitalized	12
Pellaud, C et al. ³⁸	Switzerland	196	77 (39.3)	70 (60, 80)	162	NA	49	NA	Hospitalized	12
Gregoriano, C et al. ³⁹	Switzerland	99	37 (37.4)	67 (56, 76)	NA	NA	NA	NA	Hospitalized	11
Argenziano, MG et al. ⁴⁰	USA	1000	65 (6.5)	55 (40, 69)	918	NA	386	NA	Hospitalized	13
Borghesi, A et al. ⁴¹	Italy	302	108 (35.8)	67 (57, 77)	NA	NA	NA	NA	Hospitalized	12
Toussie, D et al. ⁴²	USA	338	128 (37.9)	39 (31, 45)	NA	NA	NA	NA	Hospitalized	12
Ortiz-Brizuela, E et al. ⁴³	Mexico	140	55 (39.3)	78 (70, 88)	NA	NA	NA	NA	Hospitalized	13
Aggarwal, A et al. ⁴⁴	India	32	13 (40.6)	55 (46, 60)	22	11	24	NA	Hospitalized	11
Javanian, M et al. ⁴⁵	Iran	100	49 (49)	60.1 ± 13.9	50	NA	NA	NA	Hospitalized	12
Huang, Q et al. ⁴⁶	China	54	26 (48.1)	41 (31, 51)	18	NA	3	NA	Hospitalized	11
Pelayo, J et al. ⁴⁷	USA	223	50 (22.4)	65.9 ± 14.9	NA	NA	NA	NA	Hospitalized	12
Alkundi, A et al. ⁴⁸	UK	232	87 (37.5)	70.5 ± 15.7	NA	NA	NA	NA	Hospitalized	12
Qin, C et al. ⁴⁹	China	1875	930 (49.6)	63 (51, 70)	NA	NA	NA	NA	Hospitalized	13
Chen, Y et al. ⁵⁰	China	904	483 (53.4)	56(39, 67)	NA	NA	NA	NA	Hospitalized	13
Khamis, F et al. ⁵¹	Oman	63	10 (15.9)	48 ± 16	32	NA	NA	NA	Hospitalized	12
Gayam, V et al. ⁵²	USA	408	177 (43.4)	67 (56, 76)	NA	NA	NA	NA	Hospitalized	12
Shi, Q et al. ⁵³	China	306	156 (51)	64 (56, 72)	NA	NA	NA	NA	Hospitalized	12
Nowak, B et al. ⁵⁴	Poland	169	82 (48.5)	63.7 ± 19.6	137	NA	NA	NA	Hospitalized	12

