Increased COVID-19 Infection Susceptibility and Adverse Outcomes Due to Obesity: A Systematic Review and Meta-analysis

Xiaomin Sun
Xi'an Jiaotong University
Mohsen Mazidi
King's College London
Richard Kirwan
Liverpool John Moores University
Yixuan Li
Xi'an Jiaotong University
Bingtong Zhao
Xi'an Jiaotong University
Jayanthi Kandiah
Ball State University
Youfa Wang (youfawang@gmail.com)
Xi'an Jiaotong University

Research Article

Keywords: COVID-19, body mass index, obesity, mortality

Posted Date: March 3rd, 2021

DOI: https://doi.org/10.21203/rs.3.rs-244649/v1

Abstract

Objectives: Study bidirectional relationships between weight gain, obesity and COVID-19 infection risk during the pandemic.

Methods: MEDLINE, Embase, MedRxiv, and WHO COVID-19 Database were searched till June 2, 2020. Newspaper and internet article sources were identified using a media database. Meta-analysis was conducted using random- and fixed effect models.

Results: Ten studies published from 5 countries met inclusion criteria; five studies (provided 17 analyses/types of results) were included in meta-analysis. The studies suggested bidirectional relationships and some dose-response relationships. Meta-analysis showed obesity was associated with increased COVID-19 infection risk (Odds ratio, OR=1.69, 95% CI: 1.41, 2.02). COVID-19 risk increased with obesity (OR=1.43 (1.18, 1.73)) and severe obesity (OR=1.96 (1.49, 2.59)). Obesity was positively associated with COVID-19 mortality (OR=1.64, 95% CI: 1.20, 2.25) and its severity: admission to intensive care unit (ICU) (OR=2.01 (1.25, 3.23)), and invasive mechanical ventilation (IMV) use (OR=8.20 (2.10, 31.91)). We also observed a stronger association in younger age groups (β=-0.29 (-0.47 to -0.10)).

Conclusions: Obesity was positively associated with higher COVID-19 infection risk, severity, and mortality. Appropriate treatment of COVID-19 patients with obesity and weight management are warranted.

Introduction

As of early June 2020, the SARS-CoV-2 (COVID-19) pandemic has become a global emergency of unprecedented proportions with more than 6.9 million confirmed cases and over 400,000 deaths globally (1). In response to this pandemic, governments are implementing widespread measures to reduce the spread of the disease including quarantine, isolation, social distancing and bans on travel, both domestically and internationally (2, 3). Such measures have affected people's daily life including their eating and physical activity, and thus may affect their body weight as well.

Some initial reports from multiple countries have highlighted obesity amongst COVID-19 infected patients and particularly in more severe cases that were admitted to intensive care units (ICU) (4, 5). Some research suggests that in populations with obesity, more severe degree of obesity classification as defined by body mass index (BMI) ≥35 kg/m^2) was associated with even more serious prevalence of the disease (6), and obesity was associated with greater mortality (7). The US Centers for Disease Control and Prevention (CDC) has suggested that individuals with obesity and conditions which are associated with obesity, are amongst those at greatest risk from COVID-19 (8).

However, the link between obesity and COVID-19 infection are poorly understood, not systematically studied yet. Therefore, a comprehensive review will help shed light on this link by systematically reviewing all the accessible studies in order to provide more clarity to the currently available body of scientific evidence.

Obesity has become a global public health crisis, and the prevalence was nearly tripled between 1975 and 2016 (9, 10, 11). As of 2016, the World Health Organization estimated that over 650 million people globally suffered with obesity indicating that a significant proportion of the population are at elevated risk of COVID-19 complications and mortality (12). This obesity problem is potentially exacerbated by the many measures being used to fight COVID-19, which increase risk for development of obesity. Increased time spent at home, highlighted by mobile phone tracking reports (13), may contribute to reductions in physical activity while increased levels of stress and anxiety brought on by quarantine (14, 15, 16) may result in unhealthy food choices leading to the overconsumption of hyperpalatable and energy dense convenience foods (17).

This study reviewed research on the role obesity plays in susceptibility to COVID-19 and the risk of developing more severe, life-threatening symptoms. We also examined the evidence for the increased risk of weight-gain and subsequent development of obesity during the COVID-19 pandemic. This body of knowledge will aid health care practitioners in deciding whether the use of greater vigilance, and tailoring their testing and treatment practices to individuals with obesity is warranted for better outcomes and reductions in mortality. Information on the role of obesity in COVID-19 progression may also help the public and government agencies in determining whether engaging in activities that can result in lower adiposity or prevent the progression of obesity are likely to result in reduced risk of COVID-19 infection and/or more severe disease symptoms.

Methods And Materials

1. **Study design and data collection**

This systematic review was conducted in accordance with the Preferred Reporting in Systematic Reviews and Meta-Analyses guidelines. MEDLINE (via PubMed), Embase, MedRxiv, and WHO COVID-19 Databases were searched from 1st April, 2020 through 2nd June, 2020. Newspaper and internet article sources were identified using a media database called Nexis (https://www.lexisnexis.com/en-us/products/nexis.page). The key search terms we used included ‘coronavirus OR Severe acute respiratory syndrome OR covid-19 OR nCoV OR COVID OR SARS OR MERS OR middle east respiratory syndrome) AND (Obesity OR BMI OR body mass index OR weight OR overweight.’

To account for papers not yet indexed in databases, we also hand searched COVID-19 resource centers from the following journals and publishers, by manually trawling the collections for relevant titles: BMJ; Cambridge University Press; Elsevier; JAMA Network; The Lancet; New England Journal of Medicine; Oxford University Press; PLOS; Springer Nature; SSRN (reprints); Wiley. There was no restriction on publication type. This search was complemented by an exhaustive review of the bibliography of key articles. Results were restricted to English language articles. All retrieved studies were exported into EndNote to remove duplicates.

2. **Study/report inclusion and exclusion criteria**

All reported studies that reported results on the association between obesity and COVID-19 were included. In addition, the inclusion criteria incorporated entire comprehensive methodological study designs worldwide. We excluded articles that exclusively reported data on other respiratory viruses that did not relate to the COVID-19 clinical or epidemiological aspects, and those not written in English. We excluded editorials, correspondence letters, reviews, qualitative studies, theses, and non-full text articles.

Based on PRISMA guidelines, a flow chart was produced to facilitate transparency of the process (**Figure 1**). In total, 10 studies met our inclusion criteria and were included in this report. Of them, five studies provided adequate data and were included in meta-analysis.

