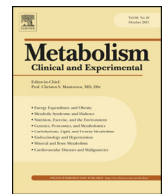




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Correspondence

An updated meta-analysis on the relationship between obesity and COVID-19 mortality


Keywords:

COVID-19
Obesity
Meta-analysis
Adjusted effect size
Mortality

Recently, Huang et al. published an article titled “Obesity in patients with COVID-19: a systematic review and meta-analysis” in the journal of *Metabolism* [1]. The authors reported that coronavirus disease 2019 (COVID-19) patients with obesity were at high risk for death based on seven studies with multivariate analyses (odds ratio = 1.49, 95% confidence interval (CI): 1.20–1.85) [1]. This study was greatly interesting, but had limited sample sizes. In addition, several eligible studies [2–5] published before August 10, 2020 were not included. To our knowledge, a considerable number of emerging studies on this topic have been reported since Huang et al.'s study was published online. Therefore, the association between obesity and COVID-19 mortality is needed to be clarified by a meta-analysis based on updated data.

This meta-analysis was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [6]. We performed a comprehensive literature search in PubMed, Web of Science and EMBASE to identify all potential studies published between January 1, 2020 and June 7, 2021. The keywords were used: “COVID-19” or “SARS-CoV-2” or “coronavirus disease 2019” and “obesity” or “obese” or “body mass index” and “mortality” or “death” or “deceased”. We included studies investigating the association between obesity and COVID-19 mortality by multivariable analyses. Preprints, reviews, duplicates, errata, comments, and studies with crude effect sizes were excluded.

The statistical analyses were done using R software (Version 3.6.3) [7]. The pooled effect size and 95% CI were estimated by a random-effects model [8,9]. I^2 statistic and Cochran's Q test were applied to evaluate statistical heterogeneity across studies [10–12]. Begg's test was used to assess publication bias [13]. Leave-one-out sensitivity analysis was performed to assess the stability of the results [14,15]. $P < 0.05$ was considered statistically significant.

The main characteristics of the included studies are summarized in Table 1. A total of 138 studies with 3,863,516 cases were included. Our results demonstrated that COVID-19 patients with obesity had a significantly higher risk for mortality compared to those without obesity (pooled effect size = 1.29, 95% CI: 1.24–1.35; Fig. 1A). Sensitivity analysis revealed that our results were stable and robust (Fig. 1B). Consistent findings were observed in the subgroup analyses by sample size, age, male percentage and setting. Begg's test indicated that there was no potential publication bias ($P = 0.331$).

Several limitations existed in this meta-analysis. First, most of the included studies were from Americas and Europe, thus the findings

should be explained with caution in other regions (such as Asia and Africa). Second, although the pooled effect size was estimated on the basis of adjusted effect sizes, the adjusted factors are not fully consistent among the included studies. Third, most of the enrolled studies are retrospective studies, thus further meta-analysis with more prospective studies should be performed to verify our results.

In conclusion, this updated meta-analysis demonstrated that obesity was significantly associated with an increased risk for COVID-19 mortality. We hope that the updated findings will contribute to more accurate elaboration and substantiation of the data reported by Huang et al. [1].

Funding

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CRediT authorship contribution statement

Yadong Wang, Haiyan Yang and Huifen Feng conceptualized the study. Hongjie Hou, Jie Xu and Yadong Wang performed literature search and data extraction. Jie Xu, Ying Wang, Huifen Feng and Haiyan Yang analyzed the data. Yadong Wang wrote the manuscript. All the authors approved the final manuscript.

Declaration of competing interest

All authors report that they have no potential conflicts of interest.

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Table 1
General information of the included studies.

