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REVIEW

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The association between excess weight and COVID-19 outcomes: An umbrella review

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Summary

This umbrella review assessed the association between excess weight and COVID-19 outcomes. MEDLINE, PsycINFO, and CINAHL were systematically searched for reviews that assessed the association between excess weight and COVID-19 outcomes. A second-order meta-analysis was conducted on the available data for intensive care unit admission, invasive mechanical ventilation administration, disease severity, hospitalization, and mortality. The quality of included reviews was assessed using the AMSTAR-2 appraisal tool. In total, 52 systematic reviews were included, 49 of which included meta-analyses. The risk of severe outcomes (OR = 1.86; 95% CI: 1.70 to 2.05), intensive care unit admission (OR = 1.58; 95% CI: 1.45 to 1.72), invasive mechanical ventilation administration (OR = 1.70; 95% CI: 1.57 to 1.83), hospitalization (OR = 1.82; 95% CI: 1.61 to 2.05), and mortality (OR = 1.35; 95% CI: 1.24 to 1.48) following COVID-19 infection was significantly higher in individuals living with excess weight compared with those with a healthy weight. There was limited evidence available in the included reviews regarding the influence of moderating factors such as ethnicity, and the majority of included reviews were of poor quality. Obesity appears to represent an important modifiable pre-infection risk factor for severe COVID-19 outcomes, including death.

KEYWORDS

association, COVID-19, mortality, obesity, overweight

1 | INTRODUCTION

In England in 2019, 27% of men and 29% of women were living with obesity, which represents a significant increase in prevalence from 13% of men and 16% of women in 1993.¹ Excess weight increases the risk of other serious diseases and reduces life expectancy,² placing a substantial strain on the health services. Indeed obesity and obesity-related illnesses are estimated to cost the UK National Health

Service £6.1 billion per annum,¹ with over 1 million hospital admissions between April 2019 and December 2020 linked to obesity.³ Coronary heart disease,⁴ multiple cancers,⁵ stroke,⁶ type 2 diabetes,⁷ and many more non-communicable diseases⁸ are more likely to develop in those living with obesity, compared with those living with a healthy weight. Excess weight is also a strong risk factor for multimorbidity.⁹ There is a growing evidence base that obesity has strong associations with the communicable Coronavirus disease 2019

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(COVID-19),^{10–12} with increased risk of infection, hospitalization, severity, and mortality.¹³

COVID-19, also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is an infectious disease caused by a novel coronavirus, first identified in Wuhan city, China.^{14,15} The COVID-19 pandemic has caused catastrophic global disruption, involving serious morbidity and mortality.¹⁶ Although most COVID-19 cases were asymptomatic or resulted in mild disease, a substantial proportion progressed to critical illness with respiratory failure requiring hospitalization, intensive care unit (ICU) admission, and invasive mechanical ventilation (IMV).¹⁷ Early epidemiological evidence in the United States that showed common comorbidities for COVID-19 were hypertension (56.6%), obesity (41.7%), and diabetes (33.8%). Indeed, obesity has been found to be a risk factor for initial COVID-19 infection,¹⁸ with people living with excess weight found to be more likely to test positive than those of a healthy weight. Additionally, people living with obesity have been found to be at a potentially higher risk of admission to an ICU than their healthy weight counterparts, with disease severity increasing with BMI.¹²

The UK is experiencing a dual epidemic of COVID-19 and obesity, which appear to interact with each other to produce severe outcomes in many groups of patients.¹³ Inequalities have been observed in adults and children living with obesity, with those residing in the most deprived areas and those who identify themselves as from Black-African, Caribbean, and South Asian ethnic groups, more likely to be living with excess weight.¹ Similar trends have been identified between socioeconomic status/ethnicity and COVID-19 prevalence and outcomes,¹⁹ with those of lower socioeconomic status and certain ethnic groups such as Black and South Asian communities being more likely to be infected and encounter a poor disease outcome.^{20–22} In the UK, obesity has been found to be associated with increased risk of ICU admission, IMV administration, and in-hospital mortality in multiple ethnic groups of patients admitted to hospital with COVID-19, with the strongest associations observed for Black ethnicities.²³

Given the vast number of reviews rapidly published, there is a need to understand the impact of excess weight on COVID-19 outcomes when looking at the entire body of available evidence and to appraise the strength of currently available reviews. The purpose of the present review was to conduct an umbrella review that investigated the association between excess body weight and the disease course of COVID-19, and whether any associations were influenced by moderating factors such as ethnicity, socioeconomic status, age, sex, or the presence of comorbidities.

2 | METHODS

This umbrella review was conducted in accordance with PRISMA guidelines²⁴ and the recommendations of Cochrane overviews of reviews.²⁵ This umbrella review was also prospectively registered in the international prospective register of systematic reviews (PROSPERO) under the registration number: CRD42021233235.

2.1 | Search strategy

Electronic bibliographic databases MEDLINE, PsycINFO, and CINAHL were searched via EBSCOhost, and no language or date restrictions were applied. The prospectively registered search strategy utilized Medical Subject Headings (MeSH), Boolean operators, and was run through to May 11, 2022 (see Supporting Information). Search results were exported to EndNote, where automated and manual deduplication was performed. Reference lists of eligible reviews were also screened for any further eligible reviews.

2.2 | Article selection

Two researchers (JM & AG) independently assessed the title and abstracts of eligible studies, with disagreements resolved by a third reviewer (LE). Articles were deemed eligible for inclusion if they were systematic reviews (with or without meta-analysis) of solely primary literature that assessed any association between excess weight and COVID-19 infection, severity, or mortality in more than one study. Systematic reviews were required to include studies, in any setting, which presented laboratory-confirmed diagnoses of COVID-19 in people living with overweight or obesity. Where laboratory-confirmed diagnosis was not specified within the potentially eligible systematic review, the protocol/registration for the review and/or the full text of each included primary study was checked to confirm diagnosis methods. If COVID-19 diagnosis method could still not be established, the corresponding author of each included primary study was contacted and allowed 4 weeks to respond. Systematic reviews were excluded if it could not be confirmed that COVID-19 was diagnosed via a laboratory technique in any included primary study. Studies were eligible for inclusion if the authors defined a group of participants as living with excess weight. This included a variety of author-defined classifications (see Table S1), which sometimes differed for specific ethnicities.

Potentially eligible papers were then retrieved, and their full text was assessed for inclusion independently by two reviewers (JM & AG), with a third used for dispute resolution (LE). Reference lists of included articles were then searched for further potentially relevant systematic reviews.

2.3 | Data extraction

A standardized pre-piloted electronic data extraction form (Microsoft Excel) was used by two researchers (AG & OS) to extract data from the included systematic reviews. Extracted data included: review characteristics, search details, characteristics of included studies/participants, COVID-19 diagnosis method, overweight/obesity definition, COVID-19 infection, severity, hospitalization, and mortality data, inferred mechanisms, any relevant data on moderators such as severity of excess weight, ethnicity, socioeconomic status, age, sex, geography, or other comorbidities, author-acknowledged limitations, funding

source, and author declarations. All data extraction was then checked by a third reviewer (JM) for accuracy.

We extracted data on COVID-19 severity as it was reported in the included review. Therefore, there are multiple author-defined definitions of COVID-19 severity, such as “poor outcome,” “severe COVID,” “severe outcome,” “severe disease,” “severity,” “severe complications,” “severe illness,” and “crucial illness,” as well as ICU admission and IMV. Occasionally, these terms include ICU admission, IMV, hospitalization, and mortality; however, it was not possible to disaggregate the data. Therefore, the present review utilizes the descriptions stated within the relevant included review.