3. **Data extraction**

Two authors independently assessed (screened titles and abstracts, reviewed full reports) the articles for inclusion and exclusion criteria and extracted data, with a third author resolving any differences. The reference lists from all identified studies and reviews were scrutinized for eligible articles. The data extraction was independently checked by the senior author.

The following data were retrieved from each study: country/setting, study sample size, age (mean or range), % of male participants, main findings relating to the association of obesity with outcomes (e.g. Odds ratio, OR), and other information of importance, such as BMI cut-offs used for classifying body weight status including obesity. In addition, in studies related to people's weight gain and obesity related behaviors the following baseline data were gathered from each study: main findings on weight gain and eating habits and physical activity.

4. **Statistical analysis**

Meta-analysis was performed using findings from five studies, which provided needed information to estimate the pooled effects on the associations between COVID-19 and obesity. The OR and 95% confidence interval (CI) were used to determine the associations between COVID-19 and obesity. Study heterogeneity was assessed using the I^2 index. The level of heterogeneity represented by I^2 was interpreted as small ($I^2 \leq 25\%$), moderate ($25\% < I^2 \leq 50\%$), substantial ($50\% < I^2 \leq 75\%$), or considerable ($I^2 > 75\%$). In our meta-analysis, a fixed-effect model was estimated when modest to moderate heterogeneity was present, and a random-effects model was estimated when substantial to considerable heterogeneity was present. Additionally, meta-regression analyses were performed in order to determine whether subjects' age (in years), and gender (male) could be related with the associations between COVID-19 and obesity.

To investigate potential sources of heterogeneity, subgroup analyses were performed based on categorical variables including country, study design, obesity classification and the severity of COVID-19. In this review, obesity classification based on BMI was defined as: 1) obesity; 2) severe obesity. The severity of COVID-19 was classified as: 1) COVID-19 admission; 2) ICU admission; 3) IMV use; 4) acute care admission; and 5) death by COVID-19.

A pre-specified sensitivity analysis was conducted to investigate the influence of a single study on the overall pool estimate by omitting one study in each turn. Publication bias was assessed by visual inspection of the funnel plot and Begg's and Egger's tests.

All statistical analyses were conducted using the Stata software version 14 (Stata Corp., College Station, Texas, USA). All analyses used two-sided tests, and p-values $<$0.05 were considered statistically significant.

Results

1. **Characteristics of the included studies**

The characteristics of the 10 included studies are summarized in **Table 1**. These studies were published in the months of April and May 2020 from 5 countries, including China (2 studies), France (2 studies), Italy (1 study), the United Kingdom (3 studies), and the United States (2 studies). The sample size of these studies varied greatly, ranging from 41 to 17,425,445. Nine studies focused specifically on COVID-19 and obesity, and one study investigated obesity related behaviors (e.g., eating and physical activity).

The study design and populations were diverse. There were 8 cohort studies, 1 cross-sectional study and 1 case report. These studies included retrospective analysis of primary care electronic health records in the general population (1 study), retrospective analysis of cohorts of COVID-19 patients (5 studies), and prospective observational cohort studies (3 studies). The duration of data collected from these studies ranged from 1 week (2 studies), to 3 weeks (3 studies), 4 weeks (1 study), 6 weeks (1 study), 10 weeks (1 study) and 12 weeks (1 study). Some studies only included adults while others incorporated children. Subjects' ages ranged from 0 to 104 years.

Only one study examined the influence of COVID-19 on obesity-related behaviors. This was a longitudinal observational study in Italy with 41 children. It reported changes in eating, physical activity and inactivity behaviors.

2. **Effect of obesity on COVID-19 infection risks**

Nine studies provided results regarding the association between obesity and COVID-19 infection and severity risks. Three studies reported that obesity was more prevalent amongst COVID-19 infected patients. In a retrospective cohort study of SARS-CoV-2 confirmed patients, compared with a non-SARS-CoV-2-infected patient control group, Simonnet et al (4) observed that obesity (BMI 30-34.9kg/m^2) and severe obesity (BMI ≥35 kg/m^2) were significantly more frequent among COVID-19 infected patients than controls (47.6% vs 25.2% and 28.2% vs 10.8%, respectively). Williamson et al (18) used data from over 17 million UK National Health Service primary care records and observed that the incidence of COVID-19 advanced with increasing severity of obesity. They reported a dose-response relationship between degree of obesity and COVID-19 infection risk. Assuming non-obese individuals had a hazard ratio (HR) of 1.00, the fully adjusted HRs for obesity class I (BMI 30-34.9kg/m^2), obesity class II (BMI 35-39.9kg/m^2) and obesity class III (BMI ≥40 kg/m^2) were 1.27, 1.56 and 2.27, respectively. An intensive care admissions report of confirmed COVID-19 cases from the Intensive Care National Audit and Research Centre (19) showed the majority of ICU admissions (71.7%) also suffered from overweight or obesity. Specifically, 31.6% of ICU admissions had overweight (BMI 25-29.9kg/m^2), 32.8% had moderate obesity (BMI 30-39.9kg/m^2) and 7.3% had severe obesity (BMI ≥40 kg/m^2).

Six studies from different countries reported on the association between obesity and severity of COVID-19 infection based on varying criteria such as admission to acute or critical care such as ICU or requirement for IMV. Overall, they suggested a positive assocatoin. In a study of 291 French patients admitted to ICU for SARS-CoV-2, Caussy et al (20) observed a doubled risk of requirement for IMV in severe obese- (BMI ≥35 kg/m^2) compared to lean patients (81.8% versus 41.9%). In a retrospective analysis of COVID-19 hospitalized patients in Wuhan, China, Hu et al (21) observed that while obesity (BMI ≥30 kg/m^2) was not associated with diagnosis of disease severity (p=0.522), it was significantly associated with unfavorable clinical outcomes (OR=3.6, p=0.009). In a retrospective cohort study of 103 US patients admitted for COVID-19, Kalligeros et al (6) observed that obesity was associated with the severity of COVID-19 presentation. Severe obesity was associated with admission to ICU (adjusted OR=5.39) while obesity and severe obesity were associated with the need for IMV (adjusted OR=6.85 and 9.99, respectively). Similarly, Lighter et al (5) performed a retrospective analysis of COVID-19 patients in a New York hospital and found that in those under 60 years old, patients with obesity (BMI 30-34.9kg/m^2) and severe obesity (BMI 35-39.9kg/m^2) had a greater risk of admission to acute care (OR 2.0 and 2.2, respectively) and admission to ICU (OR 1.8 and 3.6, respectively). A similar trend was also observed in a French cohort (4) as its multivariate regression analysis showed OR for requirement for IMV was 7.36 in patients with BMI ≥35 kg/m^2 compared with those with BMI <25 kg/m^2 (p=0.021). Another study from China of patients with metabolic associated fatty liver disease (22) reported a significant association between overweight/obesity (BMI ≥25 kg/m^2) and COVID-19 severity even after adjusting for age, sex, smoking, diabetes, hypertension, and dyslipidemia (adjusted OR=6.32, p=0.033).

