

Risks of and from SARS-COV-2 infection and COVID-19 in people with diabetes: a rapid evidence review

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Background

In the context of the COVID-19 pandemic, the World Health Organisation (WHO) and WHO Member States requested information and guidance on key topics related to COVID-19 and the virus which causes the disease, SARS-COV-2. This rapid review was commissioned to address specific key questions for WHO to provide high-quality, evidence-informed information products around COVID-19.

This review presents a summary of the latest research evidence on the effects of COVID-19 in people with diabetes (PWD).

At the outset of the pandemic, PWD were assumed to be at increased risk from COVID-19. During 2020, emerging data signalled increased risk of adverse outcomes, including mortality, in PWD, likely dependent on a range of different factors.(1, 2) It is important to establish the risks COVID-19 poses to PWD in order to enable informed decision-making by PWD, their carers, healthcare providers, and policymakers.

Therefore, in this rapid review, we set out to review the evidence regarding the extent to which PWD are at increased risk of SARS-CoV-2 infection, and/or of suffering its complications including associated mortality. In particular, we set out to analyse evidence on the following questions:

1. Is diabetes associated with increased risk of acquiring SARS-CoV-2?
2. Is diabetes associated with hospitalization with COVID-19?
3. Is diabetes associated with the severity (including ICU admission, death, and other composite measures of severity) of COVID-19 outcomes?
4. Are there differences in outcomes of SARS-CoV-2 infection within the population of people with diabetes?

Methods

A protocol was agreed in advance with the WHO and published online.(3) This was updated in 2022 at the request of WHO.(4) Methods follow a general framework for a suite of rapid reviews commissioned by WHO in respect to their scientific briefs on COVID-19 and selected non-communicable diseases. As pre-specified by WHO, systematic reviews were first identified; primary studies were then to be reviewed only if insufficient systematic reviews were found.

Searches, screening and inclusion criteria

We searched the Cochrane COVID-19 study register, Embase, MEDLINE, and LitCOVID on 3 December 2020 for published literature or literature accepted for publication but not yet published, in any language (see Appendix 1 and (4) for search strategies). Results from this search have previously been published.(5) We ran an update search of COVID-END, Epistemonikos, Europe PMC, PubMed, and TRIPdatabase on 19 October 2022.

Two reviewers screened titles and abstracts, with discrepancies resolved by discussion or referral to a third reviewer. One reviewer screened full texts for the 2020 searches; for the 2022 searches, this was done in duplicate. We selected systematic reviews (defined as any review in which at least one database was systematically searched) according to the following inclusion criteria:

- Population: people diagnosed with any type of diabetes, with no limitations by age, disease severity, or duration. Excluding people with 'pre-diabetes' (e.g., impaired glycaemic control which does not meet clinical threshold for diabetes diagnosis) and gestational diabetes.
- Exposure: SARS-CoV-2 infection.
- Comparator: Questions 1 to 3 (as above), people without diabetes. Question 4 (as above): people with diabetes, according to the following comparisons as specified in advance by WHO:
 - Type 1 vs type 2 diabetes
 - Controlled vs uncontrolled glycaemia (by HbA1c, whichever definition of control has been used)
 - Previously diagnosed diabetes vs diabetes first diagnosed at COVID-19 diagnosis
 - People treated with metformin vs people not treated with metformin

- People treated with dipeptidyl peptidase 4-inhibitors (DPP4-i) vs people not treated with DPP4-i
- People treated with insulin vs people not treated with insulin
- People with CVD/hypertension/ chronic kidney disease vs people without
- Low socioeconomic status vs high socioeconomic status
- Outcome: Rates of confirmed SARS-CoV-2 infection; admission to hospital and/or to ICU with COVID-19; death with COVID-19.

Data extraction, appraisal, and synthesis

One reviewer appraised and extracted data from systematic reviews in relation to the above review questions; data were checked by a second. We included any systematic reviews which met the above criteria. Quality was assessed using the AMSTAR-2 checklist, but focussing only on critical domains, namely: protocol registered before commencement; adequacy of literature search; justification for excluding individual studies; risk of bias from individual studies; appropriateness of meta-analytical methods; consideration of risk of bias when interpreting results; assessment of presence and likely impact of publication bias.(6) Domains were assessed according to AMSTAR-2 guidance.(6) We considered reviews judged as yes or partial yes for 6 or 7 out of the 7 critical domains of AMSTAR-2 to be higher quality, and those reviews judged as 'no' for at least two critical domains to be of lower quality. Appraisal was not used as a basis for excluding reviews but was used when considering certainty in the findings from the reviews. Data from contributing systematic reviews were narratively synthesised. 95% confidence intervals (CIs) and I^2 values are presented alongside point estimates, where available.

Results

Search results

After removing duplicates, our searches for systematic reviews returned 2178 references, 228 of which met our PECO criteria. The most common reasons for exclusion at full-text stage were 'wrong patient population' and 'not a systematic review' (see Figure 1). As we identified sufficient systematic reviews, we did not search further for primary literature (as per the process set out in our protocol).(3)

Characteristics of included reviews

Of the 228 included reviews: 65 evaluated prevalence of diabetes in cohorts with COVID-19; 156 evaluated severity of COVID-19 outcomes in PWD compared to people without diabetes, including various definitions of severity, ICU admission (47 references) and/or mortality (112 references); and 71 looked at determinants of risk from COVID-19 within PWD (note some reviews contributed data on more than one review question). Within the included reviews, date of search ranged from March 2020 to March 2022. Table 1 lists full citations for the included reviews; Table 2 shows key characteristics of included reviews. Unless stated otherwise, reviews did not specify type of diabetes they included.