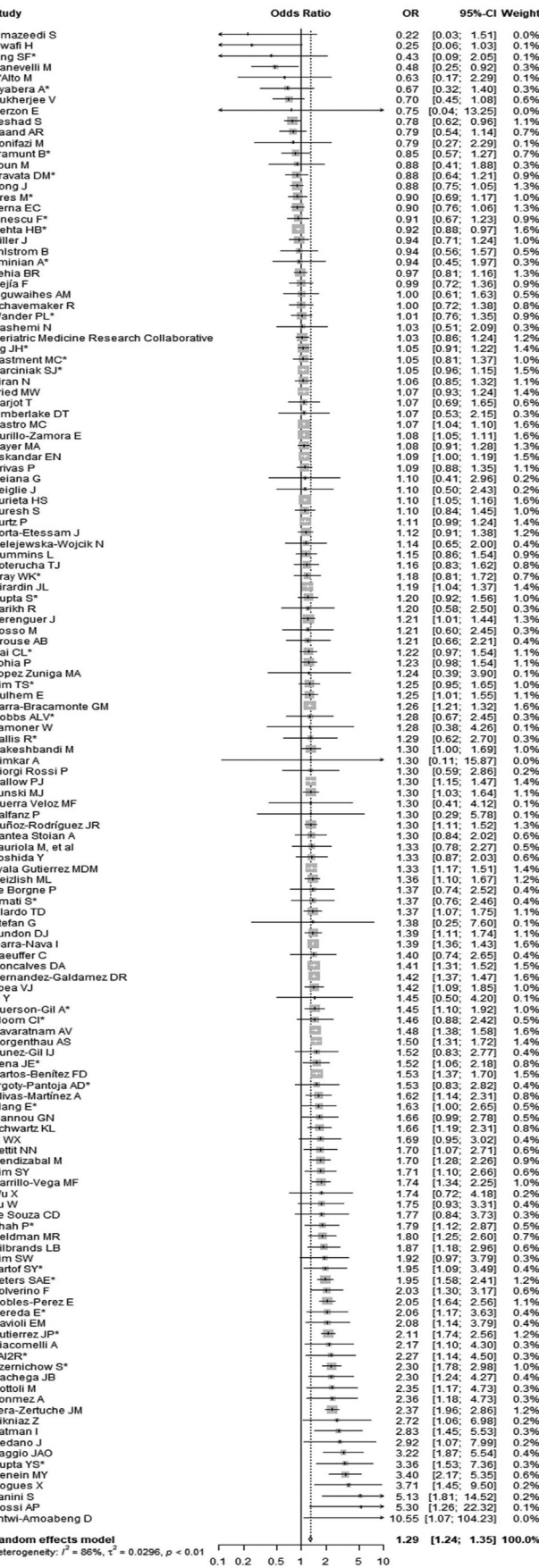
Author	Cases	Obesity (%)	Age (years)	Male (%)	Study type	Country/region	Definition of obesity	Effect size (95% CI)
Klang E*	3406	1231 (36.1)	66 ± 12.2	75.6	Retrospective study	USA	BMI ≥ 30	1.63 (1.0–2.65)
Rottoli M	482	104 (21.6)	66.2 ± 16.8	62.7	Retrospective study	Italy	BMI ≥ 30	2.35 (1.17–4.75)
Antwi-Amoabeng D	172	89 (51.7)	53 (33.5–68)	55.8	Retrospective study	USA	BMI ≥ 30	10.55 (1.07–104.45)
Deiana G	1223	NA	NA	40.8	Retrospective study	Italy	BMI ≥ 30	1.1 (0.4–2.9)
Hashemi N	363	NA	63.34 ± 16.5	55.4	Retrospective study	USA	BMI ≥ 30	1.03 (0.51–2.09)
Pettit NN	238	146 (61.3)	58.5 ± 17	47.5	Retrospective study	USA	BMI ≥ 30	1.7 (1.1–2.8)
Shah P*	522	347 (66.5)	63 (50–72)	41.8	Retrospective study	USA	BMI ≥ 30	1.79 (1.12–2.88)
Aeshad S	2541	1250 (52.3)	63.7 ± 16.5	51.1	Retrospective study	USA	BMI ≥ 30	0.775 (0.624–0.962)
Gupta S*	2215	NA	60.5 ± 14.5	64.8	Multicenter cohort study	USA	BMI ≥ 30	1.2 (0.92–1.56)
Nakeshbandi M	504	215 (43)	68 ± 15	52	Retrospective study	USA	BMI ≥ 30	1.3 (1–1.7)
Hernandez-Galdamez DR	211,003	41,344 (19.59)	45.7 ± 16.3	54.71	Cross-sectional study	Mexico	BMI ≥ 30	1.42 (1.37–1.47)
Berenguer J	4035	497 (13.8)	70 (56–80)	61	Retrospective study	Spain	BMI ≥ 30	1.21 (1.01–1.44)
Almazzeedi S	1096	44 (4)	47 ± 31.11	81	Retrospective study	Kuwait	BMI ≥ 30	0.223 (0.033–1.513)
Posso M	834	55 (6.6)	78.2 ± 9.8	46.5	Retrospective study	Spain	BMI ≥ 30	1.21 (0.6–2.45)
Tartof SY*	6916	3171 (45.9)	49.1 ± 16.6	45	Retrospective study	USA	BMI ≥ 30	1.95 (1.09–3.50)
Parra-Bracamonte GM	142,690	28,432 (20)	45 (34.0–57.0)	56	Dataset	Mexico	BMI ≥ 30	1.264 (1.207–1.323)