One study reported the association between obesity and COVID-19 mortality. Data from about 17,000 COVID-19 patients in the UK showed that any form of obesity (as defined by hospital staff) was associated with a 37% greater risk of COVID-19 mortality (HR=1.37). (7) Note that in the study from China, Hu et al (21) included death, along with progression to more severe disease presentation, in their criteria they found unfavorable outcomes, indicating mortality data alone was insufficient from this study.

2. **Effect of COVID-19 on obesity-related behaviors**

Only one published study investigated the effect of COVID-19 on obesity-related behaviors such as eating and physical activity. A longitudinal study of lifestyle factors involving 41 children and adolescents with obesity was based in Verona, Italy. Compared with previous data, lockdown was associated with an increase in number of meals a day (+1.15), an increase in number of servings of potato chips, red meat and sugary drinks (+0.54, 1.66 and 0.5, respectively), an increase in screen time and sleep time (+4.85 hours and +0.65 hours, respectively) and a decrease in time dedicated to sports (-2.3 hours/week). Therefore, more research on this topic is needed.

3. **Meta-analysis of the associations between COVID-19 and obesity**

Figure 2 and **Table 2** show that five studies (which provided 17 analyses and types of results) were included in the meta-analysis. The overall pooled analysis showed that obesity was associated with increased risk of COVID-19 infection (OR=1.69, 95% CI: 1.41, 2.02), and with large heterogeneity (I^2= 87.3%, χ^2=126.48, p< 0.001). The ORs reported by the individual studies ranged from 0.90 to 9.99.

Our subgroup analyses showed between-country differences in the associations between obesity prevalence and COVID-19 (**Table 2**): in the US (OR=1.80, 95% CI: 1.32, 2.46), the UK (OR=1.57, 95% CI: 1.23, 2.02), and China (where national obesity/overweight prevalence was much lower than that in the US and the UK) (OR=6.32, 95% CI: 1.16, 34.48). When stratified by study design, obese/overweight people had 1.66 times higher risk of getting COVID-19 infection than those non-overweight (OR=1.66, 95% CI: 1.39, 1.99) in cohort studies. In contrast, in a cross-sectional study, the reported OR for obese patients was 6.32 (95% CI: 1.16, 34.48). When stratified by obesity classifications, obesity (OR=1.43, 95% CI: 1.18, 1.73) and severe obesity (OR=1.96, 95% CI: 1.49, 2.59) were positively associated with COVID-19 risk, and obesity was positively associated with COVID-19 mortality (OR=1.64, 95% CI: 1.20, 2.25) and its severity: ICU (OR=2.01, 95% CI: 1.25, 3.23), and IMV use (OR=8.20, 95% CI: 2.10, 31.91).

Meta-regression analysis indicated that age affected the association between obesity and COVID-19 infection (β=-0.29; 95%: -0.47 to -0.10), but not gender (**Table 3**).

4. **Sensitivity analysis and assessment of publication bias**

The sensitivity analysis consistently showed that removing individual studies from the meta-analysis did not change the association estimate (**Supplemental Table 1**). The funnel plot and assessment of Egger's and Begg's tests did not reveal any significant publication bias in the association (Egger P=0.148; Begg P=0.343) (**Figure 3**).

Discussion

We systematically investigated the relationship between obesity and COVID-19 infection risk and severity. This included an examination of the risk of weight-gain and subsequent development of obesity due to government mandated containment measures. The results indicated that obesity and in particular, severe obesity are consistently and significantly associated with elevated risk of COVID-19 (our meta-analysis showed that OR=1.43 and 1.96, respectively). Obesity was also associated with an increased risk of developing more severe COVID-19 symptomology, such as admission to acute care, admission to ICU (OR=2.01), use of IMV (OR=8.20), and mortality (OR=1.64). Meta-regression also revealed that age was an important mediating factor and negatively associated with the association between COVID-19 and obesity. The association was stronger in younger people. Given the high prevalence of overweight and obesity globally, these results indicate that a large proportion of the world population may be at an increased risk of COVID-19 complications and mortality (12).

To prevent the spread of COVID-19, the unprecedented response of global governments has included measures such as quarantine, isolation, social distancing and travel bans (2, 3) which may result in an extended period of time spent in one's home. Such time in quarantine is known to result in negative emotions such as fear, nervousness and sadness (23) and eating is a known coping mechanism for dealing with stress and negative emotions (24, 25). Thus, this increased likelihood of stress eating, combined with potentially increased use of hyperpalatable, calorie-dense ultra-processed foods (26, 27, 28) which may be preferentially purchased in times of anticipated food emergency (29), may lead to overeating, body fat gain and the further development of obesity in the population. Indeed some of these obesity-promoting behaviors (increased consumption of UPFs, increased screen time and reduced physical activity) were observed in only one study to document such behaviors during a COVID-19 lockdown scenario (30). However, very limited research has reported about the impact of such measures on obesity-related behaviors such as eating and physical activity.

It is worth noting that the meta-regression revealed that age is a moderator in the association between obesity and COVID-19, which means the association of obesity and COVID-19 was greater in younger age groups. Compared with the elderly, younger people were unlikely to have diabetes, stroke and other chronic diseases, and are general considered a lower-risk group for COVID-19. Nevertheless, some studies and reports have pointed to obesity being a notable risk for COVID-19, especially among younger patients (5, 31).