In addition to the reviews listed in Table 2, we found two umbrella reviews (reviews of reviews). Characteristics of these are summarised in this paragraph; their results are integrated into the outcomes below. Harrison 2021 provided an overview of reviews of cardiovascular risk factors and cardiovascular disease and their association with COVID-19 outcomes, with searches up to November 2020.(7) They identified findings from 84 reviews, and focussed on the 32 of those that they assessed as moderate (n=31) or high (n=1) quality according to AMSTAR-2. Kastora 2022 investigated the impact of diabetes on COVID-19 mortality and hospital outcomes, with searches up

to August 2021.(8) They identified 53 eligible meta-analyses, and from these extracted data from 185 individual studies, pooling where they deemed it appropriate to do so.

AMSTAR-2 judgements (conducted for critical domains only) are summarised by domain in Table 3 and are provided in more detail in Table 4. Eight reviews (Tan 2020; Sathish 2020; Espinosa 2020; Mesas 2020; Izcovich 2020; Kobjane 2020; Ng 2022; Trskova-Schwarzbach 2021) scored yes or partial yes across all seven domains. A further 30 scored yes or partial yes across six domains, and 47 scored yes or partial yes on 5 of the 7 domains. Where systematic reviews provided conflicting answers for the same review question, we prioritised results from the higher scoring reviews. Within the included reviews, included studies were mainly retrospective observational studies. None of the reviews identified relevant randomized controlled trials.

Is diabetes associated with an increased risk of acquiring SARS-CoV-2 and/or of hospitalisation with COVID-19?

Sixty-five reviews reported some data on prevalence (Table 5). Six of these were judged to be higher quality (yes or partial yes on at least 6 of 7 AMSTAR-2 critical domains). The most recent search data within this set of reviews was January 2022. The vast majority of the data on prevalence comes from hospitalised or at the least symptomatic cohorts. Therefore, questions on acquiring SARS-CoV-2 and hospitalisation with COVID-19 are discussed together here. Few reviews looked at differences between prevalence of diabetes according to setting, but, as described below, one review indicated higher prevalence of diabetes in hospitalised than non-hospitalised (but symptomatic) cohorts. However, certainty in this finding was limited.(9)

Estimates of percentages of PWD within cohorts of people with COVID-19 were highly heterogeneous but on the whole PWD were over-represented in COVID-19 cases compared to population averages (note, population averages may also be under-representations of true diabetes prevalence due to selective diabetes screening within communities) (Table 5). Estimates from individual studies included in the retrieved systematic reviews ranged from 1.7% to 40% PWD within COVID-19 confirmed cases. The pooled estimates in the systematic reviews of PWD within COVID-19 confirmed cases ranged from 7.7% to 23%. In a cohort of people with obesity and COVID-19 this increased to 30.3%.(10) Estimates of diabetes prevalence from the six higher-quality reviews ranged from 10.8% to 22% when looking at all cases, and from 17% to 20% in subgroups with severe disease.(11-16)

Multiple reviews flagged up the presence of heterogeneity between studies. As acknowledged by the reviewers, some of this heterogeneity will be driven by different practices in recording diabetes status (e.g., on admission with COVID-19 or from previous healthcare records), but other reasons have also been investigated. Kumar 2020 (1) (judged to be higher quality) conducted the most thorough investigation of between-study heterogeneity. Their meta-regression showed that proportion of diabetes in patients with COVID-19 was influenced by age (with studies with higher patient age having higher proportion of diabetes, $p<0.001$), type of composite endpoint (with studies reporting mortality endpoint having higher proportion of diabetes, $p=0.004$), and country of study (with studies outside of China having higher proportion of diabetes, $p=0.006$)(13). All other reviews which investigated these potential causes of heterogeneity found the same patterns. Desai 2020 and Mantovani 2020 also found diabetes prevalence was higher in older compared to younger patients (as would be expected given trends in diabetes prevalence in the general population)(17, 18). Hussain 2020 also found prevalence was higher in studies conducted outside of China and Mantovani 2020 found prevalence was greater in non-Asian than in Asian countries.(18, 19) Barrera 2020, Chen 2022, Chua 2021, Du 2020, Hartmann-Boyce 2020, Mair 2020, Meng 2020, and Wang

2020 (3) also found the prevalence of diabetes was higher in patients with severe COVID-19 manifestations, indicating a relationship between diabetes and increased COVID-19 severity which is explored further below (2, 9, 14, 20-24).

Only one review directly compared prevalence of diabetes in hospitalised versus non-hospitalised cohorts with COVID-19. Mair 2020 found higher rates of diabetes in hospitalised (8%, 95% CI 5 to 10%, 13 studies, n not stated) versus community (4%, 95% CI 1 to 7%, 3 studies, n not stated) cohorts with COVID-19, suggesting that once clinically ill PWD are more likely to be admitted to hospital. (9) However, this finding should be interpreted with caution: the review was judged to have several critical weaknesses according to AMSTAR-2; confidence intervals are compatible with no difference and between-study heterogeneity does not appear to have been investigated.

Conclusion: Because of a lack of data from widespread systematic, population-based asymptomatic community testing, data are insufficient to conclude whether or not diabetes predisposes to infection with COVID-19. Data on prevalence of diabetes in symptomatic/hospitalised COVID-19 cases are heterogeneous, but on the whole suggest PWD are over-represented, particularly in hospitalised cohorts and in cohorts with severe disease. Heterogeneity may in part be driven by: age of sample, with older cohorts having a higher prevalence of diabetes and multimorbidity; geographic location, with some indication of lower estimates of prevalence of diabetes in hospitalized COVID patients in Asia compared to outside of Asia; and severity of COVID-19, with estimates higher in severe COVID-19 cohorts. There is some data from an indirect comparison that, once clinically ill with COVID-19, PWD are more likely to be hospitalised; this is consistent with the observation that PWD appear over-represented in hospitalised cohorts.