Rottoli, M et al. ⁵⁵	Italy	482	163 (33·8)	66·2 ± 16·8	NA	NA	NA	NA	Hospitalized	12
Huang, Y et al. ⁵⁶	China	1255	589 (46·9)	64(52, 70)	791	NA	236	NA	Hospitalized	9
Li, T et al. ⁵⁷	China	312	125 (40·1)	69·2 ± 7·3	241	NA	105	NA	Hospitalized	12
Zhou, X et al. ⁵⁸	China	110	50 (45·5)	57·7 ± 14·2	NA	NA	NA	NA	Hospitalized	12
Wu, F et al. ⁵⁹	China	1048	457 (43·6)	63·5	382	NA	NA	NA	Hospitalized and non- hospitalized	12
Xu, J et al. ⁶⁰	China	239	96 (40·2)	62·5 ± 13·3	162	NA	NA	NA	Hospitalized	11
Buckner, FS et al. ⁶¹	USA	105	52 (49·5)	69(23, 97)	98	NA	51	NA	Hospitalized	12
Wan, S et al. ⁶²	China	135	63 (46·7)	47(36, 55)	43	NA	40	NA	Hospitalized	13
Li, J et al. ⁶³	China	94	43 (45·7)	58·7 ± 16	39	NA	NA	13	Hospitalized	10
Cao, M et al. ⁶⁴	China	198	97 (49)	50·1 ± 16·3	69	NA	19	NA	Hospitalized	12
Sun, L et al. ⁶⁵	China	55	24 (43·6)	44 (34, 56)	18	NA	15	NA	Hospitalized	11
Huang, R et al. ⁶⁶	China	202	86 (42·6)	44 (33, 54)	55	NA	23	NA	Hospitalized	12
Labenz, C et al. ⁶⁷	Germany	42	13 (31)	68 (55, 75)	NA	NA	NA	NA	Hospitalized	11
Zhang, JJ et al. ⁶⁸	China	289	135 (46·7)	57 (22, 88)	169	NA	127	49	Hospitalized	13
Pérez, FM et al. ⁶⁹	Spain	96	33 (34·4)	63 ± 17	60	NA	17	NA	Hospitalized	10
Wang, L et al. ⁷⁰	China	116	49 (42·2)	54 (38– 69)	51	NA	NA	7	Hospitalized	13
Wang, D et al. ⁷¹	China	143	70 (49)	58 (39– 67)	50	NA	71	NA	Hospitalized	12
Güner, R et al. ⁷²	Turkey	222	90 (73·8)	50·6 ± 16·5	92	NA	50	NA	Hospitalized	12
Zhou, Y et al. ⁷³	China	304	166 (54·6)	61·5 ± 13·3	NA	NA	NA	NA	Hospitalized	12
Feng, Y et al. ⁷⁴	China	476	205 (43·1)	53 (40, 64)	205	NA	124	NA	Hospitalized	12

Brill, SE et al. ⁷⁵	UK	450	178 (39.6)	72 (56, 83)	NA	NA	NA	NA	Hospitalized	12
Shah, P et al. ⁷⁶	USA	522	304 (58.2)	63 (50, 72)	NA	NA	NA	NA	Hospitalized	13
Lagi, F et al. ⁷⁷	Italy	84	29 (34.5)	62 (51, 72)	49	NA	NA	NA	Hospitalized	12
Yang, Q et al. ⁷⁸	China	226	113 (50)	49.9 ± 15.3	NA	NA	NA	NA	Hospitalized	12
Ji, W et al. ⁷⁹	South Korea	7341	4371 (59.5)	47.1 ± 19.0	NA	NA	NA	NA	Hospitalized and non- hospitalized	13
Lee, JY et al. ⁸⁰	South Korea	694	482 (69.5)	55.9 ± 17.3	NA	NA	NA	NA	Hospitalized	13
Shahriarirad, R et al. ⁸¹	Iran	113	42 (37.2)	53.7 ± 16.6	44	NA	NA	NA	Hospitalized	12
Baqui, P et al. ⁸²	Brazil	7371	3081 (41.8)	58.3 ± 16.4	NA	NA	NA	NA	Hospitalized	12
Asfahan, S et al. ⁸³	India	20812	NA	NA	5276	NA	NA	504	Hospitalized and non- hospitalized	12
Petrilli, CM et al. ⁸⁴	USA	2729	1057 (38.7)	63 (51, 74)	2176	NA	990	NA	Hospitalized	14
Mendy, A et al. ⁸⁵	USA	689	324 (47)	49.5 ± 33.1	NA	NA	NA	NA	Hospitalized	12
Masetti, C et al. ⁸⁶	Italy	229	81 (35.4)	60.7 ± 14.2	124	NA	NA	33	Hospitalized	12
Davies, MA et al. ⁸⁷	South Africa	2978	1848 (62.1)	NA	NA	NA	NA	NA	Hospitalized	13
Huang, J et al. ⁸⁸	China	299	139 (46.5)	53.4 ± 16.7	99	NA	NA	16	Hospitalized	12
Kammar-Garcia, A et al. ⁸⁹	Mexico	13842	5853 (42.3)	46.6 ± 15.6	6270	1282	4098	1305	Hospitalized	12
Ye, C et al. ⁹⁰	China	856	417 (48.7)	46 (35-56)	242	63	154	1	Hospitalized	13
Bonetti, G et al. ⁹¹	Italy	144	49 (34)	70	92	NA	NA	70	Hospitalized	12
Ponziani, FR et al. ⁹²	Italy	515	192 (37.3)	65 (53, 77)	350	32	77	NA	Hospitalized	13
Klang, E et al. ⁹³	USA	3406	1445 (42.4)	65.94	3126	NA	NA	1136	Hospitalized	13