The proposed mechanism by which obesity may augment the risks of COVID-19 infection and severity is yet to be elucidated, but may be multifaceted. Physically, those with obesity carry excess adipose tissue and in particular, central/abdominal distribution of this adipose tissue can make breathing more difficult, resulting in less oxygen from respiration entering the blood (32). It is known that SARS-CoV-2 gains cellular entry via the angiotensin converting enzyme 2 (ACE2) receptor (33). Highman et al observed increased ACE2 expression in the bronchial epithelium of chronic obstructive pulmonary disease (COPD) patients who are overweight compared to those not overweight, which may be a route for increased SARS-CoV-2 infection of the respiratory tract (34). Obesity patients are known to have chronically higher leptin (and lower adiponectin) concentrations resulting in an unfavorable, pro-inflammatory hormonal milieu which may lead to a dysregulation of the immune response and lead to obesity-linked complications in COVID-19 (35). Similarly, those with obesity typically have chronically elevated levels of pro-inflammatory cytokines, such as Tumor Necrosis Factor- alpha, Monocyte Chemoattractant Protein-1 and Interleukin-6, which can contribute to defective innate immunity (36). Lower levels of physical activity, which may be more likely observed in individuals with obesity, may also contribute to increased risk as regular physical activity improves immune function (37).

The implications of these results are significant for the general population. One also needs recognize that those with obesity may suffer from the additional burden of weight bias and stigma (38). During this COVID-19 pandemic, the acknowledgment of obesity as a risk factor for COVID-19 might led to fat-shaming amongst the general public and, in particular, on social media. Therefore, efforts need be made to prevent weight stigma. The ultimate risk of such weight stigma is that those with obesity may avoid healthcare services even when suffering symptoms of COVID-19, which may lead to a worsening of their condition and predisposing them to other chronic diseases, and post risks to others.

Obesity is considered a top public health concern, and the prevalence was nearly tripled from 1975 to 2016 (9, 10, 11). In 2016, 39% of adults worldwide were overweight, and 13% were obese (12). In addition to obesity-related many other non-communicable chronic diseases, our study indicated that having obesity will increase the risk of contracting COVID-19, its severity and mortality. Thus, countries like the US where the prevalence of overweight and obesity has reached nearly 70% and the reported COVID-19 cases are greater than 1.1 million, government agencies and health care professionals need to take extra effort to encourage their citizens with overweight/obesity issues to take extra precautions against COVID-19.

Our findings also support the importance of the ongoing efforts worldwide in fighting the global obesity epidemic. There are major concerns that the obesity epidemic will become worse with the many dramatic changes in people's daily life, including reduced physical activity and over-consumption of unhealthy food and reduced consumption of fresh vegetables and fruits. Many sectors in the society need pay attention on such issues while they are taking efforts to fight COVID-19 and save lives.

Regarding the limitations of the individual studies used in this review, many of the studies included in this article were single-center studies which increases the likelihood of admission bias and selection bias between studies. Furthermore, due to the urgent nature of the pandemic many of the included studies did not clarify their inclusion criteria, nor did they provide specific details on the severity of disease presentation. In addition, some of the included studies were retrospective studies, therefore the influence of other confounding factors cannot be ruled out. Finally, the heterogeneous nature of the reported studies must be noted. Further, investigation is required to determine the impact of body composition (adipose tissue/fat-free mass/muscle) on clinically relevant outcomes such as hospitalization, severity of disease and mortality associated with COVID-19, as well as the mechanisms involved, which may help improve COVID-19 treatment strategies.

This study has several important strengths. It is the first study to comprehensively investigate the link between COVID-19 and obesity. Second, we analyzed data from multiple nations and different ethnicities, which may improve the generalizability of the findings to other populations. Third, we conducted meta-analysis and meta-regression analysis. Combining those results with those of the larger data sets, makes our conclusions more robust. Finally, our findings are timely and will help guide ongoing public health efforts, to contain COVID-19 and save lives.

In conclusion, obesity is positively associated with a greater risk of COVID-19 infection and there is a dose-response relationship, while age is mediating factor. Obesity is also associated with increased severity of COVID-19 infection outcomes including like admission to ICU, requirement for IMV and death. These findings highlight the need for early detection and appropriate treatment of COVID-19 in patients with obesity. They also demonstrate the importance of obesity prevention. Government agencies and policy makers should consider the potential negative health repercussions induced by altered lifestyle behaviors during COVID-19 lockdowns and how best to reduce the risk of obesity development.

Abbreviations

ACE2, angiotensin converting enzyme 2; BMI, body mass index; CDC, The Center for Disease Control and Prevention; CI, confidence interval; HR, hazard ratio; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; IMV, invasive mechanical ventilation; OR, Odds ratio, aOR, adjusted OR.

Declarations

Acknowledgement

The authors would like to thank the study participants and collaborators and staff members who have contributed to the study. In particular, we would like to thank other collaborators, Professors Shiyong Liu and Peng Nie and Mrs Lihua Yan and Guorui Ruan.

Author contributions

YW and MM contributed to the study design, data collection, and drafting the manuscript. XS, YL, BZ and RK contributed to the meta-analysis and drafting of the manuscript. All authors contributed to interpretation of the data, commented on and revised the report, and approved the final version for publication.

Sources of Funding

The project is supported in part by research grants from the China Medical Board (Grant number: 16-262), the University Alliance of the Silk Road (Grant number: 2020LMZX002) and Xi’an Jiaotong University Global Health Institute.

Potential Conflicts of Interest: None

Funding

The project is supported in part by research grants from the China Medical Board (Grant number: 16-262), the University Alliance of the Silk Road (Grant number: 2020LMZX002) and Xi'an Jiaotong University Global Health Institute

Potential Conflicts of Interest: None

Author contributions

YW and MM contributed to the study design, data collection, and drafting the manuscript. XS, YL, BZ and RK contributed to the meta-analysis and drafting of the manuscript. All authors contributed to interpretation of the data, commented on and revised the report, and approved the final version for publication.