Is diabetes associated with the severity of COVID-19 outcomes?

Two umbrella reviews and 144 individual reviews evaluated data related to this question. Of the systematic reviews, 21 were considered to be of higher quality. The latest search date was March 2022. Where investigated, all of the reviews identified increased risk of mortality and severity of COVID-19 in PWD.

Where data were pooled across studies, outcomes were most commonly calculated as risk ratios (RRs) or odds ratios (ORs), calculated as: $(\# \text{ of PWD with outcome} / \text{total } \# \text{ of people with outcome}) / (\# \text{ of PWD without outcome} / \text{total } \# \text{ of people without outcome})$. However, at times RRs or OR's were extracted from individual studies and nature of calculation was not explicitly stated. In addition to possible variation in the way they were calculated, pooled outcomes were subject to some limitations, including statistical heterogeneity and possible publication bias in some instances. Where high statistical heterogeneity or suspected publication bias were detected, this is noted in Table 6, and, where relevant, discussed below. Most analyses were based on unadjusted estimates, as authors stated pooling data from adjusted analyses proved difficult (e.g., Barrera 2020). However, results of individual studies which provided adjusted estimates are consistent with those from meta-analyses containing unadjusted data.

ICU admission

Twenty-three reviews evaluated ICU admission (Table 6). Of these, five were considered to be of higher quality (6 or 7 of 7 AMSTAR-2 critical domains as yes or partial yes). Of those sixteen that reported pooled effect estimates, ten found point estimates indicating increased association of ICU admission with COVID-19 in PWD, with confidence intervals excluding no difference. A further five found point estimates signalling increased association of ICU admission in PWD, but with wide confidence intervals that spanned no difference and are also compatible with a lower rate. One meta-analysis of two studies (n=179) found lower rates of ICU admission in PWD, but here again the

confidence intervals were very wide, the difference in risk being compatible with a 94% reduction to a greater than 900% increase.(25)

The four higher quality reviews which evaluated this outcome all found increases in ICU admission in PWD. In three, CIs excluded no difference and were compatible with a 10%-500% increase. Analyses varied in the amount of heterogeneity detected, from high statistical heterogeneity (1 analysis) to none (1 analysis). Fang 2020 compared rates of diabetes in people in ICU versus those not in ICU and found an RR of 1.88 (95% CI 1.10 to 3.23, $I^2=51\%$, 5 studies, $n=3747$).⁽²⁶⁾ Zhou 2020 (2) pooled data from 4 studies ($n=6652$) and found an OR of 2.98, 95% CI 1.49 to 5.98, $I^2=48\%$.⁽¹⁶⁾ Li 2021 (2) pooled data from 3 studies (n not stated) and found an OR of 2.24 (95% CI 0.84 to 5.95, $I^2=91\%$), and Gaba 2022 found a similar OR (2.79, 95% CI 1.79 to 4.34) when pooling data from 5 studies ($n=611$), with no evidence of statistical heterogeneity ($I^2=0\%$).^(27, 28)

Kastora 2022 (overview of reviews) pooled data from 59 studies and found diabetes increased risk of ICU admission with COVID-19 (OR 1.59, 95% CI 1.15 to 2.18, $I^2=96\%$, $n=280,825$). Heterogeneity was not explained by region or study design.¹

Mortality

Eighty-nine reviews evaluated mortality (death with COVID-19). Of those 64 which reported a pooled estimate, all found a point estimate suggesting increased risk of death with COVID-19 in PWD; 60 of these 64 pooled estimates had confidence intervals ranging from a 1.02 to 6.71 increase. Kastora 2022 (umbrella review) found an increased risk of mortality from COVID-19 in PWD (OR 1.75, 95% CI 1.61 to 2.17, $I^2=91\%$, 136 studies, $n=58,855$).⁽⁸⁾ Significant statistical heterogeneity remained within their pre-specified subgroups by geographical region and study type. Harrison 2021 (overview of reviews) did not conduct their own statistical syntheses but concluded that diabetes increased risk of mortality based on consistent findings across the 18 reviews they rated as moderate quality which investigated this outcome and population.⁽⁷⁾

Thirteen of the reviews which calculated pooled effect estimates were considered higher quality according to the AMSTAR-2 critical domains; 12 of the 13 detected a statistically significant increase in risk (in the ninth, Singh 2020⁽²⁾, the pooled estimate from only 2 studies resulted in wide CIs (RR 1.88, 95% CI 0.89 to 3.73).^(13, 16, 26, 29-34) In these studies, point estimates for pooled RRs ranged from 1.48 to 1.83, and for ORs ranged from 1.25 to 2.52. Where I^2 values were reported these were in the range of those not considered to indicate significant heterogeneity ($<40\%$) with the exception of Ssentongo 2020 ($I^2=84\%$) and Gaba 2020 ($I^2=62\%$).^(27, 33) Authors of the largest meta-analysis in this group, Izcovich 2020, used GRADE to evaluate certainty in this evidence and estimated absolute risks. In their meta-analysis of 52 studies ($n=30,303$), diabetes increased odds of mortality by an OR of 1.84 (95% CI 1.61 to 2.1, $I^2=33\%$).⁽²⁹⁾ This translated to an absolute estimated increased risk of 5.6% increase in mortality (95% CI 4.3 to 7%). They judged the evidence to be of high certainty. Though some of the contributing studies were judged to be at high risk of bias, sensitivity analysis showed that the pooled estimate was not sensitive to the removal of studies at high risk of bias and/or those which did not report adjusted estimates.