Sousa, GJB et al. ⁹⁴	Brazil	2070	1053 (50.9)	44 (34, 59)	NA	NA	NA	NA	Hospitalized	13
Brouns, SH et al. ⁹⁵	Netherlands	101	68 (67.3)	85.0 ± 8.1	NA	NA	NA	NA	Hospitalized	11
Lorente-Ros, A et al. ⁹⁶	Spain	707	264 (37.3)	66.6 ± 15.7	NA	NA	NA	NA	Hospitalized	14
Tatum, D et al. ⁹⁷	USA	125	68 (54.4)	58.7 ± 14.8	120	NA	NA	23	Hospitalized	13
Sabri, A et al. ⁹⁸	Iran	63	NA	54.1 ± 15.5	37	NA	NA	NA	Hospitalized	11
Cai, Q et al. ⁹⁹	China	383	200 (52.2)	49.2	NA	NA	NA	NA	Hospitalized	12
Pettit, NN et al. ¹⁰⁰	USA	238	125 (52.5)	58.5 ± 17	NA	NA	NA	NA	Hospitalized	12
Ji, D et al. ¹⁰¹	China	208	91 (43.8)	44.0 ± 16.3	45	NA	40	NA	Hospitalized	12
Gidari, A et al. ¹⁰²	Italy	68	23 (33.8)	64 ± 14	NA	NA	NA	NA	Hospitalized	11
Du, RH et al. ¹⁰³	China	179	82 (45.8)	57.6 ± 13.7	NA	NA	NA	NA	Hospitalized	13
Sarin, SK et al. ¹⁰⁴	Asia	228	96 (42.1)	51.1	NA	NA	NA	NA	Hospitalized	12
Ebinger, JE et al. ¹⁰⁵	USA	442	186 (42.1)	52.7 ± 19.6	NA	NA	NA	NA	Hospitalized	12
Pagnesi, M et al. ¹⁰⁶	Italy	200	69 (34.5)	62 (55, 74)	NA	NA	NA	NA	Hospitalized	14
Rastad, H et al. ¹⁰⁷	Iran	2957	1368 (46.3)	54.8 ± 16.9	749	NA	NA	301	Hospitalized	13
van Gerwen, M et al. ¹⁰⁸	USA	3703	1654 (44.7)	56.8 ± 18.2	2398	322	525	616	Hospitalized	13
Zhou, Y et al. ¹⁰⁹	China	17	11 (64.7)	41.8	5	NA	5	NA	Hospitalized	11
Grasselli, G et al. ¹¹⁰	Italy	3988	800 (20.1)	63 (56, 69)	2686	NA	NA	1926	Hospitalized	13
Xu, PP et al. ¹¹¹	China	703	321 (45.7)	46.1 ± 15.2	201	24	55	33	Hospitalized	13
Cen, Y et al. ¹¹²	China	1007	514 (51)	61 (49 , 68)	364	NA	222	43	Hospitalized	14
Soares, RCM et al. ¹¹³	Brazil	1152	494 (42.9)	NA	526	NA	NA	456	Hospitalized	10
Li, X et al. ¹¹⁴	China	548	269 (49.1)	60 (48, 69)	NA	NA	NA	NA	Hospitalized	14

Gao, S et al. ¹¹⁵	China	210	109 (51.9)	71 (67, 77)	159	NA	NA	35	Hospitalized	12
Urrea, JM et al. ¹¹⁶	Spain	172	68 (39.5)	59.1	NA	NA	NA	NA	Hospitalized	12
Rivera-Izquierdo, M et al. ¹¹⁷	Spain	238	107 (45)	64.7 ± 15.4	135	NA	NA	61	Hospitalized	12
Deng, Q et al. ¹¹⁸	China	112	55 (49.1)	65 (49, 71)	58	NA	NA	14	Hospitalized	12
Kim, DW et al. ¹¹⁹	South Korea	9148	5592 (61.0)	NA	NA	NA	NA	NA	Hospitalized and non-hospitalized	13
Hewitt, J et al. ¹²⁰	UK & Italy	1564	661 (42.3)	74 (61, 83)	NA	NA	NA	NA	Hospitalized	14

NA not available.