It should be noted that where data have been extracted *verbatim* from included reviews, we have altered language that reduced people to their medical condition. The alterations made ensure person first language throughout this report (e.g., “individual living with obesity” has replaced “obese individual”).

2.4 | Quality assessment

The quality of each included systematic review was assessed by one author (JM), with a selection checked by a second (AG) and disputes solved by a third (OS), using the Assessment of Multiple Systematic Reviews (AMSTAR 2) measurement tool.²⁶ AMSTAR 2 is a 16-item critical assessment tool for appraising the quality of systematic reviews, which is not intended to generate an overall score. AMSTAR 2 has a rating system based on weaknesses in critical domains and can therefore assist in the identification of high-quality reviews. Review classifications were scored as follows: Critically low: more than one critical flaw with or without non-critical weaknesses; Low: one critical flaw with or without non-critical weaknesses; Moderate: more than one non-critical weakness with no critical flaws; High: no or one non-critical weakness with no critical flaws.

2.5 | Quantitative synthesis

We conducted a second-order meta-analysis on the available data for disease severity, hospitalization, and mortality. Within disease severity, we examined severe outcomes, admission to ICU, and IMV separately. The majority of effect sizes were Odds Ratios, which were converted to log Odds for analyses. A small number of effects were expressed as Risk Ratios, which we used interchangeably with Odds Ratios.²⁷ However, under certain conditions (as the number of event rates increases), Odds Ratios and Risk Ratios diverge, so we also conducted sensitivity analyses removing Risk Ratios.

We estimated the degree of overlap of primary studies in each meta-analysis included in the quantitative synthesis for each outcome using the Corrected Covered Area (CCA). The CCA provides an intuitive approximation of overlap using the formula $[(N - r)/(r \times c) - r]$, where N is the sum of primary studies included across all systematic-reviews/meta-analyses (including double counting), r is the number of primary studies total, and c is the number of systematic-reviews/

meta-analyses. We used cut-offs to interpret the degree of overlap, where 0–5 is indicative of slight, 6–10 indicative of moderate, 11–15 indicative of high, and >15 indicative of very high overlap.²⁸ If it was not possible to establish the primary studies that contributed to the meta-analytic effect size, these were excluded from the calculation of the CCA. We also generated a visual matrix to examine the overlap of included primary studies in each meta-analysis for each outcome, which highlights reviews that were and were not included in the quantitative synthesis.²⁹

As there was overlap between the primary studies in the different meta-analyses, this violates the independence of the effect sizes, which in turn can artificially increase the precision of the pooled effect. As such, we conducted a sensitivity analysis in which we adjusted the precision of the pooled effect size by an inflation factor.³⁰ As this factor was unknown, we reanalyzed each model with a series of inflation factors in 10% increments until the precision meant the effect was no longer significant. We conducted a sensitivity analysis for each outcome excluding pediatric and pregnant populations. We also conducted categorical subgroup analyses on high/moderate quality versus low/critically low quality, wherever there were at least four reviews in both quality groups.³¹ Where there were not four studies in each subgroup, we present the pooled effect with the removal of high/moderate quality reviews.

Individual meta-analytic effects were pooled and the second-order meta-analysis was conducted in R using the “metafor” package. Random Effects models with a Restricted Maximum Likelihood Estimator were used. The analysis script and data can be found here [<https://osf.io/dkgjn/>].

3 | RESULTS

3.1 | Study selection

Figure 1 outlines the PRISMA flow diagram of study selection, which shows in total 52 systematic reviews^{13,32–82} met the inclusion criteria and were included in this umbrella review. A list of the records that were excluded at full text screening, with their accompanying reason for exclusion, can be found in Table S2.

3.2 | Characteristics of included reviews

All 52 included reviews were published between 2020 and 2022, from 17 different countries. The reviews originate from China ($n = 16$), USA ($n = 7$), UK ($n = 5$), Indonesia ($n = 3$), Brazil ($n = 3$), Hungary ($n = 2$), Singapore ($n = 2$), Iran ($n = 2$), Australia ($n = 2$), Spain ($n = 2$), Bangladesh ($n = 2$), Canada ($n = 1$), Korea ($n = 1$), South Africa ($n = 1$), Italy ($n = 1$), France ($n = 1$), and Taiwan ($n = 1$). Of the 52 included reviews, 49 were meta-analyses, and three were narrative systematic reviews.^{51,58,77} Two reviews were conducted with pediatric populations,^{59,66} and three were in pregnant women.^{34,71,72} As per

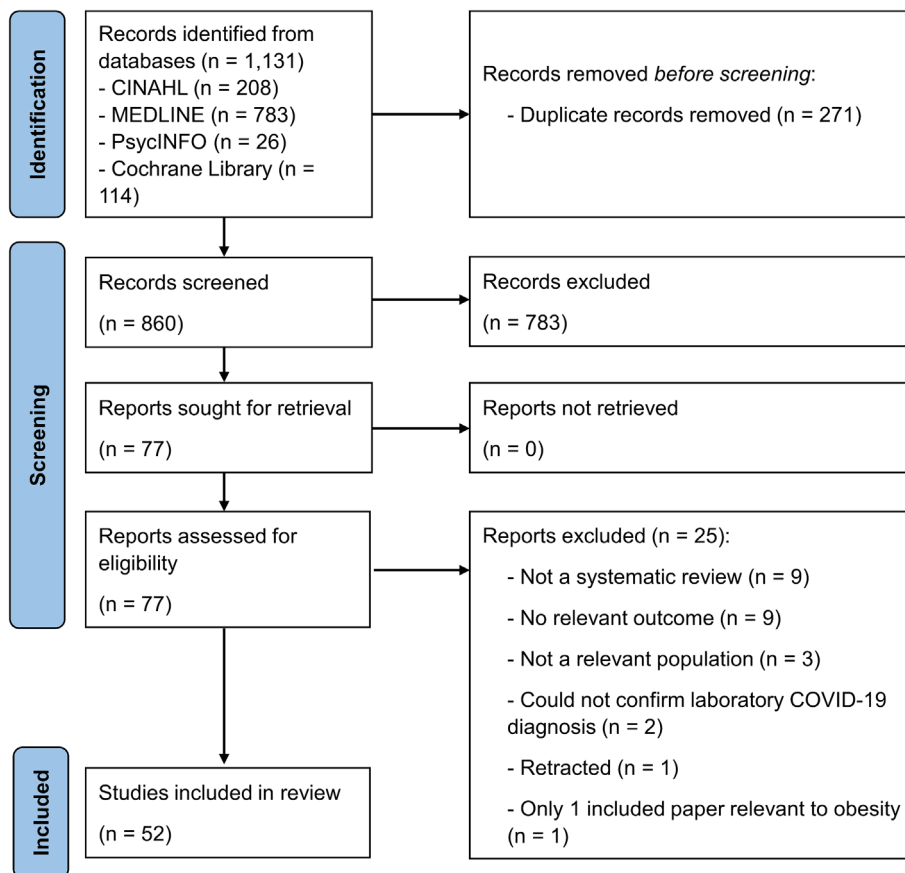


FIGURE 1 PRISMA flow diagram of study selection.

the inclusion criteria, all reviews included studies that utilized laboratory-confirmed COVID-19 diagnosis methods. Within the included reviews, there were a variety of definitions of excess weight (most commonly BMI > 25 or BMI > 30 and were often lower within included reviews to account for people who identify as Asian ethnicity), which were compared with people of a healthy weight (most commonly defined as BMI < 25). The characteristics of the included reviews, including the excess weight definition of each review, are shown in Table S1, with additional characteristics presented in Table S3. An overview of the findings of the included reviews can be found in Table 1, with additional detailed findings presented in Table S4.