References

1. WHO. WHO Coronavirus Disease (COVID-19) Dashboard 2020. Available from: https://covid19.who.int/.
2. Parmet WE, Sinha MS. Covid-19 — The Law and Limits of Quarantine. *New England Journal of Medicine* 2020;**382:** e28.
3. Sjödin H, Wilder-Smith A, Osman S, Farooq Z, Rocklöv J. Only strict quarantine measures can curb the coronavirus disease (COVID-19) outbreak in Italy, 2020. *Euro Surveill* 2020;**25**.
4. Simonnet A, Chetboun M, Poissy J, Raverdy V, Noulette J, Duhamel A*, et al.* High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. *Obesity (Silver Spring)* 2020.
5. Lighter J, Phillips M, Hochman S, Sterling S, Johnson D, Francois F*, et al.* Obesity in patients younger than 60 years is a risk factor for Covid-19 hospital admission. *Clin Infect Dis* 2020.
6. Kalligeros M, Shehadeh F, Mylona EK, Benitez G, Beckwith CG, Chan PA*, et al.* Association of Obesity with Disease Severity among Patients with COVID-19. *Obesity (Silver Spring)* 2020.
7. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L*, et al.* Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. *medRxiv* 2020**:** 2020.2004.2023.20076042.
8. CDC. Groups at Higher Risk for Severe Illness 2020 [May 14th, 2020]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/groups-at-higher-risk.html.
9. Wang Y, Beydoun MA, Min J, Xue H, Kaminsky LA, Cheskin LJ. Has the prevalence of overweight, obesity and central obesity levelled off in the United States? Trends, patterns, disparities, and future projections for the obesity epidemic. *Int J Epidemiol* 2020.
10. Wang Y, Wang L, Qu W. New national data show alarming increase in obesity and noncommunicable chronic diseases in China. *Eur J Clin Nutr* 2017;**71:** 149-150.
11. Y W, M S, Y Y. China blue book on obesity prevention and control. Beijing, 2018.
12. WHO. WHO Obesity and Overweight Factsheet 2020. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.
13. Google. COVID-19: Community Mobility Report 2020 [May 14, 2020]. Available from: https://www.google.com/covid19/mobility/.

14. Blendon RJ, Benson JM, DesRoches CM, Raleigh E, Taylor-Clark K. The public's response to severe acute respiratory syndrome in Toronto and the United States. *Clin Infect Dis* 2004;**38:** 925-931.
15. Jeong H, Yim HW, Song YJ, Ki M, Min JA, Cho J*, et al.* Mental health status of people isolated due to Middle East Respiratory Syndrome. *Epidemiol Health* 2016;**38:** e2016048.
16. Lei L, Huang X, Zhang S, Yang J, Yang L, Xu M. Comparison of Prevalence and Associated Factors of Anxiety and Depression Among People Affected by versus People Unaffected by Quarantine During the COVID-19 Epidemic in Southwestern China. *Med Sci Monit* 2020;**26:** e924609.
17. Gibson EL. Emotional influences on food choice: sensory, physiological and psychological pathways. *Physiol Behav* 2006;**89:** 53-61.
18. Williamson E, Walker AJ, Bhaskaran KJ, Bacon S, Bates C, Morton CE*, et al.* OpenSAFELY: factors associated with COVID-19-related hospital death in the linked electronic health records of 17 million adult NHS patients. *medRxiv* 2020**:** 2020.2005.2006.20092999.
19. ICNARC. ICNARC report on COVID-19 in critical care ICNARC, 2020.
20. Caussy C, Wallet F, Laville M, Disse E. Obesity is associated with severe forms of COVID-19. *Obesity (Silver Spring)* 2020.
21. Hu L, Chen S, Fu Y, Gao Z, Long H, Wang JM*, et al.* Risk Factors Associated with Clinical Outcomes in 323 COVID-19 Hospitalized Patients in Wuhan, China. *Clin Infect Dis* 2020.
22. Zheng KI, Gao F, Wang XB, Sun QF, Pan KH, Wang TY*, et al.* Obesity as a risk factor for greater severity of COVID-19 in patients with metabolic associated fatty liver disease. *Metabolism* 2020;**108:** 154244.
23. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N*, et al.* The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet* 2020;**395:** 912-920.
24. Solomon MR. Eating as both coping and stressor in overweight control. *J Adv Nurs* 2001;**36:** 563-572.
25. Timmerman GM, Acton GJ. The relationship between basic need satisfaction and emotional eating. *Issues Ment Health Nurs* 2001;**22:** 691-701.
26. Schulte EM, Avena NM, Gearhardt AN. Which foods may be addictive? The roles of processing, fat content, and glycemic load. *PLoS One* 2015;**10:** e0117959.
27. David IA, Krutman L, Fernandez-Santaella MC, Andrade JR, Andrade EB, Oliveira L*, et al.* Appetitive drives for ultra-processed food products and the ability of text warnings to counteract consumption predispositions. *Public Health Nutr* 2018;**21:** 543-557.
28. Hall KD, Ayuketah A, Brychta R, Cai H, Cassimatis T, Chen KY*, et al.* Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake. *Cell Metab* 2019;**30:** 67-77.e63.
29. Moran AJ, Khandpur N, Polacsek M, Rimm EB. What factors influence ultra-processed food purchases and consumption in households with children? A comparison between participants and non-participants in the Supplemental Nutrition Assistance Program (SNAP). *Appetite* 2019;**134:** 1-8.
30. Pietrobelli A, Pecoraro L, Ferruzzi A, Heo M, Faith M, Zoller T*, et al.* Effects of COVID-19 Lockdown on Lifestyle Behaviors in Children with Obesity Living in Verona, Italy: A Longitudinal Study. *Obesity (Silver Spring)* 2020.
31. Kass DA, Duggal P, Cingolani O. Obesity could shift severe COVID-19 disease to younger ages. *Lancet* 2020;**395:** 1544-1545.
32. Dixon AE, Peters U. The effect of obesity on lung function. *Expert Rev Respir Med* 2018;**12:** 755-767.
33. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W*, et al.* A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020;**579:** 270-273.

34. Higham A, Singh D. Increased ACE2 Expression in the Bronchial Epithelium of COPD Patients who are Overweight. *Obesity (Silver Spring)* 2020.
35. Ouchi N, Parker JL, Lugus JJ, Walsh K. Adipokines in inflammation and metabolic disease. *Nat Rev Immunol* 2011;**11:** 85-97.
36. Richard C, Wadowski M, Goruk S, Cameron L, Sharma AM, Field CJ. Individuals with obesity and type 2 diabetes have additional immune dysfunction compared with obese individuals who are metabolically healthy. *BMJ Open Diabetes Research and Care* 2017;**5:** e000379.
37. Zheng Q, Cui G, Chen J, Gao H, Wei Y, Uede T*, et al.* Regular Exercise Enhances the Immune Response Against Microbial Antigens Through Up-Regulation of Toll-like Receptor Signaling Pathways. *Cell Physiol Biochem* 2015;**37:** 735-746.
38. Rubino F, Puhl RM, Cummings DE, Eckel RH, Ryan DH, Mechanick JI*, et al.* Joint international consensus statement for ending stigma of obesity. *Nat Med* 2020;**26:** 485-497.