Supplementary Table 2

Quality appraisal of included studies according to MINORS assessment

Study	Clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoints appropriate to the aim of the study	Unbiased assessment of the study endpoint	Follow-up period appropriate to the aim of the study	Loss to follow up less than 5%	Prospective Calculation of the study size
Wang, L et al. ¹	2	2	1	2	0	2	2	1
Cao, J et al. ²	2	2	2	2	0	2	2	1
Chen, T et al. ³	2	2	1	2	0	2	2	1
Deng, Y et al. ⁴	2	2	1	2	0	2	2	1
Yuan, M et al. ⁵	2	2	1	2	0	2	1	0
Wu, C et al. ⁶	2	2	1	2	0	2	2	1
Li, K et al. ⁷	2	2	1	2	0	2	2	1
Yang, X et al. ⁸	2	2	1	2	0	2	2	0
Zhang, JJ et al. ⁹	2	2	2	2	0	2	2	1
Wang, D et al. ¹⁰	2	2	2	2	0	2	2	1
Huang, C et al. ¹¹	2	2	2	2	0	2	2	0
Wang, Z et al. ¹²	2	2	2	2	0	2	2	0
Guan, WJ et al. ¹³	2	2	1	2	0	2	2	2

Chen, T et al. ¹⁴	2	2	1	2	0	2	2	0
Chen, Q et al. ¹⁵	2	2	1	2	0	2	2	1
Zhang, G et al. ¹⁶	2	2	1	2	0	2	2	1
Zhang, R et al. ¹⁷	2	2	1	2	0	2	2	1
Nikpouraghdam, M et al. ¹⁸	2	2	1	2	0	0	0	2
Li, Y et al. ¹⁹	2	2	1	2	0	2	2	0
Zhou, F et al. ²⁰	2	2	1	2	0	2	2	1
He, R et al. ³⁶	2	2	1	2	0	2	2	1
Yang, AP et al. ²²	2	2	1	2	0	2	2	0
Borobia, AM et al. ²³	2	2	2	2	0	1	2	2
Zhang, C et al. ²⁴	2	2	1	2	0	2	2	0
Zhao, J et al. ²⁵	2	2	1	2	0	2	2	0
Yao, Q et al. ²⁶	2	2	1	2	0	2	2	2
Kayem, G et al. ²⁷	2	2	1	2	0	0	0	2
Tambe, MP et al. ²⁸	2	2	2	2	0	2	2	1
Yang, Q et al. ²⁹	2	2	1	2	0	2	2	1
Şenkal, N et al. ³⁰	2	2	1	2	0	2	2	2
Shi, S et al. ³¹	2	2	1	2	0	2	2	1
Mani, VR et al. ³²	2	2	1	2	0	2	2	1
Li, M et al. ³³	2	2	1	2	0	2	2	0
Salacup, G et al. ³⁴	2	2	1	2	0	2	2	1
Shi, S et al. ³⁵	2	2	1	2	0	2	2	2
Kalyanaraman Marcello, R. et al. ³⁶	2	2	1	2	0	2	2	2
Israelsen, SB et al. ³⁷	2	2	1	2	0	2	2	1
Pellaud, C et al. ³⁸	2	2	1	2	0	2	2	1
Gregoriano, C et al. ³⁹	2	2	1	2	0	2	2	0
Argenziano, MG et al. ⁴⁰	2	2	1	2	0	2	2	2
Borghesi, A et al. ⁴¹	2	2	1	2	0	2	2	1
Toussie, D et al. ⁴²	2	2	1	2	0	2	2	1