Yehia BR	7139	2044 (28.6)	68 (56–79)	51.3	Retrospective study	USA	Obesity	0.97 (0.81–1.16)
Ng JH*	10,482	NA	65.38 ± 15.2	59.5	Retrospective study	USA	BMI ≥ 30	1.05 (0.91–1.22)
Czernichow S*	5795	1264 (21.8)	59.7	65.4	Prospective study	France	BMI ≥ 30	2.3 (1.78–2.98)
Nimkar A	327	113 (34.6)	71 (59–82)	55.7	Retrospective study	USA	BMI ≥ 30	1.3 (0.1–14.9)
Biran N	764	276 (36.1)	65.29 ± 14	65.7	Retrospective study	USA	BMI ≥ 30	1.06 (0.85–1.32)
Giorgi Rossi P	2653	65 (2.7)	63.2	50.1	Prospective study	Italy	Obesity	1.3 (0.6–2.9)
Seiglie J	450	191 (42.4)	63.3	57.6	NA	USA	Obesity	1.1 (0.5–2.45)
Fried MW	11,721	1891 (16.1)	62	53.4	Retrospective study	USA	Obesity	1.07 (0.93–1.24)
Mukherjee V	137	104 (77.6)	59.0 (51.0–70.0)	72.3	Retrospective study	USA	BMI ≥ 30	0.7 (0.5–1.2)
Carrillo-Vega MF	9946	2053 (20.82)	48.15 ± 14.35	57.84	Dataset	Mexico	Obesity	1.74 (1.35–2.26)
Morgenthau AS	7337	1993 (27.2)	61.5 ± 18.85	55.2	Retrospective study	USA	Obesity	1.5 (1.3–1.7)
Lauriola M	377	30 (8.0)	71.8 ± 13.4	65.8	Retrospective study	Italy	Obesity	1.329 (0.779–2.268)
Miller J	3633	1758 (51.8)	58.4 ± 18.1	46.2	Retrospective study	USA	Obesity	0.94 (0.71–1.24)
Ioannou GN	10,131	78 (0.8)	63.6 ± 16.2	91	Longitudinal cohort study	USA	Obesity	1.66 (0.99–2.77)
Peters SAE*	NA	NA	NA	NA	Prospective study	UK	Obesity	1.95 (1.58–2.41)
Nachega JB	766	39 (5.1)	46 (34–58)	65.6	Retrospective study	Congo	Obesity	2.3 (1.24–4.27)
Gutierrez JP*	654,858	122,917 (18.77)	46.07 (45.84–46.30)	52.21	Public data	Mexico	Obesity	2.11 (1.74–2.56)
Mallow PJ	21,676	3029 (14.0)	64.9 ± 17.2	52.8	Retrospective study	USA	Obesity	1.3 (1.15–1.47)