Tables

Table 1. Main characteristics of studies and related findings on the associations between COVID-19 and obesity

Study ID	First author Publication Year	Country/ setting	Study design	Study sample size	Age (mean, median or range) (years)	Males (%)	Main findings on the associations, e.g. ORs 95%CI	Note: How obesity was measured
A. Associations between COVID-19 and obesity								
1	Hu et al, 2020	China	Cohort study	323	Mean 61 (range: 23-91)	51.4	Obesity prevalence: All patients: 4%, Non-severe cases: 3.8%, Severe cases: 4.3%, Critical cases 8% Outcome unfavorable: 10.7%, Favorable: 2.9%.	Obesity (BMI >30 kg/m^2).
2^	Zheng et al, 2020	China	Cross-sectional study	66	Mean 47 (range:18-75)	25.8	Compared to those with non-severe COVID-19, patients with severe disease were more obese (89.5% vs. 59.6%, p = 0.021). Association with obesity and COVID-19 severity (adjusted-OR 6.32, 95% CI 1.16–34.54).	Obesity: BMI >25 kg/m^2. All had metabolic associated fatty liver disease.
3	Caussy et al, 2020	France	Cohort study	291	NA	NA	Higher requirement for IMV in severe obesity ≥35 kg/m^2 compared to lean patients: 81.8% versus 41.9%, p=0.001.	Severe obesity: BMI ≥35 kg/m^2.
4	Simmonet et al, 2020	France	Cohort study	124	Median 60 (range: 51- 70)	73.0	Obesity and severe obesity were significantly more frequent	Obesity (BMI >30 kg/m^2) ; Class II obesity

							among SARS-CoV-2 participants than in non SARS-CoV-2 controls: 47.6% vs 25.2% and 28.2% vs 10.8%, respectively. Admission to ICU: 47.5% presented with obesity, including class II obesity in 13.7% and with class III obesity in 14.5%.	(BMI 35-39.9 kg/m^2); Class III obesity (BMI ≥40 kg/m^2).
5^	Docherty et al, 2020	UK	Cohort study	16,749	Median 72 (range: 0-104)	60.2	Mortality All obesity 1.37 (1.16-1.63, p<0.001).	as recognized by clinical staff
6	ICNARC	UK	Case report	196	Median 64 (range: 52-73)	70.9	28.6% of patients had a BMI of 25-30, 29.6% had a BMI of 30-40 and 6.6% had a BMI of 40 or higher.	Obesity (BMI >30 kg/m^2).
7^	Kalligeros et at, 2020	USA	Cohort study	103	Median 60 (range: 52-70)	61.1	1) Admission to ICU: obesity (aOR:2.65; 95% CI 0.64-10.95); and severe obesity (aOR: 5.39; 95% CI1.13-25.64). 2) Use of IMV: obesity (aOR: 6.85; 95% CI 1.05-44.82); and severe obesity (aOR: 9.99; 95% CI 1.39-71.69).	Obesity (BMI 30-34.9 kg/m^2); Severe obesity (BMI≥35 kg/m^2).
8^	Lighter et al, 2020	USA	Cohort study	3,615	<60 and ≥60	NA	1) <60 years: Admission to acute care:	Obesity BMI 30-34 kg/m^2;

							obesity OR: 2.0 (95% CI 1.6-2.6), and severe obesity OR: 2.2 (95% CI 1.7-2.9). Admission to ICU: obesity OR: 1.8 (95% CI 1.2-2.7), and severe obesity OR: 3.6 (95% CI 2.5-5.3). 2) ≥60 years Admission to acute care: obesity OR: 0.9 (95% CI 0.6-1.2), and severe obesity OR: 0.9 (95% CI 0.6-1.3). Admission to ICU: obesity OR: 1.1 (95% CI 0.8-1.7), and severe obesity OR: 1.5 (95% CI 0.9-2.3).	Severe obesity BMI >35 kg/m^2.
9^	Williamson et al, 2020	UK (England)	Cohort study	17,425,445 (5,683 COVID-19 deaths)	>18	49.9	Incidence Not obese 1.00 (ref) Obese class I: 1.27 (1.18-1.36); Obese class II: 1.56 (1.41-1.73); Obese class III: 2.27 (1.99-2.58).	Obese class I (30-34.9kg/m^2) Obese class II (35-39.9kg/m^2) Obese class III (≥40 kg/m^2)
B. Obesity related behaviors (e.g. eating and physical activity)								
10	Pietrobelli et al, 2020	Italy	Cohort study	41	Mean 13.0±3.1 (range: 6-18)	53.7	1) Meals (#/day) change: 1.15±1.56; 95% CI: 0.65/1.64	Baseline BMI was about 30.5 kg/m^2 in males and 29.7 kg/m^2 in females

	2) Potato chips change: 0.54±0.86; 95% CI: 0.26/0.81 3) Red meat change: 1.66±2.10; 95% CI: 1.00/2.32 4) Sugary drinks (#/day) change: 0.50±1.08; 95% CI: 0.16/0.84 5) Screen time (hrs/day) change: 4.85±2.40; 95% CI: 4.10/5.61 6) Sleep time (hrs/day) change: 0.65±1.29; 95% CI: 0.24/1.05 7) Sports (hrs/week) change: -2.30±4.60; 95% CI: -3.76/-0.85

Abbreviation: CI: confidence intervals; ICU: Intensive Care Unit; IMV: Invasive Mechanical Ventilation; COVID-19: Coronavirus Disease 2019; aOR, adjusted OR; WHO: World Health Organization.

^ These studies were included in our meta-analyses, because the effect sizes (OR and 95% CI) were reported.

Table 2. Overall results of meta-analysis and sub-group analysis of the associations between COVID-19 and obesity

	Number of studies/ Analyses*	Effect size (95%CI)	P value	Heterogeneity			
				I^2 (%)	χ^2	P value	Tau-squared
Total	17	1.69 (1.41, 2.02)	<0.001	87.3	126.48	<0.001	0.0838
Country							
USA	12	1.80 (1.32, 2.46)	<0.001	80.7	57.12	<0.001	0.1945
UK	4	1.57 (1.23, 2.02)	<0.001	95.1	61.29	<0.001	0.0605
China	1	6.32 (1.16, 34.48)	0.033	…	…	…	…
Study design							
cohort study	16	1.66 (1.39, 1.99)	<0.001	87.9	123.73	<0.001	0.0826
cross-sectional study	1	6.32 (1.16, 34.48)	0.033	…	…	…	…
Obesity classifications							
obesity	9	1.43 (1.18, 1.73)	<0.001	71.0	27.56	0.001	0.0417
severe obesity	8	1.96 (1.49, 2.59)	<0.001	86.7	52.55	<0.001	0.0997
COVID-19 severity							
COVID-19 admission	2	2.31 (0.56, 9.56)	0.248	67.6	3.09	0.079	0.7903
ICU admission	6	2.01 (1.25, 3,23)	0.004	77.4	22.16	<0.001	0.2290
IMV use admission	2	8.20 (2.10, 31.91)	0.002	0.0	0.07	0.786	0.0000
Acute care admission	4	1.40 (0.88, 2.22)	0.155	89.2	27.79	<0.001	0.1956
The death of COVID-19	3	1.64 (1.20, 2.25)	0.002	96.7	60.57	<0.001	0.0740

Abbreviation: CI: confidence intervals; ICU: Intensive Care Unit; IMV: Invasive Mechanical Ventilation; COVID-19: Coronavirus Disease 2019.