Ortiz-Brizuela, E et al. ⁴³	2	2	2	2	0	2	2	1
Aggarwal, A et al. ⁴⁴	2	2	1	2	0	2	2	0
Javanian, M et al. ⁴⁵	2	2	1	2	0	2	2	1
Huang, Q et al. ⁴⁶	2	2	1	2	0	2	2	0
Pelayo, J et al. ⁴⁷	2	2	1	2	0	2	2	1
Alkundi, A et al. ⁴⁸	2	2	1	2	0	2	2	1
Qin, C et al. ⁴⁹	2	2	1	2	0	2	2	2
Chen, Y et al. ⁵⁰	2	2	1	2	0	2	2	2
Khamis, F et al. ⁵¹	2	2	2	2	0	2	2	0
Gayam, V et al. ⁵²	2	2	1	2	0	2	2	1
Shi, Q et al. ⁵³	2	2	1	2	0	2	2	1
Nowak, B et al. ⁵⁴	2	2	1	2	0	2	2	1
Rottoli, M et al. ⁵⁵	2	2	1	2	0	2	2	1
Huang, Y et al. ⁵⁶	1	2	1	1	0	2	2	0
Li, T et al. ⁵⁷	2	2	1	2	0	2	2	1
Zhou, X et al. ⁵⁸	2	2	1	2	0	2	2	1
Wu, F et al. ⁵⁹	1	2	1	2	0	2	2	2
Xu, J et al. ⁶⁰	2	2	1	2	0	2	2	1
Buckner, FS et al. ⁶¹	2	2	1	2	0	2	2	1
Wan, S et al. ⁶²	2	2	2	2	0	2	2	1
Li, J et al. ⁶³	2	2	1	1	0	2	2	0
Cao, M et al. ⁶⁴	2	2	1	2	0	2	2	1
Sun, L et al. ⁶⁵	2	2	1	2	0	2	2	0
Huang, R et al. ⁶⁶	2	2	1	2	0	2	2	1
Labenz, C et al. ⁶⁷	2	2	1	2	0	2	2	0
Zhang, JJ et al. ⁶⁸	2	2	2	2	0	2	2	1
Pérez, FM et al. ⁶⁹	2	2	0	2	0	2	2	0
Wang, L et al. ⁷⁰	2	2	2	2	0	2	2	1
Wang, D et al. ⁷¹	2	2	1	2	0	2	2	1
Güner, R et al. ⁷²	2	2	1	2	0	2	2	1

Zhou, Y et al. ⁷⁸	2	2	1	2	0	2	2	1
Feng, Y et al. ⁷⁴	2	2	1	2	0	2	2	1
Brill, SE et al. ⁷⁵	2	2	1	2	0	2	2	1
Shah, P et al. ⁸¹	2	2	1	2	0	2	2	2
Lagi, F et al. ⁷⁷	2	2	1	2	0	2	2	1
Yang, Q et al. ⁷⁸	2	2	1	2	0	2	2	1
Ji, W et al. ⁷⁹	2	2	1	2	0	2	2	2
Lee, JY et al. ⁸⁰	2	2	1	2	0	2	2	2
Shahriarirad, R et al. ⁸¹	2	2	1	2	0	2	2	1
Baqui, P et al. ⁸²	2	2	0	2	0	2	2	2
Asfahan, S et al. ⁸³	2	1	1	2	0	2	2	2
Petrilli, CM et al. ⁸⁴	2	2	2	2	0	2	2	2
Mendy, A et al. ⁸⁵	2	2	0	2	0	2	2	2
Masetti, C et al. ⁸⁶	2	2	1	2	0	2	2	1
Davies, MA et al. ⁸⁷	2	2	1	2	0	2	2	2
Huang, J et al. ⁸⁸	2	2	1	2	0	2	2	1
Kammar-Garcia, A et al. ⁸⁹	2	2	0	2	0	2	2	2
Ye, C et al. ⁹⁰	2	2	1	2	0	2	2	2
Bonetti, G et al. ⁹¹	2	2	1	2	0	2	2	1
Ponziani, FR et al. ⁹²	2	2	1	2	0	2	2	2
Klang, E et al. ⁹³	2	2	1	2	0	2	2	2
Sousa, GJB et al. ⁹⁴	2	2	1	2	0	2	2	2
Brouns, SH et al. ⁹⁵	2	2	0	2	0	2	2	1
Lorente-Ros, A et al. ⁹⁶	2	2	2	2	0	2	2	2
Tatum, D et al. ⁹⁷	2	2	2	2	0	2	2	1
Sabri, A et al. ⁹⁸	2	2	1	2	0	2	2	0
Cai, Q et al. ⁹⁹	2	2	1	2	0	2	2	1
Pettit, NN et al. ¹⁰⁰	2	2	1	2	0	2	2	1
Ji, D et al. ¹⁰¹	2	2	1	2	0	2	2	1

