

A meta-analysis of the association between obesity and COVID-19

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Original Paper

Cite this article: Yang J, Ma Z, Lei Y (2021). A meta-analysis of the association between obesity and COVID-19. *Epidemiology and Infection* **149**, e11, 1–14. <https://doi.org/10.1017/S0950268820003027>

Received: 14 October 2020

Revised: 26 November 2020

Accepted: 11 December 2020

Key words:

Coronavirus; COVID-19; obesity

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Abstract

Owing to limited data, we conducted a meta-analysis to re-evaluate the relationship between obesity and coronavirus-2019 (COVID-19). Literature published between 1 January 2020 and 22 August 2020 was comprehensively analysed, and RevMan3.5 was used for data analysis. A total of 50 studies, including data on 18 260 378 patients, were available. Obesity was associated with a higher risk of severe acute respiratory syndrome-coronavirus 2 (SARS-CoV2) infection (odds ratio (OR): 1.39, 95% confidence interval (CI) 1.25–1.54; $P < 0.00001$) and increased severity of COVID-19 (hospitalisation rate: OR: 2.45, 95% CI 1.78–3.39; $P < 0.00001$; severe cases: OR: 3.74, 95% CI 1.18–11.87; $P = 0.02$; need for intensive care unit admission: OR: 1.30, 95% CI 1.21–1.40; $P < 0.00001$; need for invasive mechanical ventilation: OR: 1.59, 95% CI 1.35–1.88; $P < 0.00001$ and mortality: OR: 1.65, 95% CI 1.21–2.25; $P = 0.001$). However, we found a non-linear association between BMI and the severity of COVID-19. In conclusion, we found that obesity could increase the risk of SARS-CoV2 infection and aggregate the severity of COVID-19. Further studies are needed to explore the possible mechanisms behind this association.

Introduction

In late December 2019, a pneumonia-like disease of unknown aetiology was reported in Wuhan [1], China, which was eventually identified to be caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). This pneumonia was renamed coronavirus disease 2019 (COVID-19) and was announced by the World Health Organization (WHO) as a global pandemic on 11 March 2020. As of 8 November 2020, there have been 49 578 590 infected cases and 1 245 717 deaths reported on the WHO dashboard [2]. Clinical manifestations of COVID-19 range from no or mild symptoms to severe pneumonia, acute respiratory distress syndrome (ARDS), or even multiorgan failure and death.

A meta-analysis comprising 18 506 patients investigated the association between diabetes and COVID-19 and found diabetes was associated with a 65% higher risk for death [3]. Other risk factors, such as cardiovascular disease and hypertension, have also been shown to increase the severity of COVID [4–6]. The diseases mentioned above are usually associated with excessive adipose tissue accumulation causing metabolic and inflammatory changes [7–9]. Obesity has been identified as an independent predisposition factor for severe cases of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) infection [10], and a high genetic similarity was observed between SARS-CoV-2 and SARS-CoV (80%) and MERS-CoV (50%) [11]. These data indicate that obesity might be a risk factor for the severity of COVID-19.

One previous study in China showed that only 18.95% of survivors were overweight, and 88.24% of non-survivors had a higher body mass index (BMI) [12]. In Germany, patients with ARDS were more overweight or obese (83%) than those with healthy BMI (42%) [13]. More recently, some meta-analyses showed that obesity was associated with mortality, severity and predicted poor outcome in COVID-19 patients [14–17]. However, there are some limitations to these meta-analyses. First, the number of eligible studies is small, ranging from 9 to 14. Second, the data from other countries are scarce, and most eligible studies are from China and the USA. Third, the definition of obesity is different between Eastern and Western countries. Last, the conclusions of previous meta-analyses may be altered due to the recent emergence of a large number of studies about the association between obesity and COVID-19. Europe and North America, which have the highest prevalence of obesity cases, has become the epicentre of the COVID-19 pandemic [18]. Therefore, it is necessary to re-explore the relationship between obesity and COVID-19, including susceptibility to SARS-CoV-2 infection, which was not analysed in previous meta-analyses and poor outcomes, as we have performed in the meta-analysis presented here.

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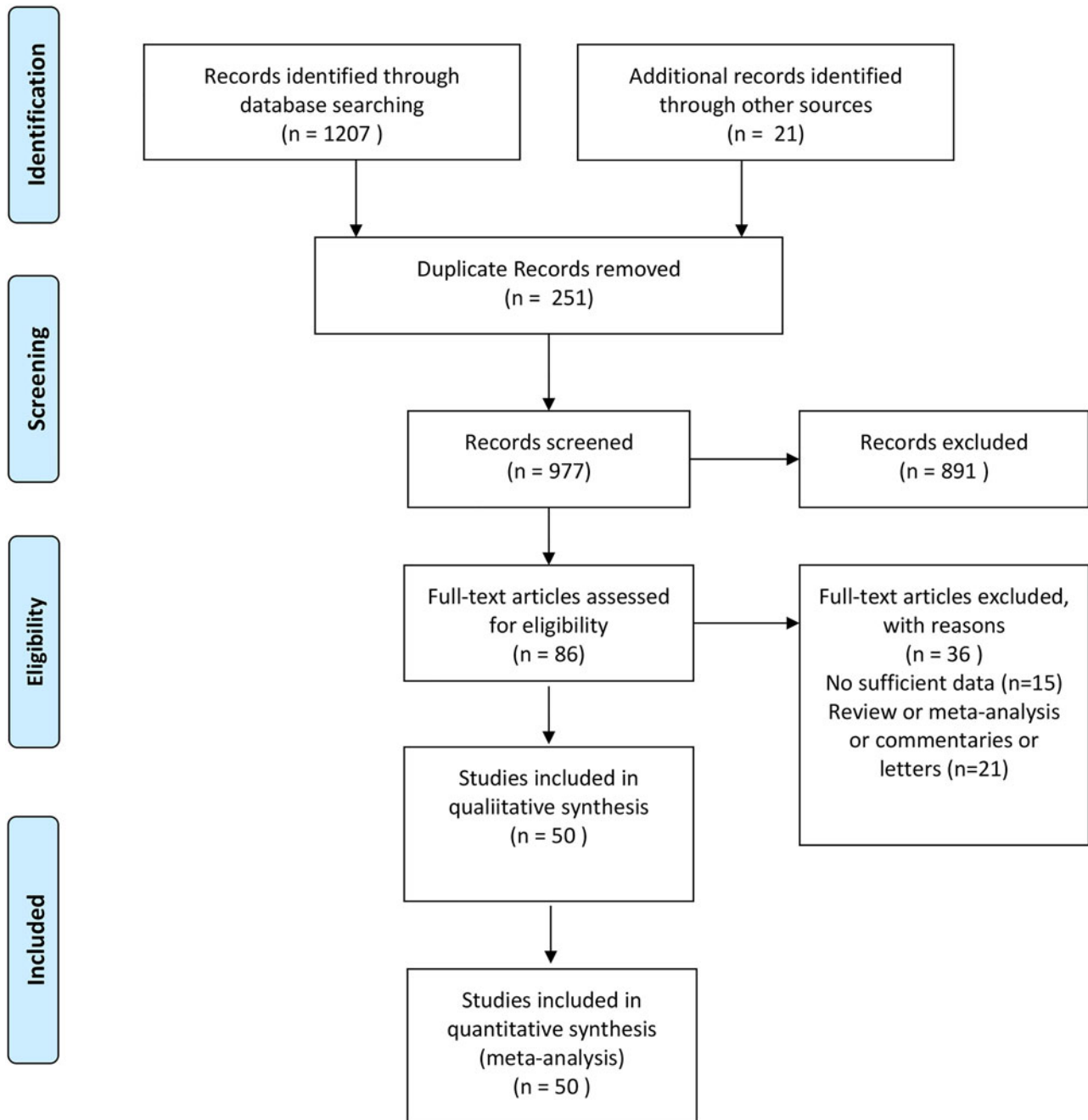


Fig. 1. Flow diagram of the literature selection process.