The number of studies included in the excess weight analysis within each included review varied substantially from 138⁸¹ to two.⁴³ There were larger reviews included that comprised as many as 217 included studies⁶⁹; however, only 27 were relevant to excess weight, as reviews on multiple COVID-19 comorbidities were eligible provided excess weight was examined. The overlap of primary studies included within each review is presented in the Supporting Information for risk of COVID-19 infection (Table S5), ICU admission (Table S6), IMV administration (Table S7), COVID-19 severity (Table S8), hospitalization (Table S9), and mortality (Table S10). These tables are supported by the list of references of included studies, giving a comprehensive list of primary studies examining the association between excess weight and COVID-19 outcomes. The total number

of included primary studies relevant to each outcome was as follows: infection risk ($n = 30$), ICU admission ($n = 50$), IMV administration ($n = 38$), severity ($n = 105$), hospitalization ($n = 78$), and mortality ($n = 153$).

3.3 | Methodological quality of included reviews

The AMSTAR-2 assessment results for each review are shown in Table S11. Of the 52 included reviews, 40 were classified as “critically low,” 11 were classified as “low,” and one⁵¹ was classified as “high.” The mean (standard deviation) of non-critical and critical weaknesses was 3 (2) and 3 (2), respectively. Notably, all but three^{47,51,72} of the included reviews lacked item 7, which requires a full list of references excluded at full-text stage and is classed as a critical domain. With item 7 excluded from the assessment, of the 52 included reviews, 30 were classified as “critically low,” 13 were classified as “low,” five were classified as moderate,^{55,58,70,74,75} and four^{45,49,51,61} were classified as “high.” It was not possible to statistically explore the differences in findings between those of moderate/high quality and those of lower quality due to the small number of moderate-/high-quality reviews for each respective outcome. Other notable areas of weakness were observed in the included reviews, such as 33/52 (63%) were not prospectively registered, 52/52 (100%) did not report on the sources of funding for the studies included within the review, and

TABLE 1 Main findings and quality of included reviews comparing the risk of COVID-19 infection, hospitalization, severity, and mortality, between individuals living with excess weight and those of a healthy weight.

Author, year	Infection	Hospitalization	Severity	Mortality	Modified AMSTAR 2 classification
Aghili et al, 2021 ³³	NR	NR	Poor outcome ↑ ICU admission ↔ IMV ↑	Mortality ↑	Critically low
Allotey et al, 2021 ³⁴	NR	NR	Severe disease ↑ ICU admission ↑ IMV ↑	Maternal mortality ↑	Low
Ashktorab et al., 2021 ³⁵	NR	NR	NR	Mortality ↑	Critically low
Booth et al., 2021 ³⁶	NR	NR	Severe outcome ↑	Mortality ↑	Critically low
Bunn et al., 2022 ⁶⁴	NR	NR	ICU admission ↑	NR	Critically low
Cai et al, 2021 ⁶⁵	NR	Hospitalization ↑	Severe disease ↑ ICU admission ↑ IMV ↑	Mortality ↑	Critically low
Chang et al., 2020 ³⁷	NR	Hospitalization ↑	Severe disease ↑ IMV ↑	NR	Low
Choi et al., 2022 ⁶⁶	NR	NR	Severe disease ↑	NR	Critically low
Chowdhury et al., 2021 ⁶⁷	NR	NR	Severe disease ↑	NR	Critically low
Chu et al., 2020 ³⁸	NR	NR	Poor outcome ↑ ICU admission ↑ IMV ↑	Mortality ↔	Low
Deng et al., 2021 ³⁹	NR	NR	Severe disease ↑ ICU admission ↑ IMV ↑	Mortality ↔	Critically low
Dessie et al., 2021 ⁶⁸	NR	NR	NR	Mortality ↑	Critically low
Du et al., 2021 ⁴⁰	NR	NR	Severe disease ↑	Mortality ↑	Critically low
Ferreira et al., 2021 ⁷⁹	NR	NR	ICU admission ↑ IMV ↑	Mortality ↔	Critically low
Foldi et al., 2020 ⁴¹	NR	NR	ICU admission ↑ IMV ↑	NR	Low
Foldi et al., 2021 ⁴²	NR	NR	ICU admission ↑ IMV ↑	NR	Critically low
Geng et al., 2021 ⁶⁹	NR	NR	Severity ↑ ICU admission ↑ ARDS ↑	Mortality ↔	Critically low
Ng et al., 2021 ⁴³	NR	NR (one study)	NR (one study)	Mortality ↔	Critically low
Ho et al., 2020 ⁴⁴	Positive test ↑	NR	Severe disease ↑ ICU admission ↔ IMV ↑	Mortality ↑	Low
Hoong et al., 2021 ⁴⁵	NR	NR	Severe disease ↑	Mortality ↑	High
Hu & Wang, 2020 ⁴⁶	NR	NR	Severity ↑ ICU admission ↑	NR	Critically low
Huang et al, 2020 ⁴⁷	NR	Hospitalization ↑	Severity ↑ ICU admission ↑ IMV ↑	Mortality ↑	Critically low
Huang et al., 2021 ⁷⁰	NR	NR	NR	Mortality ↑	Moderate
La Verde et al., 2021 ⁷¹	NR	NR	NR	Maternal Mortality ↑	Low
Lassi et al., 2021 ⁷²	NR	NR	Maternal Severity ↑	NR	Low
Li et al., 2021a ⁷³	NR	NR	Severity ↑	NR	Critically low
Li et al, 2021b ⁷⁴	NR	NR	NR	Mortality ↑	Moderate
Mahamat-Saleh et al, 2021 ⁷⁵	NR	NR	NR	Mortality ↑	Moderate

(Continues)

TABLE 1 (Continued)