Ionescu F*	3480	1767 (50.8)	64.5 ± 17.0	48.5	Retrospective study	USA	BMI ≥ 30	0.91 (0.67–1.23)
Smati S*	1965	805 (41.0)	70.1 ± 12.5	64.5	Retrospective study	France	BMI ≥ 30	1.37 (0.76–2.46)
Lunski MJ	4760	2482 (48.2)	NA	39.1	Retrospective study	USA	Obesity	1.3 (1.03–1.63)
de Souza CD	9807	13 (1.1)	70.21 ± 8.37	47.5	Cross-sectional study	Brazil	Obesity	1.77 (0.84–3.74)
Kim TS*	10,861	4090 (37.7)	65 (54–77)	59.6	Retrospective study	USA	Obesity	1.25 (0.95–1.65)
Hilbrands LB	1073	247 (23)	65	60.6	ERACODA database	26 countries	Obesity	1.87 (1.18–2.95)
Nunez-Gil IJ	1021	NA	68 (52.0–79.0)	59.5	Retrospective study	4 countries (Ecuador, Germany, Italy and Spain)	Obesity	1.52 (0.83–2.76)
Poterucha TJ	887	309 (35)	64.1	58	Retrospective study	USA	Obesity	1.16 (0.83–1.62)
Pariikh R	160	83 (51.9)	60.35	65.6	Retrospective study	USA	Obesity	1.2 (0.6–2.6)
Polverino F	3179	218 (6.9)	69.0 (57–78)	68.3	Retrospective study	Italy	Obesity	2.03 (1.3–3.17)
Saand AR	495	241 (48.7)	68.00 (58.00–77.00)	58.4	Retrospective study	USA	BMI ≥ 30	0.788 (0.544–1.14)
Filardo TD	261	109 (41.8)	58 (50–67)	67.4	Retrospective study	USA	BMI ≥ 30	1.37 (1.07–1.74)
Canevelli M	415	15 (3.6)	84.3 ± 8.1	52.8	Retrospective study	Italy	Obesity	0.48 (0.25–0.92)
D'Alto M	94	31 (33.0)	64	74.5	Prospective study	Italy	Obesity	0.626 (0.171–2.295)
FAI2R*	675	123 (22.7)	55.9	33.4	Retrospective study	France	BMI ≥ 30	2.27 (1.14–4.49)
Nyabera A*	290	89 (30.7)	77.6 ± 8.3	51.7	Retrospective study	USA	BMI ≥ 30	0.67 (0.32–1.4)
Kaeuffer C	1045	351 (33.6)	66.3 ± 16.0	58.6	Prospective study	France	BMI ≥ 30	1.4 (0.7–2.5)
Alguwaihes AM	439	178 (42.2)	55 (19–101)	68.3	Retrospective study	Saudi Arabia	Obesity	1 (0.6–1.6)