*Results from five studies (reported 17 analyses, including for different related outcomes and subgroups) were included in the meta-analysis. A fixed-effect model was fit when modest to moderate heterogeneity was present, and a random-effects model was fit when substantial to considerable heterogeneity was present.

Table 3. Results of meta-regression analyses of age and gender differences on the association between COVID-19 and obesity*

	β	95% CI	P-value	R^2
Age	-0.29	-0.47, -0.10	0.005	26.01
Gender	0.01	-0.15, 0.17	0.859	

*Meta-regression analyses based on results from five studies were performed to determine whether subjects' age (in years) and gender (% of males) affected the association between COVID-19 and obesity.

Figures

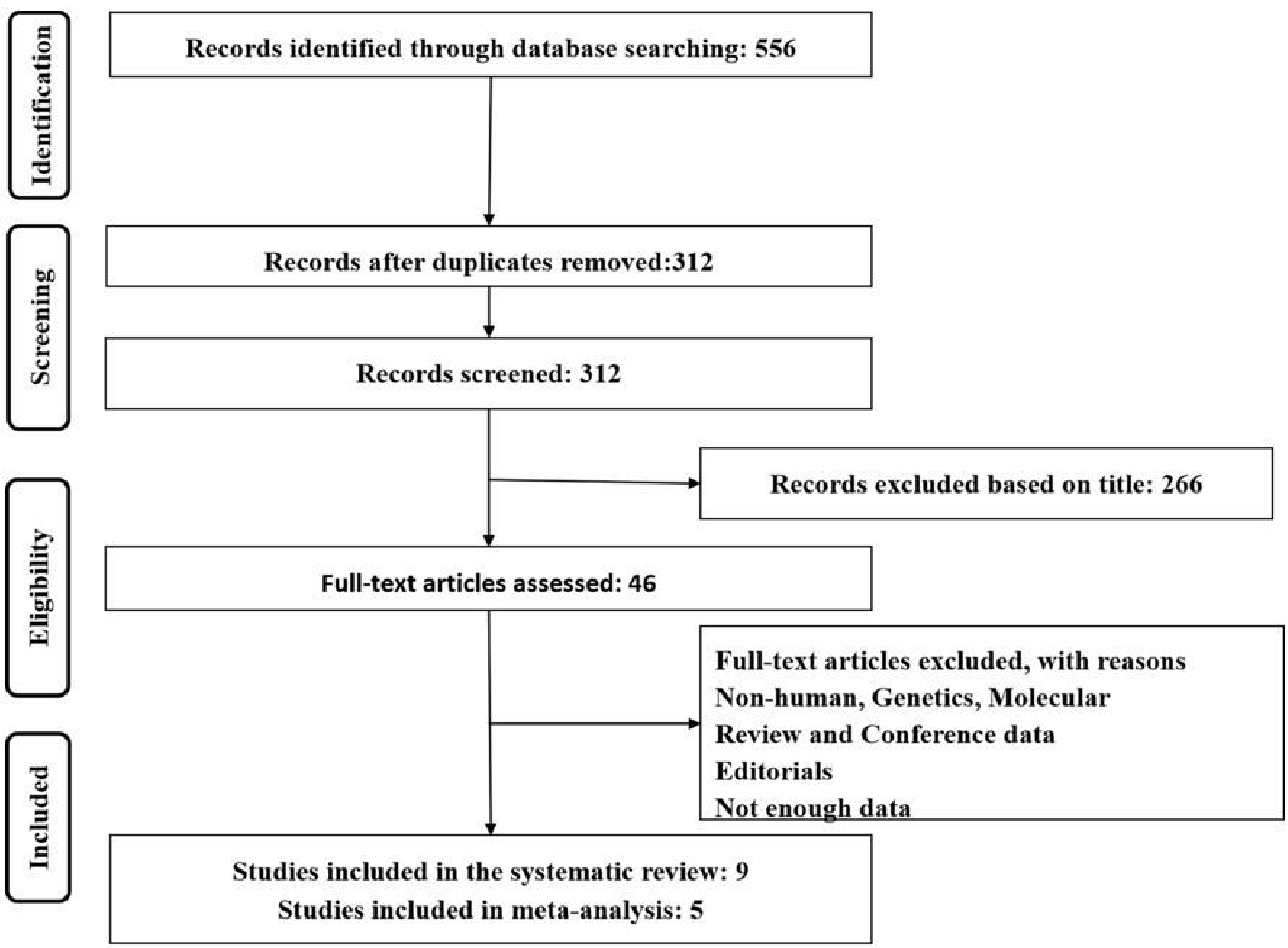
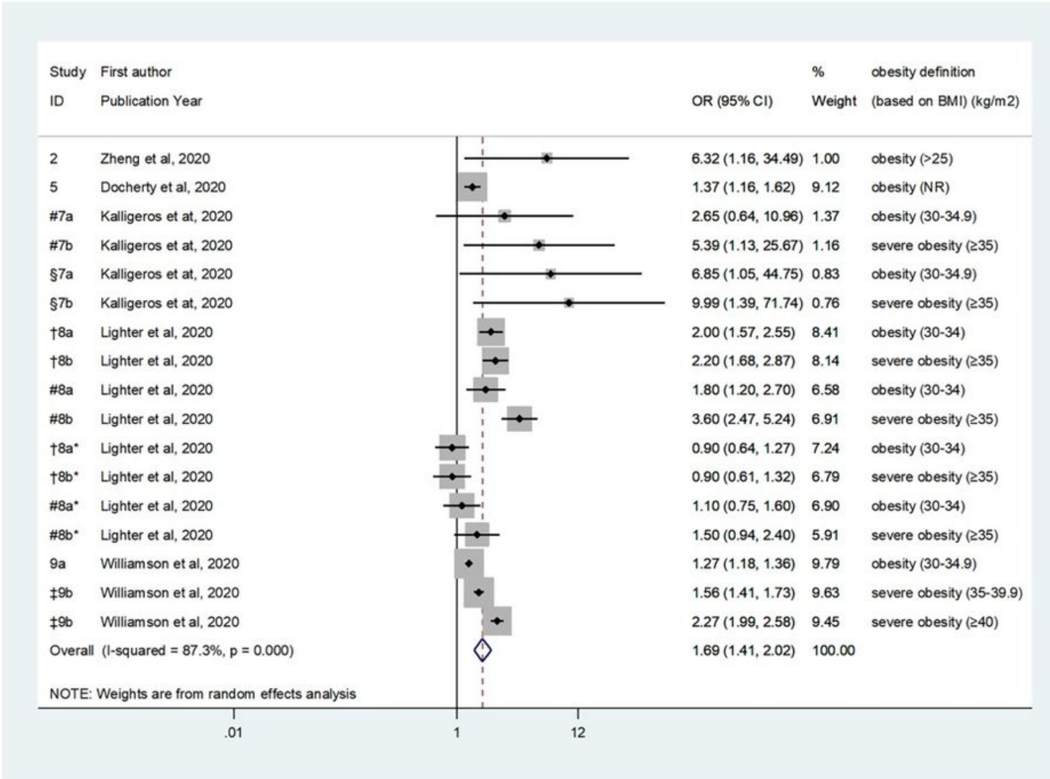