Author, year	Infection	Hospitalization	Severity	Mortality	Modified AMSTAR 2 classification
Malik et al., 2021 ⁴⁸	NR	NR	Poor outcomes ↑	NR	Critically low
Mattey-Mora et al., 2022 ⁷⁶	NR	Hospitalization ↑	NR	NR	Low
Mesas et al., 2020 ⁴⁹	NR	NR	NR	Mortality ↔	High
Noor & Islam, 2020 ⁵⁰	NR	NR	NR	Mortality ↑	Critically low
Ovalle et al., 2021 ⁷⁷	NR	NR	Severity ↑	NR	Critically low
Peres et al., 2020 ⁵¹	NR	Hospitalization ↑	Poor outcome ↑	Mortality ↔	High
Poly et al., 2021 ⁵²	NR	NR	NR	Mortality ↑	Low
Popkin et al., 2020 ¹³	Positive test ↑	Hospitalization ↑	ICU admission ↑ IMV ↑	Mortality ↑	Critically low
Pranata et al., 2020 ⁵³	NR	NR	Severity ↑ Poor outcome ↑	Mortality ↑	Critically low
Raesi et al., 2022 ⁷⁸	COVID-19 risk ↑	Hospitalization ↑	Severity ↑ ICU admission ↑ IMV ↑	Mortality ↑	Low
Sales-Peres et al., 2020 ⁵⁴	NR	NR	Severe complications ↔	NR	Low
Seidu et al., 2020 ⁵⁵	NR	NR	Severe illness ↑	Mortality ↑	Moderate
Sharma et al., 2020 ⁵⁶	NR	NR	Critical illness ↑	NR	Critically low
Soeroto et al., 2020 ⁵⁷	NR	NR	Poor outcome ↑ Severe disease ↑ ICU admission ↔	NR	Critically low
Tamara & Tahapary, 2020 ⁵⁸	NR	Hospitalization ↑	IMV ↑ Severe disease ↑	NR	Moderate
Tsankov et al., 2021 ⁵⁹	NR	NR	Severe disease ↑	NR	Critically low
Wang et al., 2022 ⁸⁰	NR	NR	ICU admission ↑	NR	Critically low
Wang et al., 2021 ⁸¹	NR	NR	NR	Mortality ↑	Critically low
Yang et al., 2020 ⁶⁰	Infection ↑	Hospitalization ↑	Severe disease ↑ ICU admission ↑ IMV ↑	Mortality ↑	Low
Yang et al., 2021a ³²	NR	NR	Severe disease ↑ Severe outcome ↑	NR	Critically low
Yang et al., 2021b ⁶¹	Positive test ↑	Hospitalization ↑	ICU admission ↑ IMV ↑	Mortality ↑	High
Zhang et al., 2021 ⁸²	NR	Hospitalization ↑	Severe disease ↑ ICU admission ↑ IMV ↑	Mortality ↔	Critically low
Zhao et al., 2020 ⁶²	NR	NR	Severe outcome ↑ ICU admission ↑	Mortality ↔↑	Low
Zhou et al., 2020 ⁸³	NR	NR	Severe disease ↑ IMV ↑	Mortality ↔	Critically low

Note: Arrows represent a significantly increased (↑), no difference (↔), or significantly decreased (↓) risk between those living with excess weight and a healthy weight control group. Reported outcome variables are defined as per included review article.

Abbreviations: ICU, intensive care unit; IMV, invasive mechanical ventilation; NR, not reported.

37/52 (71%) did not assess the potential impact of risk of bias in individual studies on the results of the meta-analysis, nor did 36/52 (69%) account for risk of bias when interpreting/discussing the results of the review.

3.4 | Infection

Five of the 52 included reviews reported COVID-19 infection as an outcome (see Table 1), which was deemed too few for second-order meta-

analysis. All five concluded a stronger association between COVID-19 infection and excess weight, compared with those of a healthy weight, with odds ratios ranging from 1.39 to 2.42. A narrative description of these five studies is presented in the Supporting Information.

3.5 | Severity

Of the included 52 reviews, 40 reported a minimum of one measure of COVID-19 severity, which resulted in a total of 76 author reported

outcomes (see Table 1). Of the 76 author-reported COVID-19 severity outcomes that were extracted from the included reviews, 72 showed that living with excess weight was associated with an increased COVID-19 severity compared with living with a healthy weight. The remaining four outcomes showed no association between disease severity and excess weight; these outcomes were ICU admission^{33,44,57} and severe complications.⁵⁴

For ICU admissions, the second-order meta-analysis had a pooled OR = 1.58 (95% CI: 1.45 to 1.72), Z = 10.67, p < .001, I² = 74%, from 21 effects (Figure 2). Seventeen of the 21 individual meta-analyses

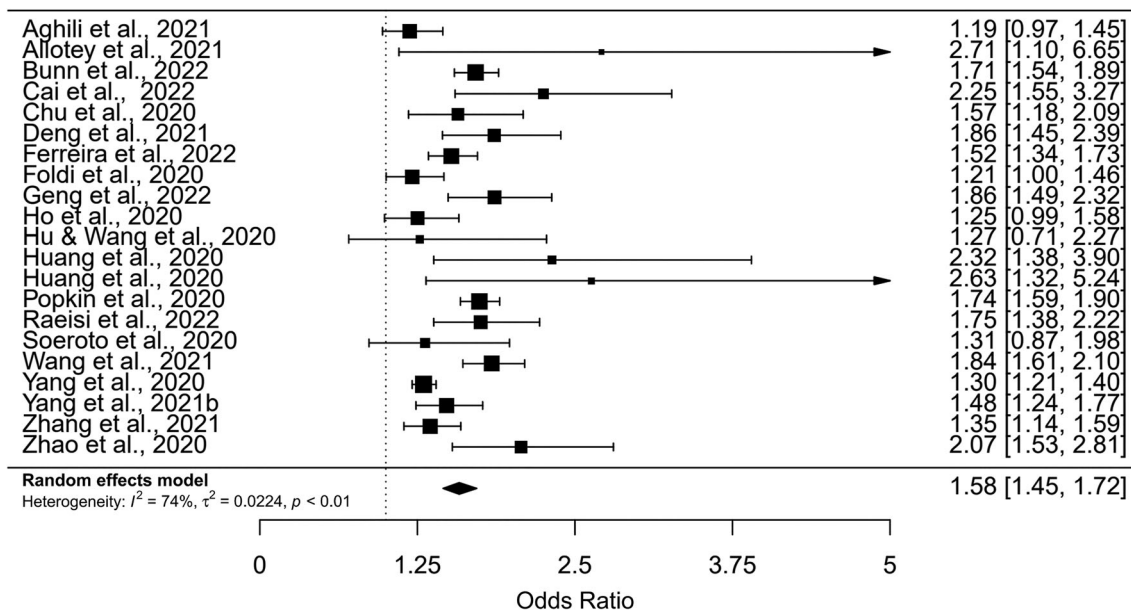


FIGURE 2 Forest plot showing the association between excess weight and intensive care unit admission with COVID-19. A higher odds ratio represents a higher risk of ICU admission in those living with excess weight compared with those of a healthy weight.

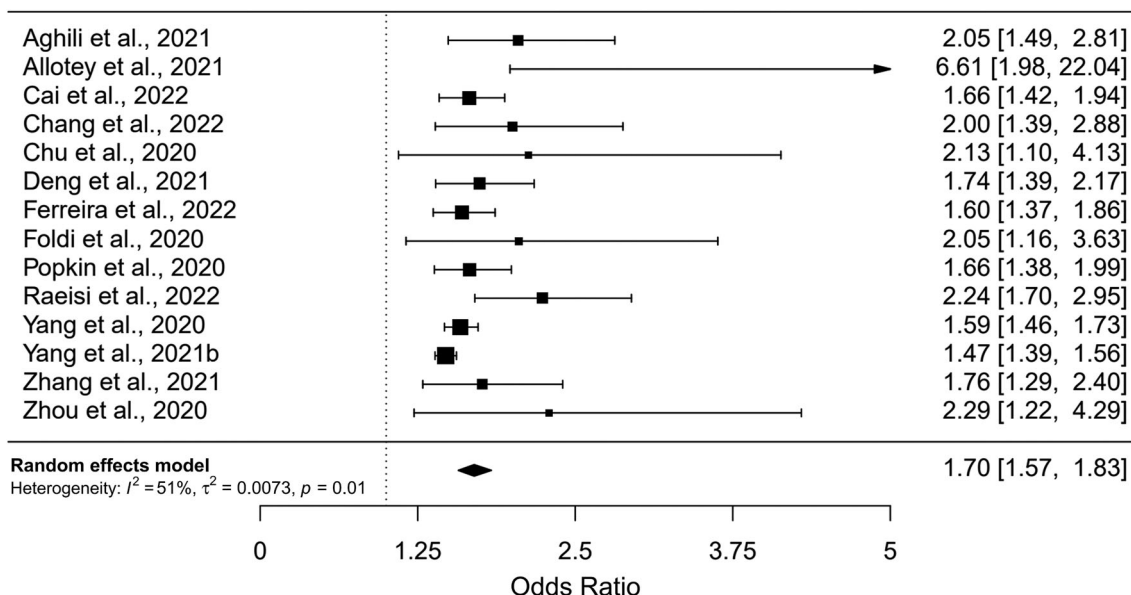


FIGURE 3 Forest plot showing the association between excess weight and invasive mechanical ventilation with COVID-19. Higher odds ratio represents a higher risk of invasive mechanical ventilation in those living with excess weight compared with those of a healthy weight.