Pantea Stoian A	432	56 (12.96)	66.97 ± 13.07	65	NA	Romania	Obesity	1.305 (0.843–2.019)
Stefan G	37	11 (30)	64 (55–71)	51	Retrospective study	Romania	Obesity	1.38 (0.25–7.58)
Murillo-Zamora E	66,123	NA	NA	60.7	Retrospective study	Mexico	Obesity	1.08 (1.05–1.11)
Ling SF*	984	20 (4.5)	74 (63–83)	54.3	Retrospective study	UK	Obesity	0.43 (0.09–2.05)
Izurieta HS	27,961	NA	75 (70–85)	48.8	Retrospective study	USA	Obesity	1.1 (1.05–1.16)
Lundon DJ	8928	631 (7.1)	58.0 ± 18.8	46.2	Cross-sectional study	USA	Obesity	1.39 (1.11–1.73)
Kim SY	4057	1159 (28.57)	40	42.5	NA	Korea	Obesity	1.71 (1.1–2.66)
Eastment MC*	25,925	12,672 (48.9)	60.4 ± 17.0	89.8	Retrospective study	USA	Obesity	1.05 (0.81–1.37)
Lanini S	379	24 (6.3)	61.67 ± 15.60	72.03	Longitudinal cohort study	Italy	Obesity	5.13 (1.81–14.5)
Schwartz KL	56,606	722 (1.3)	31	48.4	Cross-sectional study	Canada	Obesity	1.66 (1.19–2.3)
Li Y	202	92 (45.5)	58 (49–69)	54	Retrospective study	USA	BMI ≥ 30	1.45 (0.5–4.2)
Mejía F	369	157 (42.55)	59 (49–68)	65.31	Retrospective study	Peru	Obesity	0.99 (0.72–1.35)
Pena JE*	323,671	58,517 (18.1)	40.12	52.2	Retrospective study	Mexico	Obesity	1.52 (1.06–2.18)
Guerra Veloz MF	447	29 (6.5)	55.06 ± 22.55	42.5	Retrospective study	Spain	Obesity	1.3 (0.41–4.12)
Kim SW	2254	426 (28.5)	58.0 (42.0–70.0)	35.8	Retrospective study	Korea	Obesity	1.92 (0.97–3.77)
Martos-Benítez FD	38,324	8014 (20.9)	46.9 ± 15.7	58.3	Retrospective study	Mexico	Obesity	1.53 (1.38–1.71)
Hobbs ALV*	502	257 (51.6)	62 (49–71)	55.2	Retrospective study	USA	BMI ≥ 30	1.28 (0.68–2.46)
Ahlstrom B	1981	123 (6.2)	61 (52–69)	74	Retrospective study	Sweden	Obesity	0.94 (0.56–1.56)