Methods

Research strategy

This meta-analysis was performed following the PRISMA guidelines. A comprehensive search was performed using the PubMed, EMBASE and Cochrane Library databases for literature published between 1 January 2020 and 25 August 2020. The following words were utilised during the search: (COVID-19 or coronavirus or SARS-CoV-2) and (obesity or overweight or body mass index). Reference lists of eligible studies and relevant review articles were screened and evaluated for additional studies that could be used in analyses.

Inclusion and exclusion criteria

Inclusion criteria for the studies in our analyses were as follows:

- (1) Studies published in English
- (2) Studies investigating the association between obesity or overweight and COVID-19.
- (3) Studies including both adults and children diagnosed with COVID-19.
- (4) Cohort studies with prospective or retrospective designs.

Exclusion criteria from analyses were:

Table 1. Baseline characteristics of the eligible studies

Study	Region	Centre(s)	Design	Obesity <i>n</i> %	Total	Male	Age	Outcomes	NOS score
Alkhatib [19]	USA	Single	Retrospective	60.76	158	61	57	ICU admission	7
Argenziano [20]	USA	Single	Retrospective	41.85	1000	596	63 50–75	ICU admission	7
Bello-Chavolla [21]	Mexico	Multiple	Retrospective	16.42	177 133	90 582	42.58	Risk of COVID 19 infection Mortality ICU admission Need of IMV	7
Buckner [22]	USA	Multiple	Retrospective	47.31	105	53	69 23–97	Severe cases	7
Busetto [11]	Italy	Single	Retrospective	31.52	92	57	70.5 ± 13.3	Mortality ICU admission Need of IMV	8
Cai1 [23]	China	Single	Retrospective	NA	298	145	47 33–61	Severe cases	7
Cai2 [24]	China	Single	Retrospective	10.70	383	183	48.4	Severe cases	7
Caussy [25]	France	Single	Retrospective	25	340	NA	NA	Severe cases	7
Chand [26]	USA	Multiple	Retrospective	54.33	300	182	57.8 ± 12.2	Mortality	8
Chao [27]	USA	Single	Retrospective	26.09	46	31	13.1 0.4–19.3	ICU admission	7
Cummings [29]	USA	Double	Prospective	46.30	257	171	62 51–72	Mortality	8
Czernichow [28]	France	Multiple	Prospective	21.81	5795	3791	NA	Mortality	8
Docherty [30]	UK	Multiple	Prospective	10.48	20 133	12 068	73 58–82	Mortality	8
Duanmu [31]	USA	Single	Retrospective	22	100	56	45 32–65	Hospitalisation	7
Escalera-Antezana [32]	Bolivia	Single	Retrospective	5.61	107	55	43.9 ± 17.6	Mortality	8
Gao [33]	China	Multiple	Retrospective	50	150	94	48	Severe cases	7
Gerwen [34]	USA	Multiple	Retrospective	28.95	3703	2049	56.8 ± 18.2	Mortality Need of IMV Hospitalisation	8
Giannouchos [35]	Mexico	Multiple	Retrospective	16.7	236 439	120 347	42.5 ± 16.9	Risk of COVID-19 infection Hospitalisation	7
Goyal1 [36]	USA	Single	Retrospective	34.60	393	238	62.2 48.6–73.7	Need of IMV	7
Goyal2 [37]	USA	Double	Retrospective	31.12	1687	1004	66.5 53.7–77.2	Mortality	8
Giracomelli [38]	Italy	single	Prospective	16.31	233	161	61 50–72	Mortality	8

(Continued)

Table 1. (Continued.)

Study	Region	Centre(s)	Design	Obesity <i>n</i> %	Total	Male	Age	Outcomes	NOS score
Hajifathalian [39]	USA	Double	Retrospective	35.97	770	468	63.5 ± 17	Mortality ICU admission Need of IMV	8
Halasz [40]	Italy	Single	Retrospective	19.83	242	194	64 56–71	Mortality	8
Hamer [41]	UK	Multiple	Prospective	23.84	334 329	152 162	NA	Risk of COVID-19 infection	7
Hu [42]	China	Single	Retrospective	4.02	323	166	61 23–91	Severe cases	7
Hur [43]	USA	Multiple	Retrospective	53.29	486	271	59 47–69	Need of IMV	7
Jung [44]	South Korea	Multiple	Retrospective	NA	18 940	7185	53.7 ± 13.8	Risk of COVID-19 infection	7
Kalligeros [45]	USA	Single	Retrospective	47.57	103	63	60 50–72	ICU admission Need of IMV	7
Killerby [46]	Atlanta	Multiple	Retrospective	42.75	531	228	51.63	Hospitalisation	7
Kim [47]	USA	Multiple	Retrospective	46.33	2491	1326	62 50–75	ICU admission	7
Klang [48]	USA	Single	Retrospective	36.14	3406	1961	65.9	Mortality	8
Lighter [49]	USA	Single	Retrospective	37.90	3615	NA	NA	Hospitalisation ICU admission	7
Lodigiani [67]	Italy	Single	Retrospective	23.97	388	264	66	ICU admission	7
Lusignan [50]	UK	Multiple	Retrospective	21.70	3802	1612	NA	Risk of COVID-19 infection	7
Monterio [51]	USA	Single	Retrospective	35.71	112	74	61 45–74	Need of IMV	7
Nakeshbandi [52]	USA	Single	Retrospective	42.66	504	263	68 ± 15	Mortality Need of IMV	8
Ong [53]	Singapore	Single	Retrospective	NA	91	51	54.92	Mortality ICU admission Need of IMV	7
Oriz-Brizuela [54]	Mexico	Single	Prospective	21.68	309	183	43 33–54	Hospitalisation ICU admission	7
Palaiodimos [55]	USA	Single	Retrospective	NA	200	98	64 50–73.5	Mortality Need of IMV	8
Parra-Bracamonte [56]	Mexico	Multiple	Retrospective	19.92	142 690	79 280	45 34–57	Mortality	8
Petrilli [57]	USA	Multiple	Retrospective	26.81	4103	2072	52 36–65	Hospitalisation Severe cases	7
Price-Haywood [58]	USA	Single	Retrospective	49.61	3481	1394	54	Hospitalisation	7
Shah [59]	USA	Multiple	Retrospective	66.48	522	347	63 50–72	Mortality	8

Simonnet [60]	France	Single	Retrospective	NA	124	90	60 51–70	Need of IMV	7
Soares [61]	Brazil	Multiple	Retrospective	5.57	10 713	4804	NA	Hospitalisation	7
Suleyman [62]	USA	Multiple	Retrospective	56.59	463	204	57.5 ± 16.8	Hospitalisation ICU admission Need of IMV	7
Williamson [63]	UK	Multiple	Retrospective	21.82	17 278 392	8 630 403	NA	Mortality	8
Wu [64]	China	Multiple	Retrospective	NA	280	151	43.12 ± 19.02	Severe cases	7
Zachariah [65]	USA	Single	Retrospective	22	50	27	9.9	Severe cases	7
Zheng [66]	China	Multiple	Retrospective	68.18	66	49	47	Severe cases	7

IMV, invasive mechanical ventilation; ICU, intensive care unit; NA, not available; NOS, Newcastle–Ottawa quality assessment scale.