Other measures of severity

55 reviews evaluated 'severity' as a construct in and of itself; of these 10 were considered higher quality. Severity was a broad definition – in some reviews, it was not defined, or authors relied on categorisations from original study authors. In other reviews, severity was a composite score derived

¹ The authors state that heterogeneity was to some extent explained by these factors, but substantial heterogeneity remained within these groups

from set criteria, most commonly including elements such as ICU admission, mortality, oxygen levels, acute respiratory distress syndrome (ARDS), and the need for mechanical ventilation. More detail can be found in Table 6.

Of the 42 reviews which calculated a pooled estimate for severity, all found point estimates suggesting increased risk of severe disease in PWD. In 41 of 42, this effect was statistically significant (the one estimate which did not detect a statistically significant difference contained 4 studies (total n not reported) and found an OR of 2.07, 95% CI 0.89 to 4.82).(35) ORs ranged from 1.43 to 3.68; RRs ranged from 1.50 to 2.96. I^2 values tended to indicate moderate statistical heterogeneity, but with some variation. The 10 higher quality reviews all found statistically significant increases equating to, on average, over a doubling in risk of severe disease.(13, 26, 29, 30, 32, 34, 36-39) Again, Izcovich 2020 was the largest analysis deemed to be high quality and also used GRADE to evaluate certainty and calculate absolute risks. In their meta-analysis of 97 studies (n=21,381), in which severity was defined as reported by study authors or on the basis of ARDs or the requirement of ICU or invasive mechanical ventilation, they found a pooled OR of 2.51 (95% CI 2.2 to 2.87, $I^2=32\%$) and judged the evidence to be of high certainty. Estimated absolute risks were a 13.2% increase in severe COVID-19 disease (95% CI 11 to 15.5%).(29)

Kastora 2022 (umbrella review) pooled outcomes from 43 reviews evaluating 'critical' or 'severe' COVID-19 disease in PWD compared to those without; results indicated increased risk in PWD (OR 2.88, 95% CI 2.29 to 3.63, $I^2=73\%$, n=7,984). Again, heterogeneity was not explained by region or study design.(8)

Conclusion: There is consistent evidence across many systematic reviews that diabetes increases risks of severe COVID-19 disease including ICU admissions and of death with COVID-19. Most data are from retrospective studies. The largest review judged the evidence to be of high certainty regarding increased risk of severe COVID-19 and increased risk of death with COVID-19 in PWD; restricting analyses to studies at low risk of bias also showed increased risk for both outcomes in PWD. Estimates for severe disease suggest a greater than doubling increase in risk; for death, estimates suggest a slightly less than 2-fold increase in risk. There is some evidence of between-study heterogeneity, suggesting magnitude of increase may vary by study population/characteristics. Data on ICU admission again suggested increased risk in PWD.

Are there differences in outcomes of SARS-CoV-2 infection within the population of people with diabetes?

Systematic reviews which contained analyses or data regarding our pre-specified characteristics are discussed below. Only one review contained any data on socioeconomic status; Boddu 2020 reported on data from a UK cohort study which found that within PWD (as well as in the general population without diabetes) COVID-19 outcomes were worse in people from less-advantaged groups.(40)

Type of diabetes

The majority of studies in this field, and hence of reviews aggregating those studies, do not delineate between diabetes type. To some extent, this may be due to issues with recording diabetes status in hospital. Regardless, it is an area that warrants better reporting. One overview of reviews and five reviews contained some data explicitly comparing risks in type 1 versus type 2 diabetes. Kastora 2022 (overview of reviews) pooled mortality data from two small studies (total n=308) and found no clear difference when comparing type 1 and type 2 (compared to type 2, OR for COVID-19 mortality with type 1 0.68, 95% CI 0.24 to 1.87, $I^2=0\%$). (8)

Of the other four reviews, three conducted meta-analyses. Shafiee 2022, judged to be a higher quality review, pooled data from 11 studies (n=7,690,415) in people with COVID-19.(41) When comparing people with type 1 to people with type 2 diabetes, they found no significant differences between groups in terms of ICU admission (log OR -0.22, 95% CI -0.81 to 0.37) or hospitalization (log OR -0.48, 95% CI -1.38 to 0.27). Unadjusted analyses suggested reduced risk of all-cause mortality in people with type 1 compared to type 2 diabetes (log OR -0.71, 95% CI -1.38 to -0.03) but the authors descriptively report that after adjusting for age and comorbidities, risk with type 1 compared to type 2 was higher in five studies, lower in three studies, and not significantly different in two studies.

Alhumaid 2021, judged to be of lower quality, looked specifically at a subset of patients with both diabetic ketoacidosis (DKA) and COVID-19.(42) They used binary logistic regression analyses to explore the effect of demographic and biochemical parameters on death. Within their subset of people with COVID-19 hospitalised with DKA, people with type 2 diabetes were more likely to die (univariate OR 5.24, 2.07 to 15.19, multivariate OR 4.67, 2.23 to 4.31, reference group unclear) compared to those with type 1 (univariate OR 0.83, 0.23 to 2.92, multivariate OR 0.61, 95% CI 1.8 to 2.3, reference group unclear, n=243). Caution should be taken in interpreting these results as reporting is limited, the review was judged to have multiple critical weaknesses, and the latter CI are not consistent with the pooled result (they exclude the point estimate).