Table 1 (continued)

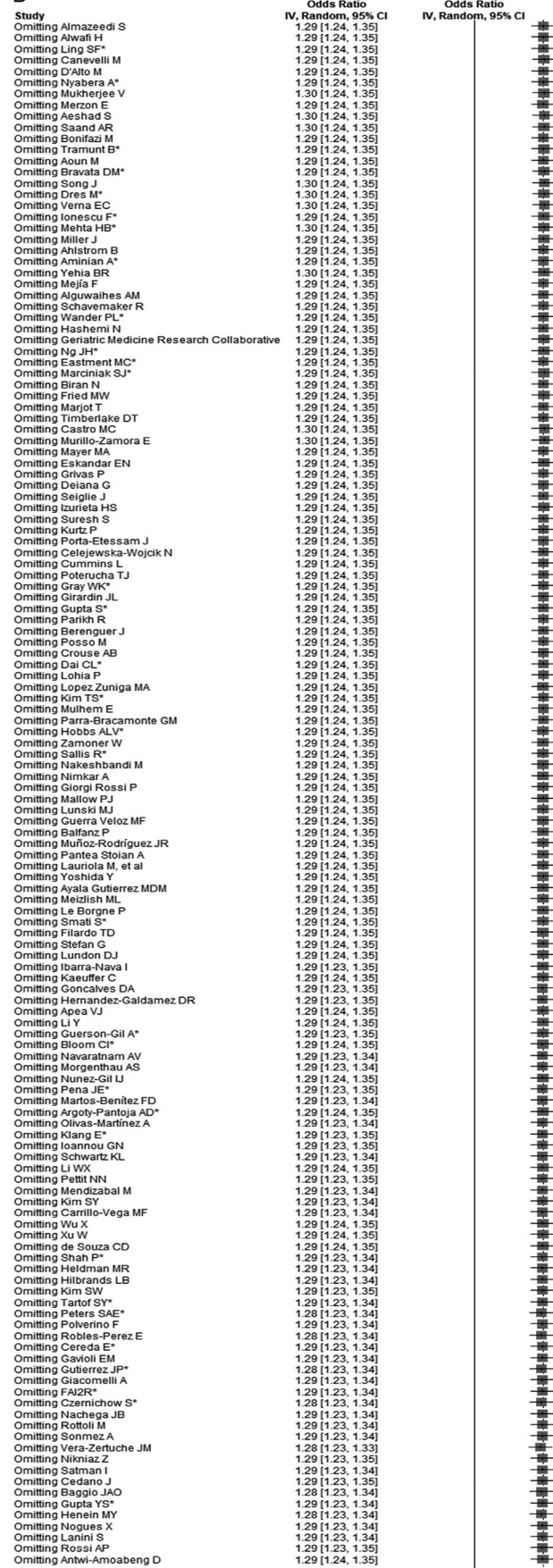
Author	Cases	Obesity (%)	Age (years)	Male (%)	Study type	Country/region	Definition of obesity	Effect size (95% CI)
Eskandar EN	4711	NA	63.4	53.3	Retrospective study	USA	BMI \geq 30	1.09 (1–1.2)
Lohia P	1871	879 (47.0)	66 (54–75)	51.6	Retrospective study	USA	BMI \geq 30	1.23 (0.98–1.54)
Apea VJ	1996	384 (19.2)	63.4	60.6	Prospective study	UK	BMI \geq 30	1.42 (1.09–1.85)
Meizlish ML	2785	NA	NA	50.1	Retrospective study	USA	Obesity	1.356 (1.101–1.67)
Mayer MA	23,844	5181 (21.7)	49.93 \pm 19.4	42.3	Retrospective study	Spain	Obesity	1.08 (0.91–1.27)
Lopez Zuniga MA	318	48 (15.2)	64.9 \pm 14.1	58.5	Prospective study	Spain	Obesity	1.238 (0.393–3.9)
Marjot T	932	248 (27)	59 (48–68)	67	Retrospective study	Three multinational registries	Obesity	1.07 (0.69–1.65)
Balfanz P	125	44 (35)	66	70	Retrospective study	Germany	Obesity	1.3 (0.29–5.74)
Olivas-Martínez A	800	357 (44.8)	51.9 \pm 13.9	61	Prospective study	USA	Obesity	1.62 (1.14–2.32)
Yoshida Y	776	409 (53.1)	60.5 \pm 16.1	47.3	Retrospective study	USA	Obesity	1.33 (0.87–2.03)
Geriatric Medicine Research Collaborative	5711	1092 (19.1)	74 (54–83)	55.2	Cohort study	12 countries	BMI \geq 30	1.03 (0.86–1.24)
Crouse AB	604	371 (61.4)	53.02	45	Retrospective study	USA	Obesity	1.21 (0.66–2.21)
Timberlake DT	275	102 (37.1)	57.9	77.1	Retrospective study	USA	Obesity	1.07 (0.53–2.14)
Cedano J	132	59 (45)	63 (53–71)	59	Retrospective study	USA	BMI \geq 30	2.92 (1.07–8.01)
Girardin JL	4210	1660 (39.4)	61.9	58.1	Retrospective study	USA	Obesity	1.19 (1.04–1.37)
Le Borgne P	1023	258 (34.1)	69.0 (58.0–79.0)	58.9	Retrospective study	France	Obesity	1.366 (0.74–2.52)
Rossi AP	95	34 (35.8)	62.46 \pm 11.81	82.1	NA	Italy	Obesity	5.3 (1.26–22.34)
Gavioli EM	437	69 (16)	67 (56–79)	48	Retrospective study	USA	Obesity	2.08 (1.14–3.78)
Dai CL*	54,645	19,763 (41.9)	47.8 \pm 19.2	47.4	Retrospective study	USA	Obesity	1.22 (0.96–1.53)
Gupta YS*	180	68 (40)	68 (59–80)	54	Retrospective study	USA	BMI > 30	3.36 (1.53–7.34)
Navaratnam AV	91,541	7920 (8.7)	71.52	55.4	Retrospective study	UK	Obesity	1.476 (1.383–1.575)
Merzon E	112	44 (39.3)	62.89 \pm 14.67	55.4	Retrospective study	Israel	Obesity	0.75 (0.04–12.49)
Zamoner W	101	22 (21.7)	57.89 \pm 15.8	54.4	Prospective study	Brazil	Obesity	1.28 (1.04–11.52)
Aoun M	231	52 (22.5)	61.46 \pm 13.99	55.4	Retrospective study	Lebanon	Obesity	0.88 (0.41–1.88)