were significant. An inflation factor of 550% would be required to reduce the precision to the point the model was non-significant. The CCA was 11.6% indicative of high overlap.

For IMV administration, the second-order meta-analysis had a pooled OR = 1.70 (95% CI: 1.57 to 1.83), $Z = 13.42$, $p < .001$, $I^2 = 51%$, from 14 effects (Figure 3). All individual meta-analyses were statistically significant. An inflation factor of 550% would be required to reduce the precision to the point the model was non-significant. The CCA was 14.6% indicative of high overlap.

The second-order meta-analysis on disease severity demonstrated a pooled OR = 1.86 (95% CI: 1.70 to 2.05), $Z = 12.73$, $p < .001$, $I^2 = 77%$, from 27 effects (Figure 4). All individual meta-analyses were statistically significant. Removal of three effect sizes that used Risk Ratios had minimal impact on the overall OR (OR = 1.91 [95% CI: 1.73 to 2.12], $Z = 12.41$, $p < .001$, $I^2 = 76%$). An inflation factor of 650% would be required to reduce the precision to the point the model was non-significant. The CCA was 6.8% indicative of moderate overlap.

Five of the nine reviews classified as either moderate or high confidence using the modified AMSTAR-2 assessment found that people living with excess weight were associated with severe disease,^{45,61} poor outcome,⁵¹ severe illness,⁵⁵ IMV,^{58,61} and ICU admission,⁶¹ compared with living with a healthy weight, with the remaining four not reporting on disease severity.^{49,70,74,75} Removal of moderate or high-rated studies did not substantially influence the pooled ORs from the second-order meta-analyses (Severity OR = 1.84 [95% CI: 1.67 to 2.03]; ICU OR = 1.59 [95% CI: 1.45 to 1.74]; IMV OR = 1.72 [95% CI: 1.60 to 1.84]).

3.6 | Hospitalization

The risk of hospitalization in people living with excess weight compared with people of a healthy weight was reported in 11 of the 52 included reviews.^{13,37,47,51,58,60,61,65,76,78,82} All 11, two of which were systematic reviews, reported a significantly stronger association in people living with excess weight for hospital admission, compared with those of a healthy weight. Two were systematic reviews, and the odds ratios from the nine meta-analyses for hospitalization ranged from 1.4 to 2.45.

The second-order meta-analysis on hospitalization rates demonstrated a pooled OR = 1.82 (95% CI: 1.61 to 2.05), $Z = 9.67$, $p < .001$, $I^2 = 83%$, from nine effects (Figure 5). All individual meta-analyses were statistically significant. An inflation factor of 500% would be required to reduce the precision to the point the second-order model was non-significant. The CCA was 5.2% indicative of moderate overlap.

Of the 11 reviews that investigated hospitalization, two systematic reviews were classified as high quality,^{51,58} one meta-analysis was classified as high quality,⁶¹ and the remaining eight meta-analyses were classified as either low or critically low, using the AMSTAR-2 assessment tool. Removal of moderate- or high-rated studies did not substantially influence the pooled ORs from the second-order meta-analyses (OR = 1.86 [95% CI: 1.63 to 2.12]).

3.7 | Mortality

Of the 52 included reviews, 33 reported on the mortality of patients with COVID-19 (see Table 1). Of those 33, 23 (70%) reported an

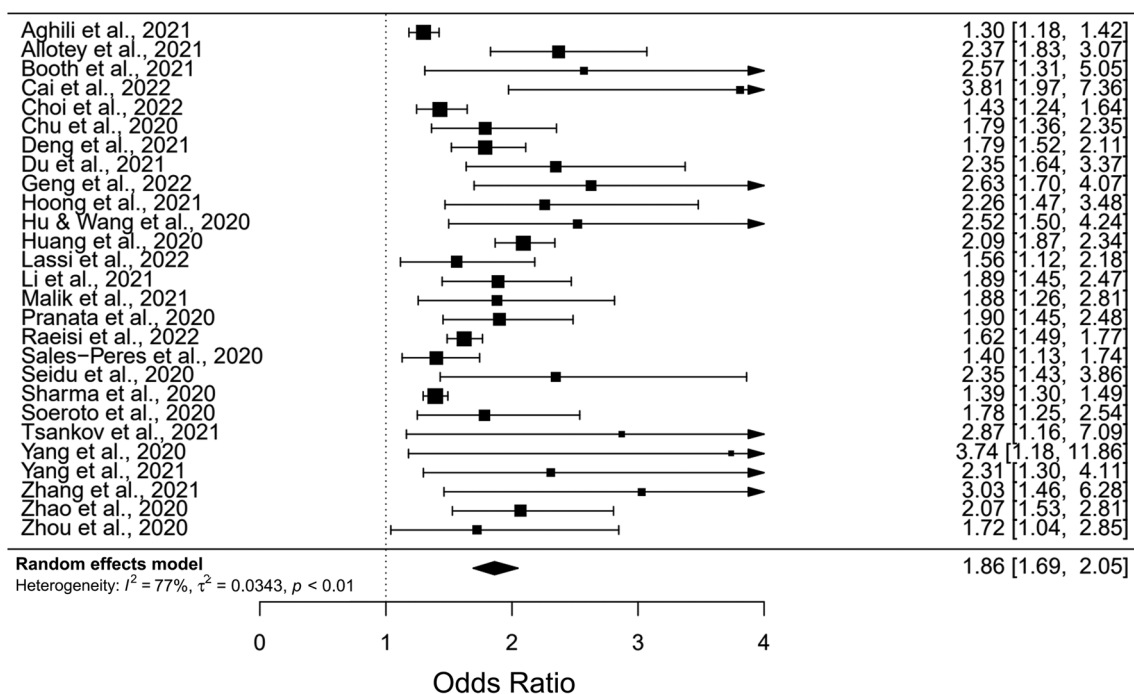


FIGURE 4 Forest plot showing the association between excess weight and COVID-19 severity. Higher odds ratio represents a higher risk of severe COVID-19 in those living with excess weight compared with those of a healthy weight.