Gidari, A et al. ¹⁰²	2	2	1	2	0	2	2	0
Du, RH et al. ¹⁰³	2	2	2	2	0	2	2	1
Sarin, SK et al. ¹⁰⁴	2	2	1	2	0	2	2	1
Ebinger, JE et al. ¹⁰⁵	2	2	1	2	0	2	2	1
Pagnesi, M et al. ¹⁰⁶	2	2	2	2	0	2	2	2
Rastad, H et al. ¹⁰⁷	2	2	1	2	0	2	2	2
van Gerwen, M et al. ¹⁰⁸	2	2	1	2	0	2	2	2
Zhou, Y et al. ¹⁰⁹	2	2	1	2	0	2	2	0
Grasselli, G et al. ¹¹⁰	2	2	1	2	0	2	2	2
Xu, PP et al. ¹¹¹	2	2	1	2	0	2	2	2
Cen, Y et al. ¹¹²	2	2	2	2	0	2	2	2
Soares, RCM et al. ¹¹³	2	2	0	2	0	0	2	2
Li, X et al. ¹¹⁴	2	2	2	2	0	2	2	2
Gao, S et al. ¹¹⁵	2	2	1	2	0	2	2	1
Urrea, JM et al. ¹¹⁶	2	2	1	2	0	2	2	1
Rivera-Izquierdo, M et al. ¹¹⁷	2	2	1	2	0	2	2	1
Deng, Q et al. ¹¹⁸	2	2	1	2	0	2	2	1
Kim, DW et al. ¹¹⁹	2	2	1	2	0	2	2	2
Hewitt, J et al. ¹²⁰	2	2	2	2	0	2	2	2

Supplementary Table 3

Assessment of publication bias and small study effect for primary outcomes

	Comorbidities		Severity		Mortality	
	Beta (95% CI)	p-value	Beta (95% CI)	p-value	Beta (95% CI)	p-value
One comorbidity	1.83 (-0.30, 3.97)	0.09	0.48 (-0.55, 1.51)	0.35	1.07 (-1.06, 3.20)	0.32
No comorbidity	-1.87 (-4.07, 0.33)	0.09	0.22 (-0.54, 0.97)	0.56	1.17 (-0.04, 2.39)	0.06
Multiple comorbidities	0.29 (-8.61, 9.20)	0.94	0.06 (-4.88, 5.00)	0.98	-1.36 (-3.61, 0.88)	0.18
HTN	1.62 (0.06, 3.17)	0.041	0.78 (0.19, 1.37)	0.011	0.65 (-0.85, 2.14)	0.39
DM	0.71 (-0.39, 1.81)	0.20	0.80 (0.34, 1.27)	0.001	-0.16 (-1.4, 1.09)	0.80
CVD	0.19 (-1.27, 1.64)	0.8	1.00 (0.53, 1.46)	< 0.001	-0.19 (-1.28, 0.9)	0.73
Obesity	4.68 (0.34, 9.02)	0.036	0.71 (-1.24, 2.66)	0.45	0.47 (-2.31, 3.25)	0.71
CVA	-0.13 (-0.52, 0.26)	0.50	0.69 (0.18, 1.20)	0.011	0.75 (-0.16, 1.65)	0.10
Lung disease	0.22 (-0.54, 0.99)	0.56	0.85 (0.47, 1.23)	< 0.001	0.52 (-0.33, 1.36)	0.22
Cancer/malignancy	0.48 (-0.18, 1.13)	0.15	0.42 (-0.07, 0.90)	0.09	-0.12 (-0.82, 0.58)	0.73
CKD/other renal disease	0.38 (-0.72, 1.48)	0.49	0.51 (-0.24, 1.26)	0.17	0.28 (-0.83, 1.40)	0.61
Liver disease	0.30 (-0.77, 1.37)	0.57	0.34 (0.04, 0.64)	0.026	0.67 (-0.43, 1.77)	0.22