Schlesinger 2021, also judged to be of lower quality, found no clear evidence in a difference in risk of death from COVID-19 when comparing type 2 to type 1 diabetes (standard rate ratio (SRR) 1.65, 95% CI 0.64 to 4.26, 2 studies, $I^2=0\%$, certainty of evidence judged to be very low).(43)

The other two reviews only presented narrative information. Both Apicella 2020 and Boddu 2020 cited data from a large UK cohort study (n=61,414,47).(40, 44, 45) Adjusted for age, sex, deprivation, ethnicity, and geographical region, compared with people without diabetes, the risk of in-hospital COVID-19-related death was markedly higher in people with type 1 diabetes than with type 2 (type 1 OR 3.51 (95% CI 3.16–3.90); type 2 OR 2.03 (1.97–2.09)).(45)

No reviews explicitly considered differential risks in other types of diabetes (this was not something we set out to investigate).

Newly diagnosed diabetes

Three reviews contained some data on diabetes diagnosed at time of COVID-19 infection. Sathish 2020, judged to be of higher quality, conducted a meta-analysis of eight studies (n=3700) to estimate prevalence of newly diagnosed diabetes in hospitalised COVID-19 patients.(46) They estimated a pooled proportion of 14.4% (95% CI 5.9 to 25.8%) but data were highly heterogeneous ($I^2=98\%$). Of note, this area may also be particularly prone to publication bias, as reports with higher-than expected levels of newly diagnosed diabetes may be more likely to be written and subsequently published.

As described above Alhumaid 2021, judged to have two or more critical weaknesses, looked specifically at a subset of patients with both diabetic ketoacidosis (DKA) and COVID-19.(42) Within their subset of people with COVID-19 hospitalised with DKA, people with newly diagnosed diabetes had ORs consistent with increased risk of mortality, but with CIs encompassing no difference; again, caution should be taken in interpreting these results due to limitations in reporting and conduct (univariate OR 1.67, 95% CI 0.31 to 2.11; multivariate OR 1.3, 95% CI 0.51 to 1.99; reference group not specified, n=243).

Boddu 2020, which was judged to have two or more critical weaknesses according to AMSTAR-2, did not conduct meta-analysis but notes that SARS-CoV-2 can trigger severe diabetic ketoacidosis at

presentation in people with new-onset diabetes.(40) The authors note that at present there is no evidence that SARS-CoV-2 induces diabetes on its own accord. Acute infection, stress and steroids can all also raise blood glucose. Distinguishing between new diabetes *caused* by COVID-19 and newly diagnosed diabetes which was already present prior to COVID-19 infection but was exacerbated and/or detected due to measurements taken at hospital also is a challenge. A global registry of patients with COVID-19-related diabetes (covidien.e-dendrite.com) has been set up to monitor this.

Glucose control

Eleven systematic reviews contained some data on glucose control; ten were judged to have two or more critical weaknesses according to AMSTAR-2 (2, 40, 42-44, 47-52) and one was judged of higher quality (53). Kastora 2022 (overview of reviews) compared mortality between those with an HbA1c above >70mmol/mol, and those with HbA1c ≤70 mmol/mol; risk was higher in those with higher HbA1c (HR 2.75, 95% CI 2.60 to 2.91, $I^2=0\%$, 5 studies, n not reported).

Five of the other systematic reviews pooled data in meta-analyses; all found point estimates suggesting increased risks with higher blood glucose, but many of these estimates were imprecise. Praticchiazzo 2022, the one review of this group to be judged of higher quality, pooled data from studies in people with diabetes and found that HbA1c was linearly associated with increased COVID-19 mortality or worsening when considered as a continuous variable (OR 1.01, 95% CI 1.01 to 1.01, $p<0.0001$, $I^2=39\%$, four studies, n not reported). (53) When restricting analyses only to mortality, results were similar but no longer statistically significant (OR 1.01, 95% CI 0.95 to 1.08, $p=0.73$, $I^2=0\%$, two studies, n not reported). Zhu 2021, judged to have multiple critical weaknesses, reported that the association between elevated HbA1c as a continuous variable and adverse prognosis of COVID-19 was not statistically significant (OR, 1.02; 95%CI, 0.95–1.09, four studies, n participants NR, $I^2=0\%$), but that when reduced to a dichotomous variable higher HbA1c contributed to an increase risk of mortality from COVID-19 (OR, 2.300; 95% CI 1.679 to 3.150, six studies, n=1180, $I^2=48\%$; cut off point for higher HbA1c varied across trials).(52) Schlesinger 2021 (judged to have multiple critical weaknesses, n not reported) found very low certainty evidence of no difference in COVID-19 mortality in people with diabetes based on HbA1c when pooling data from 2 studies (53-75 versus <53 mmol/mol SRR 1.08, 95% CI 0.57 to 2.06, $I^2=34\%$; >75 versus <53 mmol/mol SRR 0.95, 95% CI 0.50 to 1.79, $I^2=0\%$).(43) Lack of evidence of a difference persisted when pooling four studies providing data on risk per 20 mmol/mol HbA1c difference (SRR 1.05, 95% CI 0.80 to 1.35, $I^2=0\%$, low certainty evidence). By contrast, they judged there to be moderate certainty of an increased risk based on blood glucose at administration when comparing ≥11 versus <6 mmol/l (SRR 8.60, 95% CI 2.24 to 32.83, 2 studies, $I^2=0\%$) and when evaluating risk based on 1mmol/l difference in blood glucose at admission (SRR 1.10, 95% CI 1.05 to 1.16, 2 studies $I^2=0\%$, low certainty evidence). The difference was not statistically significant when comparing 6-11 versus <6 mmol/l at admission (SRR 2.76, 95% CI 0.56 to 13.51, 2 studies $I^2=0\%$, low certainty evidence).