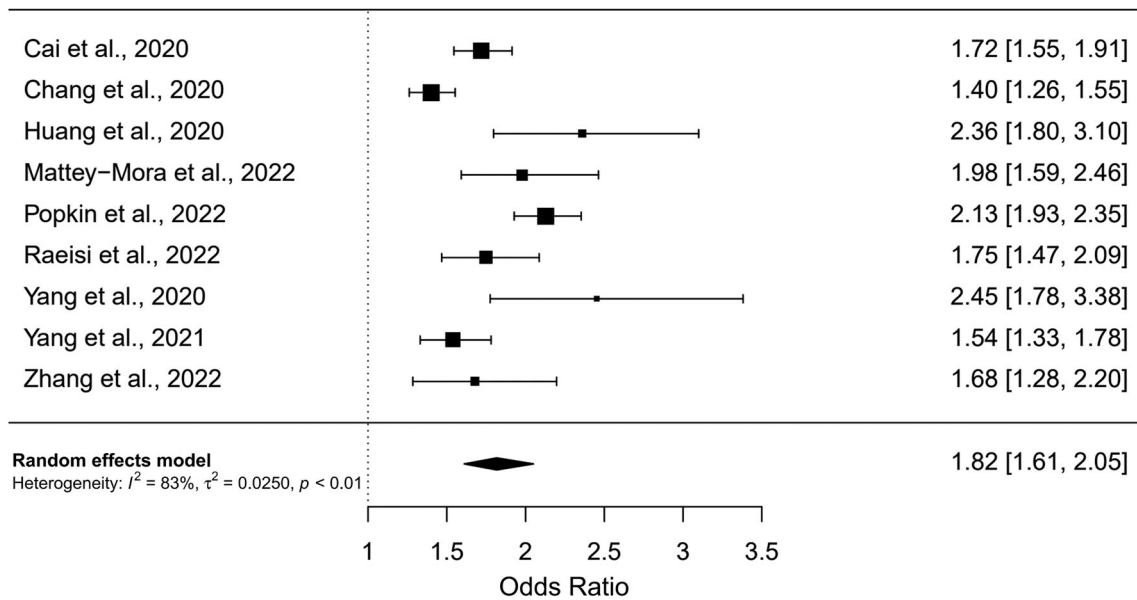


FIGURE 5 Forest plot showing the association between excess weight and hospitalization with COVID-19. Higher odds ratio represents a higher risk of hospitalization in those living with excess weight compared with those of a healthy weight.

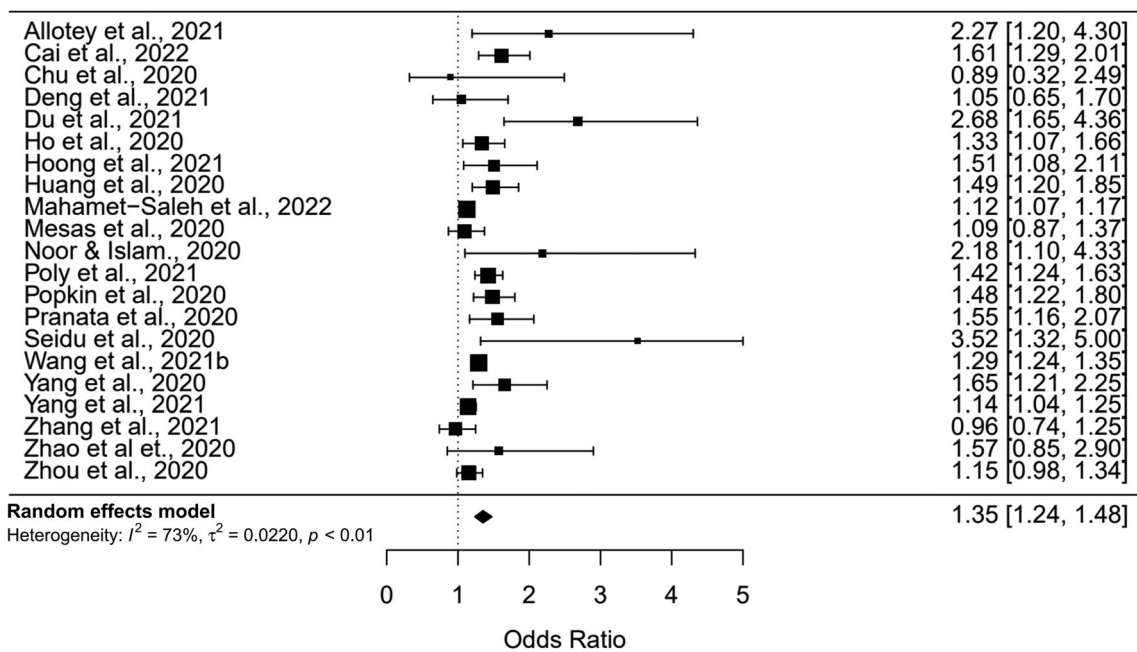


FIGURE 6 Forest plot showing the association between excess weight and mortality with COVID-19. Higher odds ratio represents a higher risk of mortality in those living with excess weight compared with those of a healthy weight.

increased mortality, nine (27%) reported no association, and Zhao et al.⁶² reported no association for BMI ≥ 30 kg/m² but a significant association for BMI ≥ 35 kg/m².

The second-order meta-analysis on mortality demonstrated a pooled OR = 1.35 (95% CI: 1.24 to 1.48), $Z = 6.67$, $p < .001$, $I^2 = 73\%$, from 21 effects (Figure 6). Fifteen of the 21 individual meta-analyses were statistically significant. Removal of four effect sizes that used a Risk Ratio did not substantially influence this

(OR = 1.35 [95% CI: 1.22 to 1.49], $Z = 6.05$, $p < .001$, $I^2 = 72\%$). An inflation factor of 350% would be required to reduce the precision to the point the model was non-significant. The CCA was 5.1% indicative of moderate overlap.

Of the nine reviews classified as either moderate or high confidence by AMSTAR-2 assessment, one did not report on mortality,⁵⁸ six reported an association between mortality and excess weight,^{45,55,61,70,74,75} and two reported no association.^{49,51} A

subgroup analysis demonstrated no significant difference between studies rated as low versus moderate or high ($\chi^2(1) = 1.78, p = .182$). Low quality OR = 1.40 (95% CI: 1.26 to 1.56), moderate or high quality OR = 1.23 (95% CI: 1.08 to 1.40).

3.8 | Moderators

3.8.1 | Excess weight

Deng et al.³⁹ observed for every 5 kg/m² increase in BMI the OR values for IMV use and ICU admission in COVID-19 patients were 1.16 (95% CI: 1.10–1.23) and 1.2 (95% CI: 1.11–1.30), respectively. Similarly, Du et al.⁴⁰ found a 1.09-fold increased risk (OR: 1.09, 95% CI: 1.04–1.14) of critical COVID-19 for each 1 kg/m² increase in BMI and a 1.19-fold increased risk (OR: 1.19, 95% CI: 1.08–1.30) of critical COVID-19 for each 2 kg/m² increase in BMI. They also found the mortality of patients with COVID-19 increased by 6% (OR = 1.06, 95% CI = 1.02–1.10) for each 1 kg/m² increase in BMI. Huang et al.⁷⁰ demonstrated a J-curved relationship between BMI and COVID-19 mortality, indicating that both individuals with a COVID-19 diagnosis and living with underweight or obesity had a higher mortality risk than patients with a healthy weight.