Beta regression coefficient, CI confidence interval, HTN Hypertension, DM Diabetes mellitus, CVD Cardiovascular disease, CVA Cerebrovascular accident, CKD Chronic kidney disease.

Supplementary Table 4

Demographic characteristics by geographic regions

Demographic characteristics	Overall	Asia	Europe	Latin America	USA	South Africa
Number of studies	120	72	26	5	16	1
Number of subjects (%)	125446	63462 (50.6%)	13929 (11.1%)	24575 (19.6%)	20602 (16.4%)	2978 (2.4%)
Age; mean (95% CI)	56.2 (52.6, 59.8)	54.4 (50.8, 58.0)	64.8 (61.9, 67.8)	50.2 (42.6, 57.9)	60.4 (57.7, 63.1)	NA
Gender [§] Total Female Meta-proportion of female; (95% CI)	104670 48446 (46.3) 0.45 (0.43, 0.47)	42587 22056 (51.8) 0.47 (0.45, 0.50)	13929 5386 (38.7) 0.39 (0.34, 0.45)	24575 10536 (42.9) 0.44 (0.41, 0.48)	20601 8620 (41.8) 0.45 (0.42, 0.47)	2978 1848 (62.0) 0.62 (0.60, 0.64)

NA Not available, CI confidence interval.

[§]Gender information was not available for 20875 patients from Asian study and 1 patient from a USA study, meta-proportion for female gender was calculated after excluding a European study that included only pregnant women.

Supplementary Table 5

Comparison of proportion estimates of underlying medical diseases and associated COVID-19 severity and mortality between geographic regions

	Asia vs. Europe	Asia vs. Latin America	Asia vs. USA	Europe vs. Latin America	Europe vs. USA	Latin America vs. USA
	p-value	p-value	p-value	p-value	p-value	p-value
Comorbidities						

One comorbidity	<0.001	0.768	<0.001	0.055	0.009	0.001
Multiple comorbidities	0.273	0.837	0.056	0.309	0.677	0.124
HTN	<0.001	0.659	<0.001	0.583	0.045	0.235
DM	0.010	0.239	<0.001	0.761	<0.001	0.006
CVD	<0.001	0.027	<0.001	0.846	0.113	0.221
Obesity	0.257	0.640	0.640	0.287	0.006	0.001
CVA	0.852	NA	0.119	0.657	0.852	0.657
Lung disease	0.002	0.936	<0.001	0.047	0.036	0.001
Cancer/malignancy	<0.001	NA	<0.001	NA	0.417	NA
CKD/other renal disease	0.003	0.814	<0.001	0.067	0.064	0.001
Liver disease	0.673	0.601	0.580	0.950	0.972	0.911
Severity						
Total	0.526	0.897	0.046	0.629	0.052	0.328
One comorbidity	0.021	0.914	0.296	0.209	0.235	0.649
No comorbidity	0.250	0.611	0.463	0.640	0.598	0.985
Multiple comorbidities	0.049	0.519	0.027	0.017	0.579	0.002
HTN	0.027	0.251	0.071	0.710	0.574	0.563
DM	0.037	0.711	0.022	0.761	0.914	0.787
CVD	0.158	0.447	0.033	0.615	0.522	0.711