- (1) Review articles, letters or commentaries.
- (2) Duplicate studies.
- (3) Studies in which data were not available.

Data assessment

Two individual authors (Jiao Yang and ZhiYing Ma) independently extracted the following information: study design, age, gender, susceptibility to COVID-19, the severity of COVID-19 (need for hospitalisation, severe cases, need for intensive care unit (ICU) admission, need for invasive mechanical ventilation (IMV) and mortality). Severe COVID-19 was defined according to the American Thoracic Society guidelines.

Statistical analysis

RveMan5.3 (Cochrane Collaboration) was used to analyse data with associated odds ratios (OR) and corresponding 95% confidence intervals (CIs). The generic inverse variance approach was used for the meta-analysis. A $P < 0.05$ was identified as statistically significant. The I^2 statistic was used to assess the heterogeneity among the studies analysed. An $I^2 > 50\%$ or $P < 0.1$ indicated heterogeneity, for which the random-effects model was utilised. Otherwise, the fixed-effects model was used. In addition, publication bias was evaluated through visual inspections of funnel plots, and the quality of eligible studies was assessed using the Newcastle–Ottawa Quality Assessment Scale.

Results

Study characteristics

A total of 50 studies [11, 19–67] that included 18 260 378 subjects were eligible for the meta-analysis. Out of these 50 studies, 44 were retrospective and 6 were prospective cohort studies. Twenty-five studies were conducted in the USA, 6 in China, 4 in Italy, 4 in the UK, 4 in Mexico, 3 in France and 1 in Brazil, Singapore, South Korea and Bolivia. The incidence of obesity, defined as BMI ≥ 30 , varied from 5.57% to 68.48% in this meta-analysis. Detailed search strategies and characteristics of eligible studies are presented in Fig. 1 and Table 1, respectively. The Newcastle–Ottawa Quality Assessment Scale scores for all included studies were equal to or more than 6, as shown in Table 1, which is acceptable for a meta-analysis.

Outcomes

Risk of COVID-19

Five studies involving 753 597 cases mentioned the association between obesity and the risk of SARS-CoV2 infection. We used the random-effects model for analysis due to a high heterogeneity ($P < 0.00001$ and $I^2 = 92\%$) between studies. This model suggested that obese subjects had a higher risk of SARS-CoV2 infection as compared to those without obesity (OR: 1.39; 95% CI 1.25–1.54; $P < 0.00001$) (Fig. 2).

Severity of COVID-19

Hospital admission: We conducted a stratified analysis to assess the relationship between BMI ranges and the need for hospital admission in patients with COVID-19. Patients with a BMI 25–29.9, BMI ≥ 30 and BMI ≥ 35 had higher rates of hospital admission than those with a BMI < 25 (OR: 2.09, 95% CI 1.22–3.60, P :

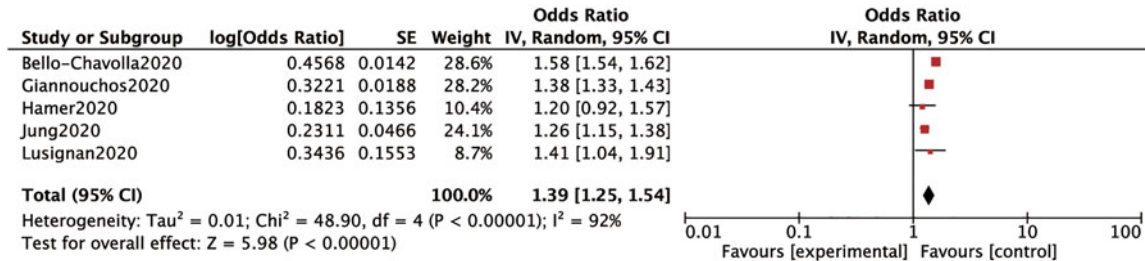


Fig. 2. Forrest plot depicting the risk of COVID-19.

0.007; OR: 2.45, 95% CI 1.78–3.39, $P < 0.00001$ and OR: 2.63, 95% CI 1.55–4.47, $P: 0.0003$, respectively) (Fig. 3). However, no significant increases in hospital admission rates were found for patients with a BMI between 30 and 34.9 (OR: 1.10, 95% CI 0.88–1.37, $P: 0.4$) than those with a healthy weight, as shown in Figure 3.

Severe cases: Ten studies reported on the association between BMI and severe cases of COVID-19. Four trials comprising 794 patients showed that those with severe diseases had a higher BMI than those with mild disease (OR: 1.18, 95% CI 1.09–1.27, $P < 0.0001$) (Fig. 3). In addition, patients with a BMI ≥ 30 had a higher prevalence of severe cases than those with BMI < 30 (OR: 3.74, 95% CI 1.18–11.87, $P: 0.02$) (Fig. 3).

ICU admission: Eleven studies evaluated the incidence of ICU care in COVID-19 patients. A stratified analysis on the association of the different BMI classes and the rate of ICU admission was conducted. Patients with COVID-19 with a BMI ≥ 30 , BMI ≥ 35 and ≥ 40 had a higher probability of requiring ICU admission than those with a BMI < 30 (OR: 1.30, 95% CI 1.21–1.40, $P < 0.00001$; OR: 1.86, 95% CI 1.31–2.63, $P: 0.0005$ and OR: 1.96, 95% CI 1.27–3.02, $P: 0.002$, respectively), as shown in Figure 4. However, patients with a BMI ≥ 25 or BMI 30–34.9 showed no significantly higher rate of ICU admission than those with a BMI < 25 or BMI < 30 (OR: 3.10, 95% CI 0.76–12.61, $P: 0.11$ and OR: 1.44, 95% CI 0.74–2.81, $P: 0.28$, respectively) (Fig. 4).

IMV: Thirteen studies assessed the association between BMI and the need for IMV in patients with COVID-19. We compared the requirement of IMV in different BMI groups and found that the need for IMV was notably raised in patients with a BMI ≥ 25 , BMI ≥ 30 , BMI ≥ 35 and BMI ≥ 40 compared to those with a BMI < 25 (OR: 1.40, 95% CI 1.13–1.73, $P: 0.002$; OR: 1.59, 95% CI 1.35–1.88, $P < 0.00001$; OR: 5.22, 95% CI 2.46–11.07, $P < 0.0001$ and OR: 1.97, 95% CI 1.24–3.12, $P: 0.004$, respectively) (Fig. 5).

Mortality

Fourteen studies investigated the association between different BMI categories and mortality. As shown in Figure 6, the mortality was significantly higher in patients with a BMI ≥ 30 , BMI 35–39.9 and BMI ≥ 40 than those with a BMI < 30 (OR: 1.65, 95% CI 1.21–2.25, $P: 0.001$; OR: 1.91, 95% CI 1.04–3.49, $P: 0.04$ and OR: 1.71, 95% CI 1.32–2.22, $P < 0.0001$, respectively). Nevertheless, patients with a BMI between 25 and 29.9 and a BMI between 30 and 34.9 did not have a statistically significant higher risk of mortality than those with a BMI < 25 (OR: 1.10, 95% CI 0.84–1.45, $P: 0.48$ and OR: 1.38, 95% CI 0.94–2.04, $P: 0.1$) (Fig. 6).