3.8.2 | Ethnicity, socioeconomic status, and geography

Although some reviews used a lower BMI cut-off for the definition of overweight/obesity in studies including data from those of Asian ethnicity (see Table S1), just one of the 52 included reviews explicitly investigated how the relationship between obesity and COVID-19 may be influenced by ethnicity. Raeisi et al.⁷⁸ categorized participants from just two ethnicities (Caucasian and East-Asian) and found that obesity was consistently associated with hospitalization, IMV, ICU admission, and mortality in Caucasians with COVID-19. However, the relationship between obesity and IMV, ICU admission, and mortality was non-significant in East-Asian populations with a COVID-19 diagnosis. Two studies included in their limitations that data on ethnicity and socioeconomic status were limited and precluded analysis.^{40,55} Seidu et al.⁵⁵ reported that ethnicity and socioeconomic status are linked to obesity and worse COVID-19 outcomes; however, they were unable to investigate these links due to insufficient data. Additionally, we did not find any evidence within the included reviews on the relationship between excess weight and COVID-19 risk, or prognosis being moderated by geography.

3.8.3 | Age

Chu et al.³⁸ found that people living with excess weight who were <60 years had a strong positive association between excess weight and poor composite outcomes of COVID-19, which included severe

COVID-19, need for ICU care, IMV, mortality, and disease progression (OR: 2.86, 95% CI: 1.55–5.28). They found that this association became weaker in people ≥60 years (OR: 1.52, 95% CI: 1.05–2.19). This finding is mirrored by the findings of Mesas et al.⁴⁹ who observed a stronger association, albeit not significant, between excess weight and COVID-19 mortality for people ≤60 years (OR: 1.62, 95% CI: 0.92–2.83) compared with people ≥60 years (OR: 0.90, 95% CI: 0.67–1.20).

3.8.4 | Sex

There was no evidence that the relationship between excess weight and COVID-19 outcomes is moderated by sex.^{40,49}

3.8.5 | Comorbidities

A detailed list of the reported comorbidities in each review can be found in Appendix S3. The majority of the included reviews included studies with multiple patient comorbidities or did not report on patient comorbidities. However, Zhao et al.⁶² excluded studies in which subjects had known diabetes or other fatal chronic diseases that may induce the severity of COVID-19 such as cancer, severe autoimmune disease, chronic kidney disease, cirrhosis, and liver failure. They found that excess weight was a risk factor for a severe COVID-19 outcome (severe manifestations, admission to ICU, and requirement for mechanical supports), but not for mortality. Additionally, Mesas, Cavero-Redondo, Álvarez-Bueno, Sarriá Cabrera, Maffei de Andrade, Sequí-Dominguez, and Martínez-Vizcaíno⁴⁹ found that living with excess weight was associated only with mortality in studies with fewer comorbidities.

4 | DISCUSSION

This umbrella review provides a comprehensive summary of the evidence on the association between excess weight and COVID-19 outcomes. The findings suggest a stronger association between weight and risk of disease severity, hospitalization, and mortality in those living with excess weight compared with their healthy-weight counterparts. Additionally, we found some evidence that the association between excess weight and COVID-19 outcomes is moderated by the severity of excess weight, age, and comorbidities. Specifically, weight associations with adverse outcomes were stronger in individuals living with a higher degree of excess weight, who were younger, and who had fewer comorbidities. It appears that older age, and larger number of comorbidities, confound the observed association between excess weight and COVID-19 prognosis, as these factors are significant independent risk factors,^{84,85} and weight often declines with comorbidities due to reverse causality linked to unintentional weight loss. Interestingly, within the included reviews, we found limited data on how ethnicity may influence the observed association, with no data

presented on socioeconomic status, or geography. The lack of reporting in this area should be addressed in any future reviews. Although the overall quality of the included reviews was poor, there was no observed difference in terms of the findings between the higher and lower ranking reviews.

The finding that excess weight is associated with a higher risk of catching COVID-19, compared with healthy weight, is supported by analyses of data from UK Biobank. Yates et al.⁸⁶ found that both BMI and waist circumference were associated with testing positive for COVID-19 in a dose-response fashion, and adjustment for possible confounders did not change the results. The adjusted odds ratio for BMI ranges of 25–<30, 30–<35, and ≥ 35 kg/m² was 1.31 (95% CI: 1.05–1.62), 1.55 (1.19–2.02), and 1.57 (1.14–2.17), respectively, compared with a healthy weight reference group. These UK-derived odds ratios broadly align with the odds ratios reported in the five included reviews,^{13,44,60,61,78} which ranged from 1.39 to 2.42. It should be noted that in many primary studies exploring the association between excess weight and COVID-19 infection, testing was done in hospitals. Therefore, it is possible that this finding, to some extent, is artefactual linked to ascertainment bias as the individuals living with excess weight were more likely to be admitted to hospital with COVID-19.⁸⁷

Of the 76 author-reported COVID-19 severity outcomes that were extracted from the included reviews, 72 (96%) showed a stronger association between weight and COVID-19 severity in people living with excess weight compared with those of a healthy weight. The remaining four outcomes showed no association between disease severity and excess weight; these outcomes were ICU admission^{33,44,57} and severe complications.⁵⁴ These four reviews were all classified as critically low confidence using the AMSTAR-2 assessment. Additionally, the three reviews t showed no association for ICU admission; all showed other metrics of COVID-19 severity to be worsened in people living with excess weight.^{33,44,57} These findings therefore support the conclusion that living with excess weight is associated with a more severe COVID-19 prognosis compared with living with a healthy weight. This finding also aligns with a prospective community-based cohort study of 6.9 million people in England, which identified J-shaped associations between BMI and admission to hospital due to COVID-19 and death.⁸⁷ This was in addition to a linear association between BMI and ICU admission. UK Biobank analyses have shown BMI to be linearly associated with higher risk of hospitalization and death from COVID-19.⁸⁸ Therefore, hospital admission and ICU admission processes could consider expediting ICU admission based on the expectation of more severe disease prognosis in people living with excess weight.

A significant association between excess weight and COVID-19-related mortality was observed in 15 of the 21 meta-analyses in which data were available for umbrella meta-analysis. Our findings are substantiated by recent large cohort studies in England,⁸⁹ Brazil,⁹⁰ and the United States.⁹¹ The OpenSAFELY study examined over 17 million adults in England and showed that a BMI > 40 was associated with a near doubling (HR: 1.92 CI: 1.72–2.13) of death from COVID-19 compared with people who were not living with obesity, in

a model adjusted potential confounders including for age, sex, smoking, index of multiple deprivation quintile, and comorbidities.⁹² In addition, UK Biobank analyses have shown BMI to be associated with a higher risk of hospitalization and death from COVID-19, particularly in people under 70 years (in agreement with our age-related findings), and in South Asian and African-Caribbean populations.⁸⁸ It should be noted that the observed association between excess weight and COVID-19-related mortality may be influenced by reverse causality, as those who are most likely to die with COVID-19 include the elderly and those with other conditions associated with underweight weight status.

Findings from included reviews,^{39,40,53} and findings from large UK studies,^{86–88,92} suggest a broadly linear relationship between excess weight and COVID-19 outcomes, with higher risk of COVID-19 infection and worse outcomes as BMI increases. These data suggest that if an individual could lower their BMI, for example, from 36 to 31 kg/m², it could meaningfully reduce their risk of COVID-19 infection and severe disease, despite their BMI still classifying them as living with obesity. However, this remains to be proven as adequately powered randomized controlled trials of the effects of weight loss on COVID-19 risk and severity are yet to be concluded. Whether relatively small amounts of weight loss can decrease COVID-19 severity is an area for future research.