Figure 1

Flow chart diagram of studies selected for investigating the relationship between obesity and Covid-19



Five studies (17 analyses) were included. A fixed-effect model was estimated when modest to moderate heterogeneity was present, and a random-effects model was estimated when substantial to considerable heterogeneity was present.

a. obesity; b. severe obesity.

‡ Severe obesity was divided into two categories in this article: severe obesity I (35-39.9 kg/m^2) and II (≥40 kg/m^2).

The COVID-19 patients in these articles needed Intensive Care Unit (ICU) admission;

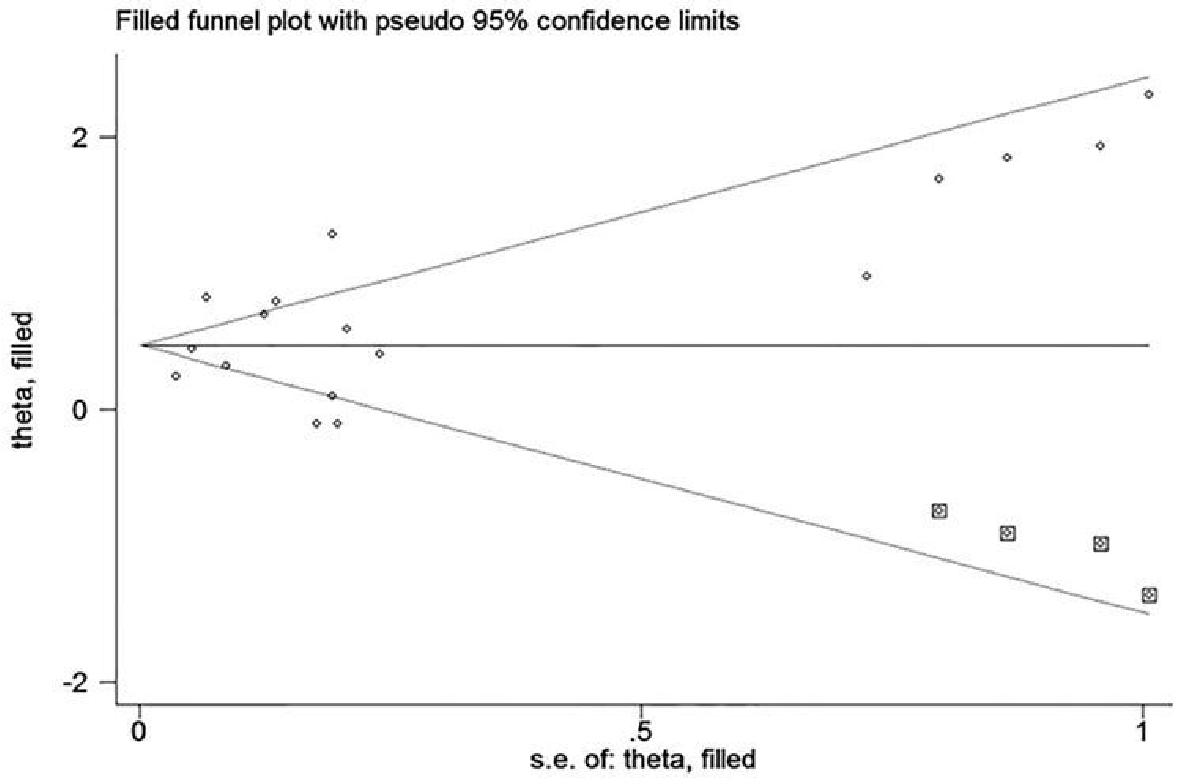
§The COVID-19 patients in these articles needed Invasive Mechanical Ventilation (IMV) use;

† The COVID-19 patients in these articles needed acute care admission.

* indicates age ≥60; age groups were classified as under and over 60 years in the study reported by Lighter et al, 2020.

Figure 2

Meta-analysis of associations between COVID-19 and obesity: Odds ratios and 95% confidence intervals based on mixed models Five studies (17 analyses and types of results) were included. A fixed-effect model was estimated when modest to moderate heterogeneity was present, and a random-effects model was estimated when substantial to considerable heterogeneity was present. a. obesity; b. severe obesity. ‡ Severe obesity was divided into two categories: severe obesity I (35-39.9 kg/m2) and II (≥40 kg/m2). # The COVID-19 patients in these articles needed Intensive Care Unit (ICU) admission; § The COVID-19 patients in these articles needed Invasive Mechanical Ventilation (IMV) use; † The COVID-19 patients in these articles needed acute care admission. * indicates age ≥60; age groups were classified as under and over 60 years in the study reported by Lighter et al, 2020.



Five studies (17 analyses) were included in the meta-analysis of the associations between COVID-19 and obesity). We used the trim method to make the funnel plot.

Figure 3

Funnel plot for publication bias Five studies (17 analyses) were included in the meta-analysis of the associations between COVID-19 and obesity). We used the trim method to make the funnel plot.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- XiaominCovidobesityTable.docx
- SupplementalTable1.pdf