Publication bias

The publication bias was assessed using a visual funnel plot. No obvious publication bias was found for the outcomes assessed

(a) risk of COVID-19; (b) hospital admission; (c) severe cases; (d) ICU admission; (e) need of IMV) as shown in Figure 7.

Discussion

Our study found obesity increased the prevalence of SARS-CoV2 infection and the severity of COVID-19 (as assessed by the need for hospitalisation, severe cases, need for ICU admission, need for IMV and mortality). Patients with overweight presented with a higher rate of hospitalisation and higher requirement of IMV. However, a non-linear association between BMI and the severity of COVID-19 was found. To our knowledge, this study is the largest meta-analysis conducted so far to comprehensively explore the association between obesity and COVID-19.

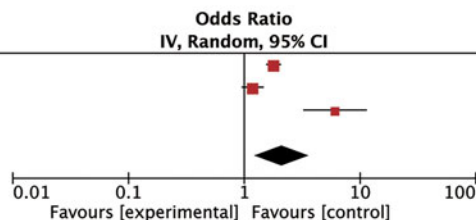
Yates *et al.* analysed UK biobank data and found that overweight and obese patients were at a higher risk of getting the SARS-CoV-2 in a dose–response manner. Compared to a healthy weight, overweight, obese and severely obese (BMI ≥ 35) subjects had a 1.31-, 1.55-, or 1.57-fold higher probability of SARS-CoV-2 positivity [68]. Chadeau-Hyam *et al.* reported that severe obesity is independently associated with the risk of obtaining COVID-19 with an odds ratio > 1.05 by analysing the data from Public Health England [69]. In our meta-analysis, patients with a BMI ≥ 30 had a 1.39 times higher chance of having COVID-19 than those with a healthy weight, which was in line with previous studies.

Obesity was the most prevalent condition in inpatients with COVID-19 aged 18–49 years in a study conducted by Garg *et al.* [70], which suggests that obesity may increase the hospitalisation rate of patients with COVID-19. A prospective study in New York revealed that an increase in BMI (e.g. BMI > 40 with 2.6 odds) in patients with COVID-19 was strongly associated with hospital admission [71]. In our meta-analysis, the odds ratios for hospitalisation rate were 2.09, 2.45 and 2.63 for patients with a BMI of 25–29.9, ≥ 30 and ≥ 35 , respectively. This suggests that a higher BMI predicts a higher hospitalisation rate for patients with COVID-19. However, no significant association between patients with a BMI 30–34.9 and hospital admission was found, which may be attributed to the limited number of eligible studies reporting on this BMI group.

A study conducted in China reported that there were no patients with underweight who developed severe COVID-19, and that obese patients progressed to severe cases (39% in the obese group, 29.3% in the overweight group and 19.2% in the healthy weight group) [23]. An observational study revealed that severely ill patients had a higher BMI (mean, 24.78 vs. 23.20) than patients with non-severe disease [72]. This indicated that a higher BMI increased the chance of COVID-19 severity. Here, we found that BMI was a major influential factor for COVID-19 progression to severity (OR: 1.18). In addition, obese patients

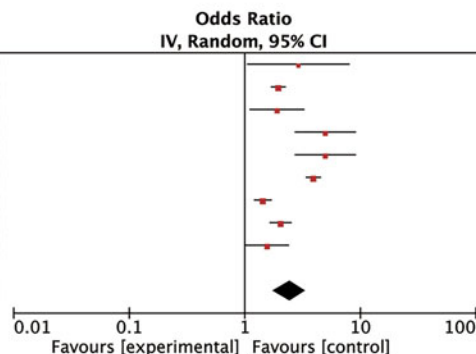
a: BMI 25–29.9 and hospital admission

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Gerwen2020	0.5808	0.0751	37.9%	1.79 [1.54, 2.07]
Hamer2020	0.1655	0.1106	36.7%	1.18 [0.95, 1.47]
ORTIZ-BRIZUELA	1.8028	0.3221	25.4%	6.07 [3.23, 11.41]
Total (95% CI)			100.0%	2.09 [1.22, 3.60]
Heterogeneity: $\tau^2 = 0.20$; $\chi^2 = 26.66$, $df = 2$ ($P < 0.00001$); $I^2 = 92\%$				
Test for overall effect: $Z = 2.68$ ($P = 0.007$)				



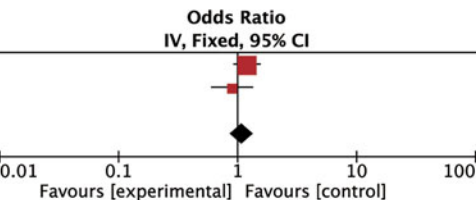
b: BMI ≥ 30 and hospital admission

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Duanmu2020	1.0674	0.5202	5.8%	2.91 [1.05, 8.06]
Gerwen2020	0.6669	0.0753	13.7%	1.95 [1.68, 2.26]
Giannouchos2020	0.6419	0.2789	10.0%	1.90 [1.10, 3.28]
Killerby2020	1.6029	0.3107	9.4%	4.97 [2.70, 9.13]
ORTIZ-BRIZUELA	1.6029	0.3107	9.4%	4.97 [2.70, 9.13]
Petrilli2020	1.3655	0.077	13.7%	3.92 [3.37, 4.56]
Price-Haywood2020	0.3577	0.0895	13.5%	1.43 [1.20, 1.70]
Soares2020	0.7129	0.1114	13.2%	2.04 [1.64, 2.54]
Suleyman2020	0.4445	0.2208	11.2%	1.56 [1.01, 2.40]
Total (95% CI)			100.0%	2.45 [1.78, 3.39]
Heterogeneity: $\tau^2 = 0.19$; $\chi^2 = 98.10$, $df = 8$ ($P < 0.00001$); $I^2 = 92\%$				
Test for overall effect: $Z = 5.48$ ($P < 0.00001$)				



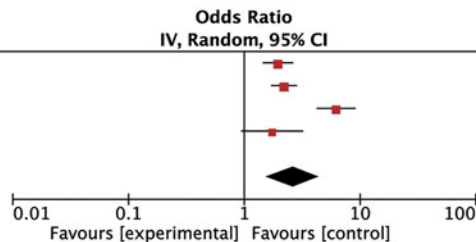
c: BMI 30–34.9 and hospital admission

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Hamer2020	0.1823	0.1356	70.0%	1.20 [0.92, 1.57]
Lighter2020	-0.1054	0.2069	30.0%	0.90 [0.60, 1.35]
Total (95% CI)			100.0%	1.10 [0.88, 1.37]
Heterogeneity: $\chi^2 = 1.35$, $df = 1$ ($P = 0.24$); $I^2 = 26\%$				
Test for overall effect: $Z = 0.85$ ($P = 0.40$)				