Despite the lack of available data in the included reviews that examined the potential influence of ethnicity and socioeconomic status as effect moderators, there are relevant primary studies that have investigated this. A large prospective study in England⁸⁷ found a significant interaction ($p < 0.0001$) between BMI and ethnicity with a higher HR per kg/m² above 23 kg/m² for people who identify as Black ethnicity when compared with those who identify as White ethnicity, for hospital admission (1.07 [1.06–1.08] vs. 1.04 [1.04–1.05]) and mortality (1.08 [1.06–1.10] vs. 1.04 [1.03–1.04]). No differences were observed between other ethnic group and those who identify as a white ethnicity. More research is needed on the effect of ethnicity on the association between excess weight and COVID-19 outcomes, as well as the potential influence of regional fat distribution.

We observed no evidence in the included reviews to suggest that sex moderates the association between excess weight and COVID-19 risk/outcomes. However, it does appear that age has an important moderating influence, with the association being stronger in individuals below 60 years of age. This is supported by prospective data collected in 6.9 million community-based people in England that suggests that BMI is a greater risk factor for COVID-19 severity for younger people (aged 20–39 years) than for older people (≥ 80 years),⁸⁷ and also supported by data from the UK biobank that showed a clear interaction in BMI to COVID-19 outcome risks in those below and above 70 years of age.⁸⁸ These data also fit with findings in the general population where BMI is more strongly linked to all-cause mortality in younger people, likely due to less reverse causality in this group,⁹³ with strengths of association closer to findings from genetic studies, as summarized.⁹⁴ As expected, when comorbidities were examined, they confounded the association between excess weight and COVID-19 outcomes. Many comorbidities, which are

associated with weight loss, are significant independent risk factors for COVID-19 severity,^{84,85} therefore, this reverse causality may help explain the confounding of the association between COVID-19 outcomes and excess weight.

There are a variety of plausible biological mechanisms linking excess weight and COVID-19 risk and outcomes. It appears likely that these may act cumulatively, and to different extents in different individuals, to influence the observed association. An in-depth examination of potential biological mechanisms is provided in a number of reviews,^{95–99} including some previously mentioned reviews.^{33,42,47,48,53} Although these reviews highlight multiple potential biological mechanisms, further research is needed to fully elucidate the mechanistic explanations for the observed association.

It is important to note that factors not described in the included reviews may play a role in the differentiation of disease outcomes by weight status. People living with excess weight face not only unique biological vulnerabilities and structural disparities but also weight stigma. This stigma can lead to, and exacerbate, mental health conditions and result in the delayed or avoidance of care because of bias and humiliation experienced in healthcare settings.^{100,101} Additionally, it appears likely that physical activity levels are also associated with COVID-19 prognosis. Sallis et al.¹⁰² identified 48,440 adult patients with a COVID-19 diagnosis and linked their self-reported physical activity levels to their disease outcome. They found that patients with COVID-19 who were consistently inactive (<10 min per week) had a greater risk of hospitalization (OR: 2.26; 95% CI: 1.81 to 2.83), ICU admission (OR: 1.73; 95% CI: 1.18 to 2.55), and death (OR: 2.49; 95% CI: 1.33 to 4.67) due to COVID-19 than patients who were consistently physically active for >150 min per week. This threshold aligns with the UK Chief Medical Officers' Physical Activity Guidelines.¹⁰³ Although physical activity and excess weight are interlinked, a sensible recommendation to reduce population-level COVID-19 hospitalization and mortality is to promote physical activity. This is particularly important given the pandemic has been found to have reduced physical activity levels.¹⁰⁴

4.1 | Limitations

There are limitations to the present umbrella review. First, the overall quality of the included reviews was generally poor, likely associated with the rapid publication rate that occurred during the peak of the COVID-19 pandemic. Despite this, we did not identify any systematic differences in outcomes between the different levels of quality rated using the AMSTAR-2 tool. Second, it should be noted that the semantics of disease severity differ between primary studies and between reviews. Additionally, the criteria for outcomes such as hospitalization, ICU admission, IMV administration, and even mortality reporting may be different between hospitals and between countries. Definitions of excess weight/overweight/obesity within the included reviews also varied. We did not include reviews that were published in languages other than English, and this may impact the results.

It should be noted that this umbrella review includes reviews published up to May 2022. Since this date, a large Cochrane Review has been published that concludes the association of obesity with mortality, and requiring a breathing tube is of high certainty but presents no data on the potential moderating influences of ethnicity or socioeconomic status.¹⁰⁵ The findings of this Cochrane Review, which includes studies published up to April 2021, largely align with the findings of this umbrella review. Although it appears that new evidence is being published at pace in this area, there seems to be consensus that excess weight is substantially associated with more severe adverse outcomes of COVID-19. However, importantly, the influence of moderating factors appears to be missing in systematic reviews.

4.2 | Future considerations

Further research on the mechanisms explaining the association between excess weight and COVID-19 would be beneficial. This research may lead to the possibility of identifying therapeutic targets and creating tailored treatment approaches to mitigate the risk of COVID-19 infection and/or poor outcomes in people living with excess weight. Additionally, large-scale interventions that show the effect of meaningful intentional weight loss (via lifestyle, pharmacotherapy, or surgery) on risk of COVID-19 infection, and risk of poor outcomes of COVID-19, would be of interest.

The COVID-19 pandemic has reduced access to weight management services and support for individuals living with excess weight, particularly around lockdowns, when face-to-face weight management services were suspended.¹⁰⁶ It is vital that people living with excess weight are offered weight management services where needed. Finally, the most effective strategy to protect against severe COVID-19 outcomes is vaccination. To the best of our knowledge, COVID-19 vaccine trials have shown no difference in vaccine efficacy between BMI groups.^{107–109} Indeed, a population-based cohort study has found a similar level of protection from severe COVID-19 in individuals with excess weight compared with those of a healthy weight.¹¹⁰

4.3 | Conclusions

This umbrella review found evidence that living with excess weight was associated with worse COVID-19 outcomes, and potentially COVID-19 infection. The COVID-19 pandemic has highlighted excess weight as a modifiable risk factor, that if appropriately addressed, could help mitigate the impact of COVID-19. The pandemic has therefore expedited the need for renewed emphasis on, and investment in, weight management services, as well as population strategies to help people live healthier lives. Unfortunately, we identified very limited reporting on the influence of factors that may moderate the association between excess weight and adverse COVID-19 outcomes. This should be addressed in future systematic reviews and meta-analyses.

AUTHOR CONTRIBUTIONS

Jamie Matu, Alison Feeley, Lisa Mabbs, Jamie Blackshaw, and Louisa Ells conceived the study. Jamie Matu, Alison Feeley, Lisa Mabbs, Jamie Blackshaw, and Louisa Ells designed the study protocol. Jamie Matu searched the literature. Jamie Matu, Alex Griffiths, Oliver M. Shannon, Rhiannon Day, and Duncan Radley conducted literature sifting and data extraction. Andrew Jones conducted statistical analyses. All authors contributed to critically appraising the analyzed data. Jamie Matu and Naveed Sattar wrote the manuscript. All authors revised and approved the final manuscript. The corresponding author attests that all authors listed meet authorship criteria and that no others meeting the criteria have been omitted. All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

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CONFLICT OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

The analysis script and data can be found here [<https://osf.io/dkgin/>].

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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