Chen 2020 set out to assess the impact of COVID-19 on blood glucose, and pooled data from three trials (n=222) in PWD comparing blood glucose or glycated haemoglobin (HbA1c) levels between patients classed as having severe versus mild disease (definition not provided)(47). The pooled mean difference (MD) in blood glucose was 2.21 mmol/L (95% CI 1.30 to 3.13, $I^2=0\%$), indicating a statistically significantly greater elevation in blood glucose in patients with severe disease. HbA1c was also higher in patients with severe disease, but the estimate was also compatible with no difference (MD 0.29%, 95% CI -0.59 to 1.16, $I^2=68\%$) when pooling the two small studies providing data (n=179). Lee 2020 set out to determine the effects of hyperglycaemia on complications of COVID-19. They pooled results from 8 studies (including 681 PWD) and found that hyperglycaemia was associated with worse COVID-19 prognosis (in both PWD and people without diabetes).(49)

Pooled results showed an increased association of admission to ICU (OR 2.7, 95% CI 0.98 to 7.35, I^2 NR) and of death with COVID-19 (OR 7.2, 95% CI 2.7 to 19.2, I^2 NR) in PWD with hyperglycaemia compared to those with 'controlled blood glucose' (not defined).

The remaining six reviews did not conduct meta-analyses relevant to this question, but all described an association between higher blood glucose and worse COVID-19 outcomes, citing individual studies to support these assertions.(2, 40, 44, 48, 50, 51) As infection and steroids can in themselves raise blood glucose levels, determining the direction of association between high blood glucose when hospitalised with COVID-19 and worse COVID-19 outcomes is challenging. A number of reviews also cited data from large (mainly UK-based) cohort studies which used last-measured HbA1c, taken prior to COVID-19 infection, which provides a better picture of longer-term blood glucose control. These studies also found significant associations between higher HbA1c (defined as $>10\%$ (86 mmol/mol)) and worse COVID-19 outcomes, including ICU admission and ARDS.(1, 45) However, Alhumaid 2021 found that in a subset of patients with both diabetic ketoacidosis (DKA) and COVID-19, there was no evidence of statistically significant differences in mortality outcomes based on HbA1c (reference group not provided).(42)

Selected medications

We focussed on metformin, DPP4-i, and insulin.

Insulin

Kastora 2022 (overview of reviews) pooled data on mortality in studies comparing insulin use to non-insulin use in people with diabetes and COVID-19; risk was higher in those using insulin (HR 2.80, 95% CI 2.29 to 3.44, $I^2=43\%$, 7 studies, n not reported). This was consistent with results from a further six systematic reviews evaluating associations between insulin use and COVID-19 outcomes. Of the three judged to be of higher quality:

- Kan 2021 restricted studies to populations with type 2 diabetes; pooled results from seven of these (n not reported) showed greater COVID-19 mortality in insulin users than in insulin non-users (pooled OR, 2.20; 95% CI, 1.34–3.60). Statistical heterogeneity was high ($I^2=80.6\%$), with five of the studies showing increased risk with confidence intervals excluding no difference, one showing no difference, and one with a point estimate indicating lower risk in those using insulin but with confidence intervals encompassing no difference as well as clinically significantly increased risk.(54)
- Nguyen 2022 also restricted studies to populations with type 2 diabetes.(55) Pooled data from 33 studies (n not reported) showed that insulin users were more likely to die during COVID-19 hospitalization than non-users (OR 1.70, 95% CI 1.33 to 2.19). Statistical heterogeneity was very high statistical ($I^2=97\%$) but for the most part appeared to be driven by magnitude rather than direction of association; all but 5 of the 33 studies had point estimates indicating increased risk in insulin users, and in the 5 where point estimates indicated reduced risk, 95% CI incorporated the possibility of increased risk.
- Chen 2022 (2) conducted a Bayesian network meta-analysis and did not explicitly restrict to populations with type 2 diabetes.(56) Fourteen studies had data on insulin use (n not reported). Insulin treatment was associated with a greater risk of death from COVID-19 (OR 1.38, 95% CI 1.24 to 1.54, $I^2=66\%$).

The three reviews judged to have significant limitations also had findings consistent with the above. Wang 2022 found that insulin use was significantly associated with a higher risk of death people with diabetes and COVID-19 compared to those who did not use insulin (OR 2.59, 95% CI: 1.66–4.05; $P < 0.0001$; $I^2=57\%$) (57), as did Schlesinger 2021 (RR 1.75, 95% CI 1.01 to 3.03, n = 5 studies, authors judged evidence to be high certainty).(43) Yang 2021 (2) also found a non-statistically significant

association with increased in-hospital admission for COVID-19 in people with diabetes using insulin compared to people with diabetes not using insulin (OR 1.23, 95% CI 0.65 to 2.33).(58)

DPP4i

Kastora 2022 (overview of reviews) pooled data on mortality in five studies comparing DPP4i use to non-use (which could include other diabetes medications, or no diabetes medications); pooled data were highly heterogenous with two studies showing statistically significant increased risk in those using DPP4-I, and three showing statistically significant reduced risk in those using DPP4i. This variation was also present in the other 14 reviews evaluating associations between DPP4i use and COVID-19 outcomes. Of the five judged to be of higher quality, results were conflicting, with one finding DPP4i use was associated with statistically significantly increased risk, another finding they were associated with statistically significantly reduced risk, two finding point estimates consistent with reduced risk but 95% CI incorporating no difference and increased risk, and one with point estimates suggesting increased risk but 95% CI also incorporating no difference and reduced risk:

- Nguyen 2022 found an increased risk of mortality in patients with T2D on DPP-4i compared to those not using DPP4i (OR 1.26, 95% CI 1.22 to 1.31, 28 studies, n not reported).(55) Statistical heterogeneity was high ($I^2=82\%$), with 9 of the 28 studies having point estimates consistent with reduced risk; of these two had 95% CI excluding no difference.
- Chen 2022 (2), not explicitly restricted to populations with type 2 diabetes, found 21 studies with data on DPP4i (n not reported).(56) DPP4i use was associated with a lower risk of death from COVID-19 than non-use (OR 0.88, 95% CI 0.78 to 1.00, $I^2=63\%$); this association remained when restricting to those studies adjusting for age, gender and other characteristics.
- Kan 2021 (restricted to populations with type 2 diabetes) pooled results from eight studies (n not reported) and found no difference in COVID-19 mortality between DPP4-I users and non-users (pooled OR, 0.72; 95% CI, 0.51 to 1.01.; $P=0.057$, $I^2=46\%$).(54)
- Han 2022 included 31 studies in 66,914 participants with COVID-19, and found no evidence of a clear association between DPP4i and mortality from COVID-19 (OR 0.95, 95% CI 0.72 to 1.26) or poor composite outcomes (OR 1.27, 95% CI 0.91 to 1.77) in PWD.(59)
- Hariyanto 2021 included data from 10 studies (n=7012) evaluating the impact of DPP4i in people with COVID-19 and diabetes. Pooled analyses indicated no clear association with DPP4i and severe COVID-19 (OR 1.07, 95% CI 0.87 to 1.31, $I^2=0\%$) or mortality (OR 1.14, 95% CI 0.87 to 1.51, $I^2=8\%$).(60)

Of the remaining nine studies:

- Three found point estimates indicating reduced risk, but confidence intervals incorporating the possibility of no difference. Patoulas 2021 described a 'non-significant decrease in 3%' in those using DPP4i compared to those who didn't in the risk for COVID-19 related death (95% CI 0.67 to 1.41, $I^2=83\%$).(61) Bonora 2021 found no clear evidence of a difference when pooling seven studies with unadjusted data (RR 0.81, 95% CI 0.57 to 1.15, $I^2=55\%$) or when pooling data from the three studies adjusting on participant characteristics (RR 0.74, 95% CI 0.47 to 1.16, $I^2=64\%$).(62) In their main model testing the association between DPP4i use and mortality, Pal found no significant association (OR 0.79, 95% CI 0.46 to 1.36), but significant heterogeneity ($I^2=80\%$). In a subgroup analysis restricted to in-hospital use of DPP4i pooled data suggested benefit (OR 0.37, 95% CI 0.23 to 0.58) and no heterogeneity ($I^2=0\%$).(63)
- Three found statistically significant reductions in mortality in people using DPP4i. Rakhmat 2021 found that DPP4i were associated with lower mortality in patients with COVID-19 (RR 0.76, 95% CI 0.60 to 0.97, $I^2=44.5\%$). Their meta-regression showed that the association was significantly affected by metformin (OR 1.02, 95% CI 1.00 to 1.04 and ACEI/ARB use OR 1.04,

95% CI 1.01 to 1.07).(64) Similarly, Zein 2022 reported that DPP4i use was associated with reduced mortality (OR 0.75, 95% CI 0.56 to 0.99, $I^2=42.9\%$) and that this association was affected by metformin (OR 1.03, 95% CI 1.01 to 1.06, $p = 0.010$) and ACEI/ARB use (OR 1.06, 95% CI 1.02 to 1.10, $p = 0.004$).(65) Yang 2021 found that the use of DPP4i inhibitors was associated with decreased mortality due to COVID-19 (OR 0.58, 95% CI 0.34 to 0.99, $I^2=51.1\%$).(66)

- Three studies did not provide meta-analyses for this comparison. Apicella 2020 noted that though there is speculation that DPP4-i could, hypothetically, reduce virulence (by acting as a co-receptor for a subset of coronaviruses and hence interfering with binding), there is no clinical evidence of this.(44) They cite two studies which found no associations between glucose-lowering drugs (as prescribed/taken prior to COVID-19 illness) and COVID-19 outcomes in people hospitalised with COVID-19. Flaherty 2020 sounded a note of possible optimism regarding the role of DPP4i as possible receptors for SARS-CoV-2, but calls for further research to investigate their role.(67) Carrasco-Sanchez 2022 summarises an expert consensus exercise on the effectiveness and safety of DPP4i in treating patients with diabetes and COVID-19. They stated there was no clear evidence that DPP4i impact risk of 'contagion', there was no evidence that DPP4i were unsafe in this context, and that there was some evidence that DPP4i may reduce mortality in hospitalized patients with COVID-19, but not in outpatients.(68)

Metformin

Kastora 2022 (overview of reviews) pooled data on mortality in studies comparing metformin use to non-use in populations with diabetes; risk was lower in those using metformin (HR 0.60, 95% CI 0.54 to 0.67, $I^2=58\%$, 7 studies, n not reported). Though I^2 indicated moderate statistical heterogeneity, all studies showed statistically significantly reduced risk in those using metformin.

A further fourteen reviews contributed information on this comparison. Of the six reviews considered higher quality, five found metformin to be associated with statistically significant reduced risks from COVID-19 (see summaries of each below), and the sixth (which contained the smallest number of studies) found a point estimate indicative of reduced risk, but confidence intervals narrowly incorporating no difference (OR 0.81, 95% CI 0.64 to 1.01, $I^2=41.6\%$, 8 studies)(69):