Porta-Etessam J	5399	NA	64.27 \pm 16.93	59.2	NA	Spain	Obesity	1.12 (0.91–1.39)
Li WX	1249	353 (28.3)	36 (27–50)	61.9	Retrospective study	China	BMI \geq 30	1.69 (1.12–3.57)
Suresh S	1989	1031 (52)	63.82 \pm 16.55	50	Retrospective study	USA	Obesity	1.1 (0.83–1.44)
Sonmez A	9213	870 (9.4)	61	43.3	Retrospective study	Turkey	Obesity	2.36 (1.18–4.74)
Ibarra-Nava I	416,546	79,635 (19.1)	46.1	53.1	Retrospective study	Mexico	Obesity	1.39 (1.35–1.42)
Bloom CI*	65,653	6007 (9.1)	75.7	56.3	Prospective study	UK	Obesity	1.46 (0.88–2.42)
Giacomelli A	520	92 (17.7)	61 (50–72)	76	Prospective study	Italy	Obesity	2.17 (1.1–4.31)
Argoty-Pantoja AD*	412,017	77,566 (18.8)	45.3	53.2	Longitudinal analysis	Mexico	Obesity	1.53 (0.83–2.81)
Satman I	18,658	1024 (5.5)	53	44	Retrospective study	Turkey	Obesity	2.83 (1.45–5.53)
Grivas P	4966	1704 (34)	66 (56–76)	49	Retrospective study	USA	Obesity	1.09 (0.88–1.35)
Wu X	1091	285 (26.1)	59 (49–67)	46.7	Retrospective study	China	Obesity	1.74 (0.73–4.21)
Muñoz-Rodríguez JR	12,126	2100 (18.8)	66.4	53.3	Prospective study	Spain	Obesity	1.3 (1.1–1.5)
Mehta HB*	137,119	37,318 (27.2)	76	34	Retrospective study	USA	BMI > 30	0.92 (0.88–0.97)
Schavemaker R	1099	324 (29.5)	64.77 \pm 10.91	73	Cohort study	UK	Obesity	1 (0.72–1.38)
Bonifazi M	263	51 (19.4)	45.3 (40.4–48.4)	62.4	Retrospective study	Italy	BMI \geq 30	0.79 (0.27–2.27)
Mulhem E	3219	1642 (51.0)	65.2 (52.6–77.2)	49	Retrospective study	USA	Obesity	1.25 (1.01–1.56)
Kurtz P	4188	NA	63 (49–76)	64	Prospective study	Brazil	Obesity	1.11 (0.99–1.24)
Sallis R*	48,440	24,831 (51.3)	47.5 \pm 16.97	38.1	Retrospective study	USA	BMI \geq 30	1.29 (0.62–2.72)
Mendizabal M	2211	383 (17.3)	54.3 \pm 17.3	60.6	Prospective study	11 Latin American countries	Obesity	1.7 (1.3–2.3)
Alwafi H	706	88 (12.5)	48.0 \pm 15.6	68.5	Retrospective study	Saudi Arabia	BMI \geq 30	0.25 (0.06–1.01)
Baggio JAO	59,659	138 (0.2)	41	44.6	Retrospective study	Brazil	Obesity	3.22 (1.87–5.54)
Vera-Zertuche JM	15,529	3215 (20.7)	46.6 \pm 15.5	57.8	Retrospective study	Mexico	Obesity	2.37 (1.96–2.86)
Nikniaz Z	317	76 (24.0)	65.09 \pm 13.29	51.4	Prospective study	Iran	Obesity	2.72 (1.13–7.44)
Ayala Gutierrez MDM	13,940	2711 (19.4)	67.3	57.1	Retrospective study	Spain	Obesity	1.33 (1.17–1.51)
Cereda E*	222	68 (30.6)	58.6 \pm 11.2	77.9	Prospective study	Italy	BMI \geq 30	2.06 (1.17–3.63)
Cummins L	1781	481 (27.1)	51.74	55.2	Retrospective study	UK	Obesity	1.15 (0.86–1.55)