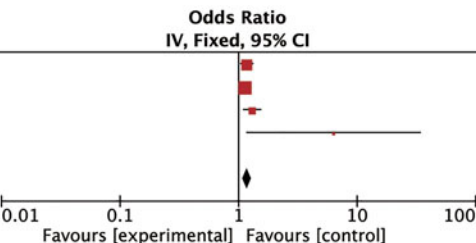
d: BMI ≥ 35 and hospital admission

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Hamer2020	0.6678	0.1547	26.6%	1.95 [1.44, 2.64]
Lighter2020	0.7885	0.1315	27.3%	2.20 [1.70, 2.85]
Petrilli2020	1.8245	0.1975	25.2%	6.20 [4.21, 9.13]
Suleyman2020	0.5528	0.3151	20.9%	1.74 [0.94, 3.22]
Total (95% CI)			100.0%	2.63 [1.55, 4.47]
Heterogeneity: $\tau^2 = 0.25$; $\chi^2 = 25.98$, $df = 3$ ($P < 0.00001$); $I^2 = 88\%$				
Test for overall effect: $Z = 3.59$ ($P = 0.0003$)				



e: BMI and severe cases

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Cai1 2020	0.157	0.065	35.5%	1.17 [1.03, 1.33]
Gao2020	0.1222	0.0573	45.7%	1.13 [1.01, 1.26]
Wu2020	0.2624	0.0899	18.6%	1.30 [1.09, 1.55]
Zheng2020	1.8437	0.865	0.2%	6.32 [1.16, 34.43]
Total (95% CI)			100.0%	1.18 [1.09, 1.27]
Heterogeneity: $\chi^2 = 5.51$, $df = 3$ ($P = 0.14$); $I^2 = 46\%$				
Test for overall effect: $Z = 4.23$ ($P < 0.0001$)				



f: BMI ≥ 30 and severe cases

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Buckner2020	0.4625	0.419	17.1%	1.59 [0.70, 3.61]
Cai2 2020	1.2238	0.4527	16.9%	3.40 [1.40, 8.26]
Causy2020	0.6729	0.281	18.0%	1.96 [1.13, 3.40]
Hu2020	0.2485	0.5826	15.9%	1.28 [0.41, 4.02]
Petrilli2020	2.7583	0.0957	18.7%	15.77 [13.08, 19.03]
Zachariah2020	2.6672	0.8531	13.5%	14.40 [2.71, 76.65]
Total (95% CI)			100.0%	3.74 [1.18, 11.87]
Heterogeneity: $\tau^2 = 1.85$; $\chi^2 = 93.44$, $df = 5$ ($P < 0.00001$); $I^2 = 95\%$				
Test for overall effect: $Z = 2.24$ ($P = 0.02$)				

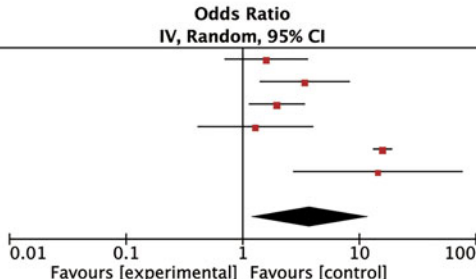
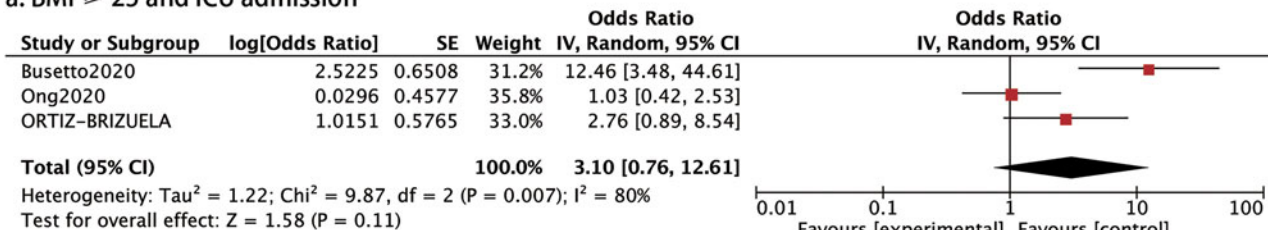
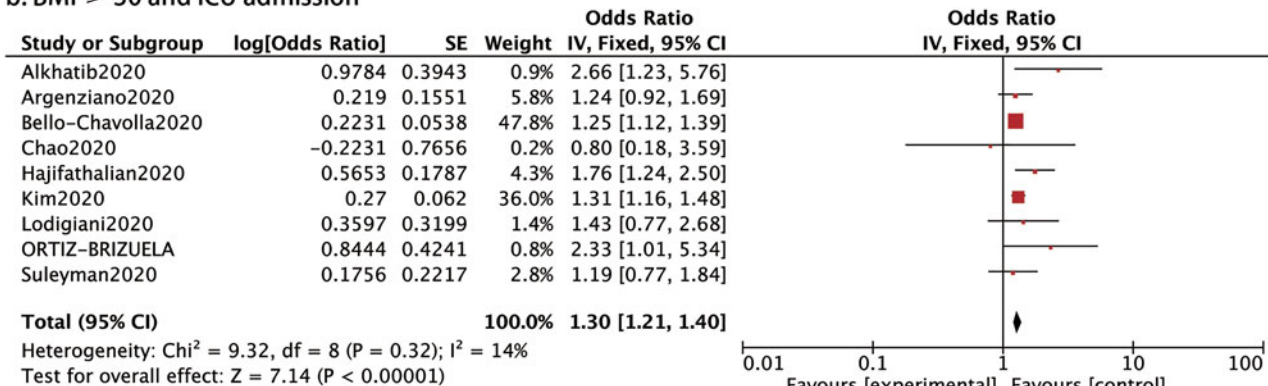


Fig. 3. Forrest plot showing the severity of COVID-19: (a) BMI 25–29.9 and hospital admission, (b) BMI ≥ 30 and hospital admission, (c) BMI 30–34.9 and hospital admission, (d) BMI ≥ 35 and hospital admission, (e) BMI and severe cases, (f) BMI ≥ 30 and severe cases.

a: BMI \geq 25 and ICU admissionb: BMI \geq 30 and ICU admission

c: BMI 30-34.9 and ICU admission

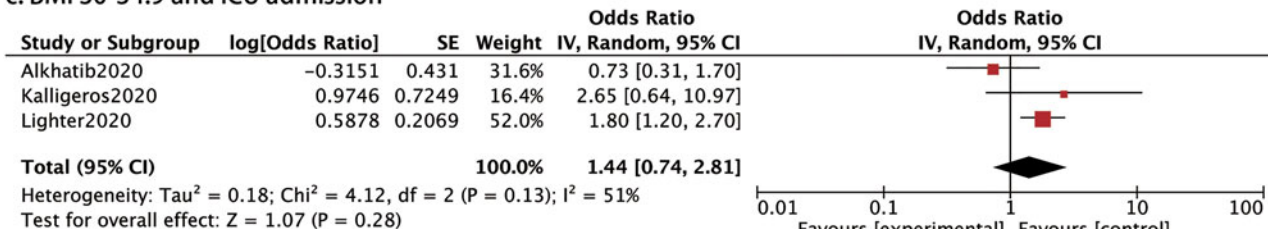
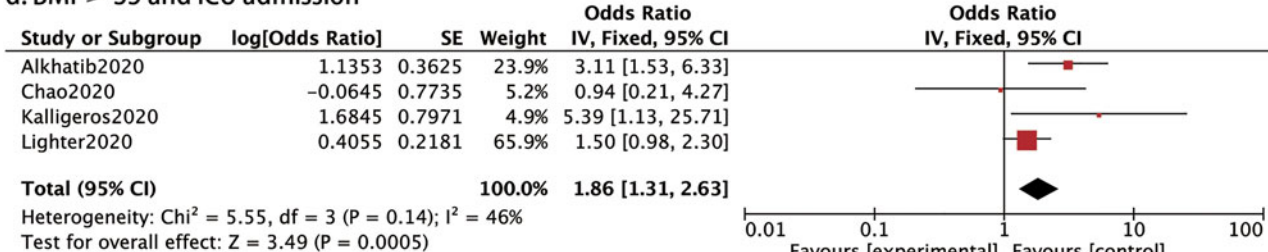
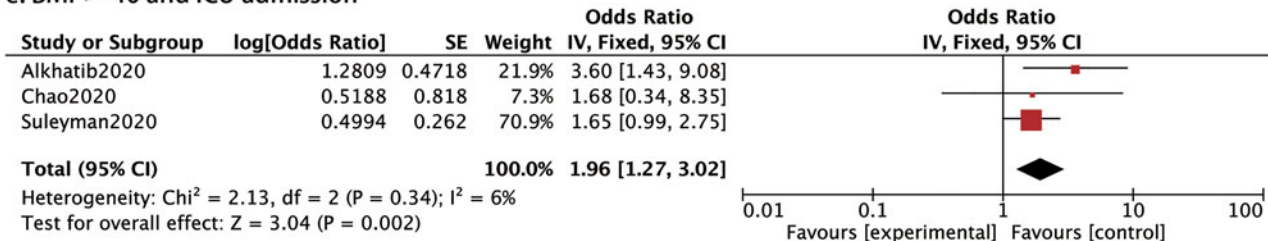
d: BMI \geq 35 and ICU admissione: BMI \geq 40 and ICU admission