Obesity	0.447	0.816	0.582	0.730	0.665	0.878
CVA	0.531	NA	0.026	0.713	0.531	0.713
Lung disease	0.216	0.661	0.035	0.830	0.590	0.905
Cancer/malignancy	0.535	NA	0.715	NA	0.751	0.751
CKD/other renal disease	0.027	NA	<0.001	NA	0.583	0.583
Liver disease	0.660	0.660	0.442	1.00	0.824	0.824
Mortality						
Total	0.045	0.436	0.427	0.546	0.450	0.943
One comorbidity	0.096	0.558	0.866	0.576	0.293	0.721
No comorbidity	0.112	0.221	0.943	0.957	0.313	0.389
Multiple comorbidities	0.139	NA	0.065	0.273	NA	0.273
HTN	0.120	NA	0.888	NA	0.245	0.245
DM	0.001	<0.001	0.340	0.131	0.025	0.001
CVD	0.033	0.011	0.145	0.299	0.616	0.170
Obesity	0.072	NA	0.003	0.072	0.160	0.003
CVA	NA	NA	0.672	NA	NA	0.672
Lung disease	0.218	0.060	0.465	0.360	0.075	0.023
Cancer/malignancy	0.035	NA	0.508	0.096	0.035	0.096
CKD/other renal disease	0.011	<0.001	0.499	0.118	0.020	0.001

Liver disease	0.166	0.034	0.829	0.500	0.284	0.080
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NA Not available, *HTN* Hypertension, *DM* Diabetes mellitus, *CVD* Cardiovascular disease, *CVA* Cerebrovascular accident, *CKD* Chronic kidney disease.

Supplementary Table 6

Comparison of proportion estimates of underlying medical diseases and associated COVID-19 severity and mortality between age groups

	Age ≤ 50 years Vs 50 years < Age ≤ 65 years	Age ≤ 50 years Vs Age > 65 years	50 years < Age ≤ 65 years vs. Age > 65 years
	p-value	p-value	p-value
Comorbidities			
One comorbidity	<0.001	<0.001	0.001
Multiple comorbidities	0.001	0.022	0.278
HTN	<0.001	<0.001	0.001
DM	0.023	<0.001	0.008
CVD	0.666	<0.001	<0.001
Obesity	0.094	0.286	0.562
CVA	0.405	0.157	0.070
Lung disease	0.257	0.018	0.076
Cancer/malignancy	0.047	0.004	0.068
CKD/other renal disease	0.273	<0.001	<0.001
Liver disease	0.474	0.935	0.542
Severity			

One comorbidity	0.886	0.866	0.790
No comorbidity	0.127	0.482	0.884
Multiple comorbidities	0.001	NA	NA
HTN	0.981	0.646	0.610
DM	0.850	0.511	0.557
CVD	0.423	0.764	0.712
Obesity	0.991	0.508	0.471
CVA	0.442	0.893	0.667
Lung disease	0.362	0.631	0.927
Cancer/malignancy	0.486	0.615	0.331
CKD/other renal disease	0.122	0.161	0.799
Liver disease	0.977	0.629	0.625
Mortality			
One comorbidity	0.153	0.010	0.064
No comorbidity	0.110	0.054	0.311
Multiple comorbidities	0.205	0.558	0.885
HTN	0.635	0.447	0.610
DM	0.794	0.823	0.479
CVD	0.580	0.246	0.297

Obesity	0.615	0.743	0.442
CVA	0.416	0.199	0.296
Lung disease	0.744	0.716	0.187
Cancer/malignancy	0.319	0.254	0.651
CKD/other renal disease	0.534	0.319	0.447
Liver disease	0.318	0.503	0.957

NA Not available, *HTN* Hypertension, *DM* Diabetes mellitus, *CVD* Cardiovascular disease, *CVA* Cerebrovascular accident, *CKD* Chronic kidney disease.

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