Castro MC	176,559	NA	NA	NA	Retrospective study	Brazil	Obesity	1.07 (1.04–1.1)
Guerson-Gil A*	3499	1472 (42.1)	65 (55–76)	55.27	Retrospective study	USA	BMI \geq 30	1.45 (1.09–1.91)
Gray WK*	117,438	10,426 (8.9)	70.5	54.6	Retrospective study	UK	Obesity	1.18 (0.81–1.72)
Song J	5621	1260 (22.4)	50.21	41.2	Retrospective study	Korea	Obesity	0.883 (0.751–1.054)
Dres M*	1199	NA	74 (72–78)	73	Prospective study	France	BMI \geq 30	0.9 (0.69–1.16)
Bravata DM*	13,510	5940 (44.0)	67.58	90.8	Observational cohort study	USA	BMI \geq 30	0.88 (0.64–1.21)
Verna EC	1070	184 (17.2)	60	52.5	Retrospective study	USA	Obesity	0.9 (0.76–1.06)
Xu W	1131	320 (28.3)	36 (26–50)	61	Retrospective study	China	Obesity	1.75 (1.21–4.32)
Celejewski-Wojcik N	116	43 (37.1)	61 (51–70)	78.4	Prospective study	Poland	Obesity	1.14 (0.65–2.01)
Goncalves DA	182,700	6470 (3.5)	NA	56.6	Retrospective study	Brazil	Obesity	1.411 (1.309–1.521)
Heldman MR	1051	365 (34.7)	57.4	62.2	Multicenter cohort study	USA	Obesity	1.8 (1.2–2.5)
Aminian A*	2839	1357 (47.8)	52.7 \pm 20.1	46.4	Retrospective study	USA	BMI \geq 30	0.94 (0.45–1.97)
Robles-Perez E	70,531	9906 (14.0)	NA	43.2	Retrospective study	Mexico	Obesity	2.05 (1.67–2.6)
Henein MY	213	122 (57.3)	49.6 \pm 12	NA	Retrospective study	Egypt	Obesity	3.403 (1.902–4.694)
Marciniak SJ*	85,006	NA	NA	NA	Prospective study	UK	Obesity	1.05 (0.96–1.15)
Wander PL*	35,879	15,147 (52)	60.3 \pm 17.0	89	Retrospective study	USA	BMI \geq 30	1.01 (0.76–1.35)
Tramunt B*	2380	929 (39.0)	70 (61–79)	63.5	Retrospective/Prospective study	France	BMI \geq 30	0.85 (0.57–1.27)
Nogues X	678	68 (8.1)	62.1	59.1	Prospective study	Spain	Obesity	3.71 (1.45–9.5)

Note: The age (years) was expressed as mean \pm standard deviation (SD) and median (interquartile range, IQR). BMI, body mass index; CI, confidence interval; NA, not available; UK, United Kingdom; USA, the United States of America. * indicates the combined effect size and 95% CI were used.

A



B



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Fig. 1. (A) The forest plot demonstrated the significant relationship between obesity and the increased risk for mortality among patients with coronavirus disease 2019 (COVID-19) on the basis of 138 eligible studies with a total of 3,863,516 cases reporting adjusted effect estimates and (B) Leave-one-out sensitivity analysis indicated that our results were stable and robust. * indicates the combined effect size and 95% CI were used.