Fig. 4. Forrest plot showing the severity of COVID-19: (a) BMI \geq 25 and ICU admission, (b) BMI \geq 30 and ICU admission, (c) BMI 30–34.9 and ICU admission, (d) BMI \geq 35 and ICU admission, (e) BMI \geq 40 and ICU admission.

were 3.74 times more likely to get severe COVID-19 than those with BMI < 30. These data together indicate that obesity or a high BMI increases the chance of severe cases.

A large international multicentre study showed that the mean BMI of critically ill patients was 28.1, and the overall prevalence of

obesity was 37.5% [73]. Cai *et al.* also reported that patients with a BMI \geq 24 (OR = 1.258, P = 0.005) were more likely to be admitted to the ICU [74]. However, we failed to find a positive association between overweight and the risk of ICU admission. However, patients with BMI \geq 30 and BMI \geq 35 showed a 1.30- and

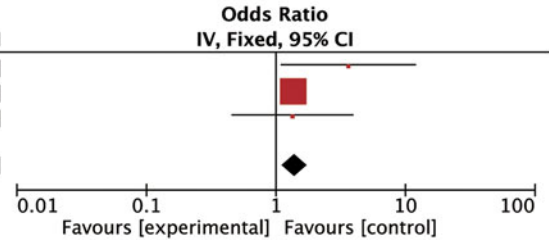
a; BMI ≥ 25 and need for IMV

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio	
				IV, Fixed, 95% CI	
Busetto2020	1.2865	0.6124	3.2%	3.62	[1.09, 12.02]
Gerwen2020	0.305	0.1133	92.9%	1.36	[1.09, 1.69]
Ong2020	0.2927	0.5529	3.9%	1.34	[0.45, 3.96]

Total (95% CI) 100.0% 1.40 [1.13, 1.73]

Heterogeneity: $\text{Chi}^2 = 2.49$, $\text{df} = 2$ ($P = 0.29$); $I^2 = 20\%$

Test for overall effect: $Z = 3.07$ ($P = 0.002$)

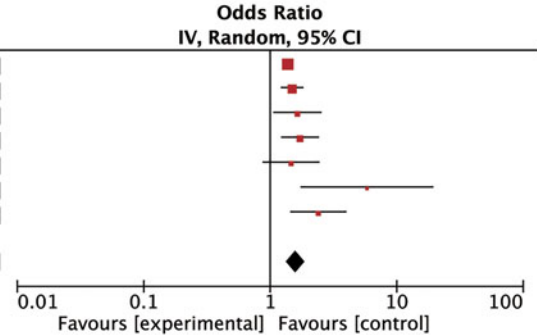
b: BMI ≥ 30 and need for IMV

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio	
				IV, Random, 95% CI	
Bello-Chavolla2020	0.3185	0.0527	33.1%	1.38	[1.24, 1.52]
Gerwen2020	0.3989	0.1043	24.1%	1.49	[1.21, 1.83]
Goyal1 2020	0.4945	0.2234	10.4%	1.64	[1.06, 2.54]
Hajifathalian2020	0.5423	0.1752	14.4%	1.72	[1.22, 2.42]
Hur2020	0.3784	0.2641	8.0%	1.46	[0.87, 2.45]
Monterio2020	1.7613	0.616	1.8%	5.82	[1.74, 19.47]
Nakeshbandi2020	0.8755	0.2606	8.2%	2.40	[1.44, 4.00]

Total (95% CI) 100.0% 1.59 [1.35, 1.88]

Heterogeneity: $\text{Tau}^2 = 0.02$; $\text{Chi}^2 = 11.15$, $\text{df} = 6$ ($P = 0.08$); $I^2 = 46\%$

Test for overall effect: $Z = 5.51$ ($P < 0.00001$)

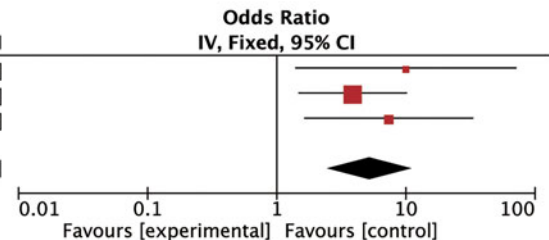
c: BMI ≥ 35 and need for IMV

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio	
				IV, Fixed, 95% CI	
Kalligeros2020	2.3016	1.0063	14.6%	9.99	[1.39, 71.80]
Palaiodimos2020	1.3533	0.4939	60.5%	3.87	[1.47, 10.19]
Simonnet2020	1.9961	0.7691	24.9%	7.36	[1.63, 33.23]

Total (95% CI) 100.0% 5.22 [2.46, 11.07]

Heterogeneity: $\text{Chi}^2 = 0.98$, $\text{df} = 2$ ($P = 0.61$); $I^2 = 0\%$

Test for overall effect: $Z = 4.30$ ($P < 0.00001$)

d: BMI ≥ 40 and need for IMV

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio	
				IV, Fixed, 95% CI	
Hur2020	0.6523	0.3754	39.0%	1.92	[0.92, 4.01]
Suleyman2020	0.6931	0.2999	61.0%	2.00	[1.11, 3.60]

Total (95% CI) 100.0% 1.97 [1.24, 3.12]

Heterogeneity: $\text{Chi}^2 = 0.01$, $\text{df} = 1$ ($P = 0.93$); $I^2 = 0\%$

Test for overall effect: $Z = 2.89$ ($P = 0.004$)

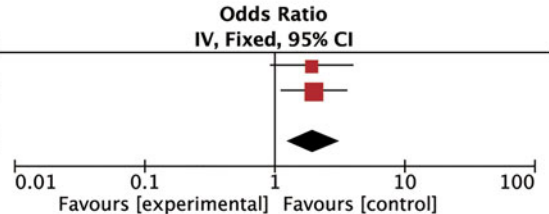


Fig. 5. Forrest plot showing the severity of COVID-19: (a) BMI ≥ 25 and need for IMV, (b) BMI ≥ 30 and need for IMV, (c) BMI ≥ 35 and need for IMV, (d) BMI ≥ 35 and need for IMV, (e) BMI ≥ 40 and need for IMV.

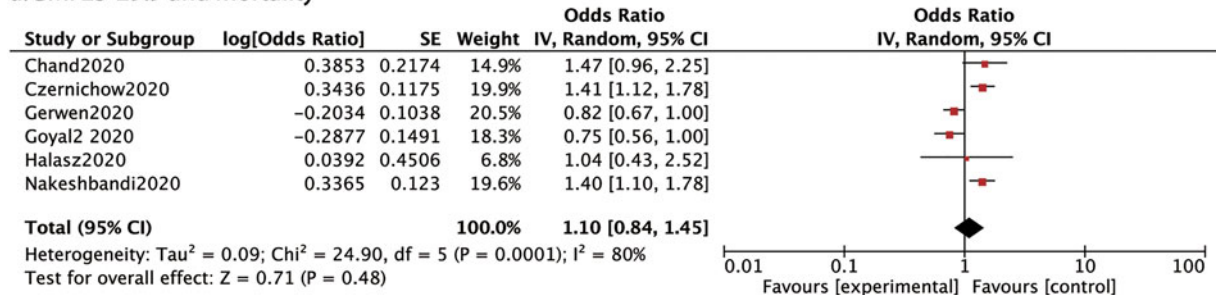
1.86-fold odds of requiring ICU admission compared to those with a BMI < 30 . Therefore, there might be a positive correlation between the severity of obesity and the risk of ICU admission. Surprisingly, patients with BMI 30–34.9 presented no significant risk of ICU admission compared to those with BMI < 30 , which should be confirmed in future studies.

Simonnet *et al.* reported data from the Lille University centre, showing that severe obesity (BMI ≥ 35) was associated with a higher requirement for mechanical ventilation compared to patients with a healthy weight (81.8% vs. 41.9%) [60]. In Singapore, Ong *et al.* found that a BMI ≥ 25 was significantly associated with mechanical ventilation (OR 1.16) [53]. Moreover, Chetboun *et al.* reported that the relationship between BMI and the risk of the need for IMV was linear, and the odds were 3.06-fold higher in patients with a BMI ≥ 40 [73]. In our meta-analysis, the odds of IMV risk in patients with BMI ≥ 25 and BMI ≥ 30 were 1.40 and 1.59 times higher than those with

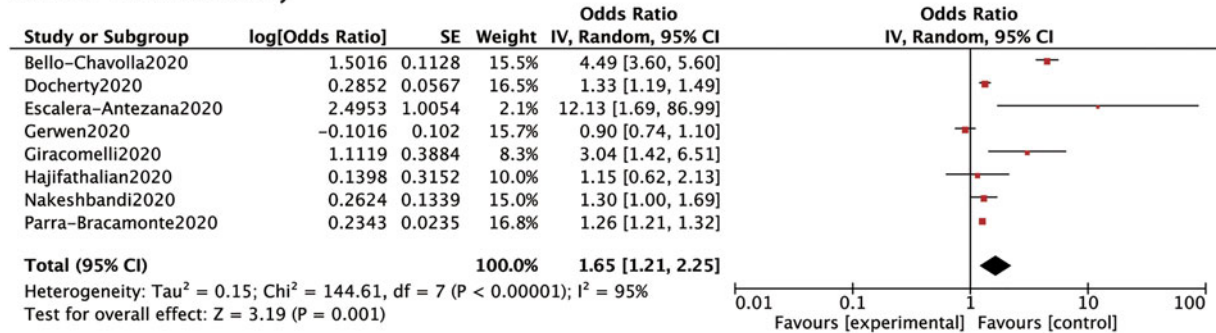
BMI < 25 and BMI < 30 . For severely obese patients (BMI ≥ 35) diagnosed with COVID-19, the odds of requiring IMV were 5.22. However, for morbidly obese patients (BMI ≥ 40), the odds were 1.97. It appears that no significant linear relationship exists between higher BMI and the requirement of IMV, which is in contrast to previous studies [73].

A retrospective analysis of 112 patients with COVID-19 showed that 88.2% of non-survivors had a BMI ≥ 25 compared to 18.8% of survivors [75]. Asare *et al.* showed that 733 of 1930 deaths from COVID-19 were contributed to obesity alone in patients without reported comorbid conditions such as hypertension and cardiovascular disease [76]. On the contrary, no difference in the mortality rates was found between those with obesity and the non-obesity arm [77]. In the study, patients with a BMI between 25 and 29.9 had no significant higher risk of mortality compared to those with a BMI < 25 . However, the odds ratio of mortality in patients with COVID-19 with a BMI ≥ 30 , BMI 35–39.9 and BMI ≥ 40

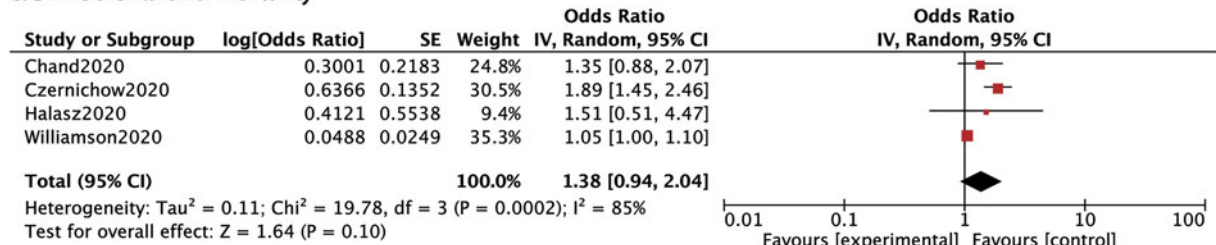
a: BMI 25-29.9 and mortality



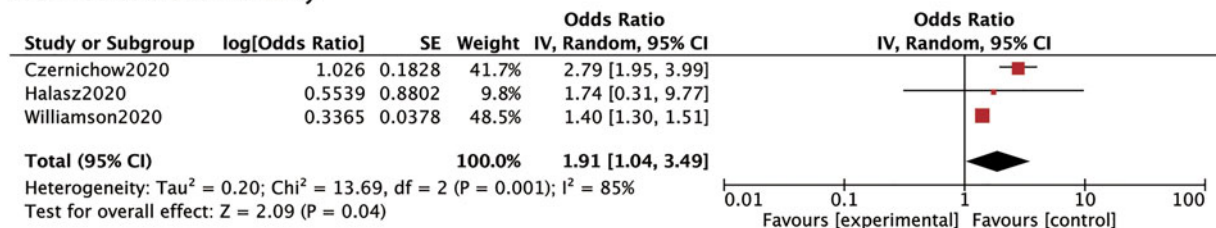
b: BMI ≥ 30 and mortality



c: BMI 30-34.9 and mortality



d: BMI 35-39.9 and mortality



e: BMI ≥ 40 and mortality

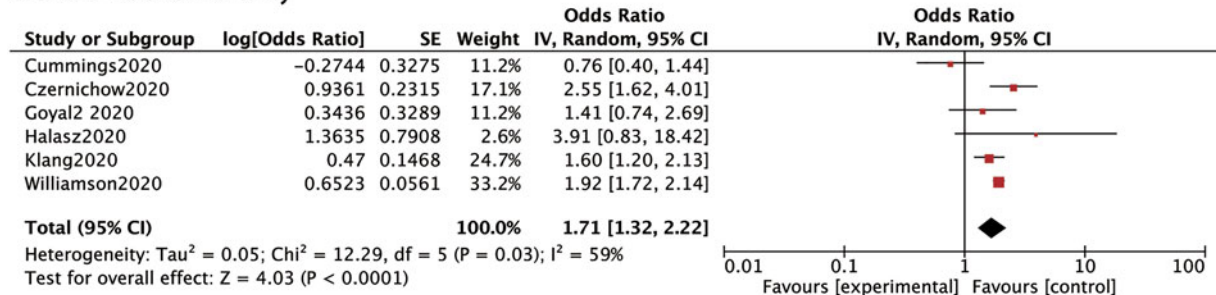


Fig. 6. Forrest plot showing mortality caused by COVID-19: (a) BMI 25–29.9 and mortality, (b) BMI ≥ 30 and mortality, (c) BMI 30–34.9 and mortality, (d) BMI 35–39.9 and mortality, (e) BMI ≥ 40 and mortality.

were 1.65, 1.91 and 1.71, respectively. This suggests a positive relationship between obesity and mortality in patients with COVID-19. Surprisingly, patients with a BMI between 30 and 34.9 did not have a higher mortality risk.

The mechanism behind the finding that overweight or obesity may aggravate COVID-19 remains to be elucidated. Possible mechanisms have been presented in previous studies. Ziegler *et al.* reported that angiotensin-converting enzyme 2 (ACE2)

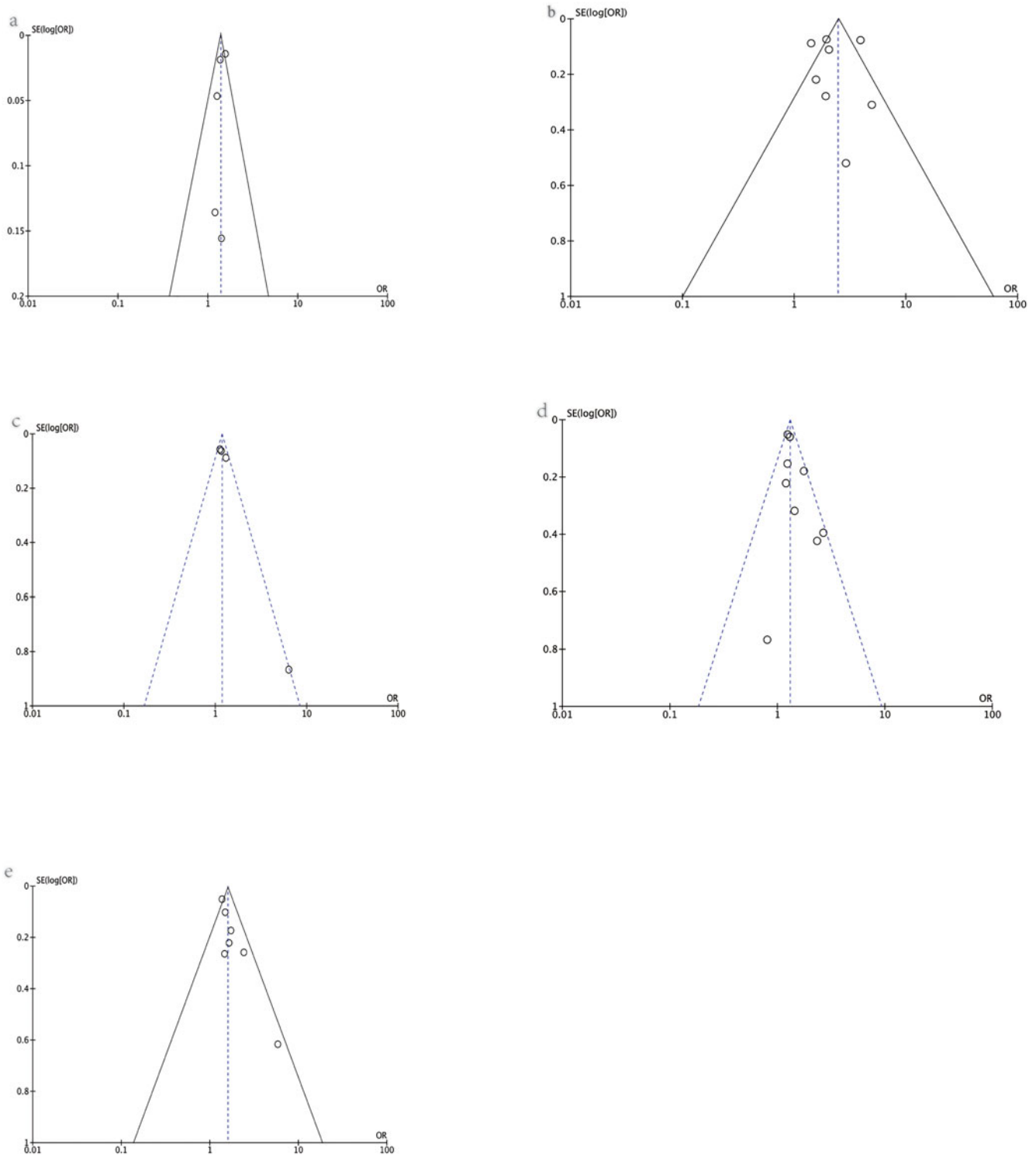


Fig. 7. Funnel plot of various outcomes: (a) risk of COVID-19, (b) hospital admission, (c) severe cases, (d) ICU admission, (e) the need for IMV.

facilitates cellular entry of SARS-CoV-2 [78]. Higher concentrations of ACE2 are not only expressed on lung tissues [79, 80], such as bronchial smooth muscle cells and alveolar epithelium, but also on extrapulmonary tissues, specifically the heart, kidney, ileum, jejunum and adipose tissues [79, 81]. The ACE2 gene-expression profile was assessed in the HCCDB gene-expression database, demonstrating that ACE2 gene expression was higher in

human subcutaneous and visceral adipose tissue than in human lung tissue [82], indicating excess adiposity may induce higher susceptibility of SARS-CoV-2 infection and higher infection severity in patients with COVID-19. Moreover, studies show that obesity disrupts the immune system, limiting its capacity to deal with a new virus like SARS-CoV-2 [83]. In severe cases, patients may have a cytokine storm, characterised by the overproduction of IL-6,

TNF- α , monocyte chemoattractant protein-1 and leptin, resulting in an increased risk of vascular hyperpermeability and multiorgan failure [84, 85]. Besides, respiratory physiology is altered in patients with obesity, resulting in decreased functional residual capacity and expiratory reserve volume, leading to subsequent ventilation–perfusion abnormalities and hypoxaemia [86, 87]. In addition, obesity has been associated with a high risk of developing venous thromboembolism [88], which is frequently reported in COVID-19 cases and is correlated with a poor prognosis [89].

There are some limitations of this study that should be noted. First, most studies included here were retrospective and were conducted in the USA. Additional prospective studies from other countries should be performed to validate the results presented here. Second, patients suffering from a SARS-CoV2 infection with BMI 30–34.9 presented no significant differences in hospitalisation rates, the need for ICU admission, or mortality compared with those without obesity. This might be attributed to the few eligible studies for this group of patients, and further studies are required to confirm these data. Third, we may have excluded some studies from this meta-analysis that reported outcomes related to obesity without mentioning the terms (obesity or overweight or body mass index). Last, experimental parameters such as c-reactive protein, interleukin-6, and coagulation index were not evaluated in this study.

In conclusion, obesity might increase the risk of SARS-Cov2 infection and aggravate the severity of COVID-19.

Conflict of interest. None declared.

Data availability statement. The data that support the findings of this study are openly available in at <http://doi.org/10.1017/S0950268820003027>.

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