- Kan 2021 (restricted to populations with type 2 diabetes) pooled results from 15 studies (n not reported) and found reduced COVID-19 mortality in those using metformin compared to those not using metformin (pooled log OR -0.37; 95% CI -0.59 to -0.16.; $P=0.002$, $I^2=59\%$).(54)
- Nguyen 2022 (also restricted to populations with type 2 diabetes) also found metformin to be associated with significantly reduced mortality when comparing users with non-users (OR 0.54, 95% CI 0.47 to 0.62, 42 studies, n participants not reported).(55) Statistical heterogeneity was high ($I^2=82\%$) but appeared to for the most part be driven by magnitude rather than direction of effect; of the 42 studies, only 2 had point estimates consistent with increased risk, and of these only one had confidence intervals excluding the null.
- Chen 2022 (2) conducted a Bayesian network meta-analysis; they did not explicitly restrict to populations with type 2 diabetes.(56) Twenty-five studies had data on metformin use (n not reported). Metformin was associated with a lower risk of death from COVID-19 than non-use (OR 0.74, 95% CI 0.67 to 0.81, $I^2=61\%$).
- Han 2022 included 31 studies in 66,914 participants with COVID-19 and any type of diabetes, and found metformin was associated with statistically significantly lower risks of mortality (OR 0.62, 95% CI 0.50 to 0.76) or poor composite outcomes (OR 0.83, 95% CI 0.71 to 0.97).(59)

- Ganesh 2022, one of the largest reviews, found metformin was significantly associated with lower mortality in COVID-19 patients with diabetes in both unadjusted (OR 0.61 [95% confidence interval: 0.53–0.71], $P < .00001$, $I^2 = 70\%$) and adjusted (OR 0.78 [95% confidence interval: 0.69–0.88], $P < .00001$, $I^2 = 67\%$) models.(70) They considered data from 32 cohort studies in 2.9 million people, and graded the certainty of this evidence as low, downgrading results based on risk of bias and because all studies were non-randomized.

Of the remaining eight reviews (those considered lower quality), six conducted meta-analyses, all of which found a clinically and statistically significant association between metformin use prior to COVID-19 diagnosis and reduction in death with COVID-19:

- Hariyanto 2020 pooled 5 studies, and found an RR of 0.54 (95% CI 0.32 to 0.90, $I^2=54\%$, $n=6937$) for metformin use in PWD. The authors caution that confounding was not taken into account in most studies, and that none of the studies stated the dose or duration of metformin treatment in their samples.(71) In addition, all five studies were retrospective.
- Kow 2020 pooled 5 studies ($n=8121$), all of which were in PWD, and four of which are identified by the authors as reliable given their large-scale and adjustments for multiple confounding factors. They found an OR of 0.62 (95% CI 0.43 to 0.89, $I^2=29\%$). (72)
- Lukito 2020 pooled 9 studies ($n=10,233$). They tested sensitivity between non-adjusted and adjusted models and found that regardless of model used, metformin was associated with a reduction in death with COVID-19 (non-adjusted model (OR 0.45, 95% CI 0.25 to 0.81; $I^2=63.9\%$; adjusted model (OR 0.64, 95% CI 0.43 to 0.97; $I^2= 52.1\%$)). However, there was some indication of small study effects.(73)
- Poly 2021 (16 studies, n not reported) found metformin use was associated with a 35% decrease in risk of mortality among patients with COVID-19 (RR 0.65, 95% CI 0.54 to 0.80, $I^2 =76\%$). (74)
- Schlesinger 2021 found users of metformin compared with non-users of metformin were at lower relative risk of dying (RR 0.50, 95% CI 0.28 to 0.90, 4 studies, authors judged certainty of evidence to be moderate).(43)
- Yang 2021 (1) (17 studies, $n=20,719$) found metformin was associated with significantly decreased mortality (OR 0.64, 95% CI 0.51 to 0.79) and significantly decreased severity (OR 0.81, 95% CI 0.66 to 0.99).(75)

Of note, metformin is consistently shown to be associated with lower mortality in a range of conditions (e.g., breast cancer (76), not just COVID-19), which is thought to be driven by confounding by indication; these findings should not be immediately interpreted as suggesting that metformin has a protective effect in COVID-19 illness without further investigation. The remaining reviews did not provide pooled estimates but rather narratively summarised results from individual studies.(67, 77) Multiple review authors emphasised the need for data from randomized controlled trials to achieve clarity on whether the observed associations above are causal in nature.

Selected co-morbidities

We focus here on PWD with concurrent cardiovascular disease, hypertension, or chronic kidney disease. Considering the high prevalence of these co-morbidities in PWD, there was a notable paucity of data in this area.

Six reviews considered co-morbidities relevant to our review. Only one was judged to be of higher quality: Corona 2021 found their observed increased risk of COVID-19 related mortality in people with diabetes was reduced in studies reporting a higher proportion of patients with CKD and/or hypertension, but that no such relationship was shown based on CVD. (78) No further information was available, as investigating this was not a central aim of the review.

Two lower-quality reviews pooled data on risks from co-morbidities *within* populations with diabetes and COVID-19. Maddaloni 2021 found that risk of mortality was significantly increased in those with concurrent CVD (OR 2.91, 95% CI 2.13 to 3.97, 4 studies, $I^2=0\%$).⁽⁷⁹⁾ Schlesinger 2021 (judged to have 4 critical weaknesses) pooled data from 22 studies in 17,687 and found that CVD and CKD were both associated with statistically significantly increased risk of COVID-19 related death (CVD standard rate ratio (SRR) 1.56, 95% CI 1.09 to 2.24, 8 studies, $I^2=70\%$; CKD SRR 1.93, 95% CI 1.28 to 2.90, $n = 6$ studies, $I^2=81\%$).⁽⁴³⁾ Evidence for both was judged to be of moderate certainty (n and reasons for judgements not provided).

Two further lower quality reviews considered co-morbidities in their analyses. Huang 2020 evaluated the impact of diabetes on a composite poor outcome in people with COVID-19 pneumonia and found a statistically and clinically significant association (see Table 6).⁽⁸⁰⁾ They used meta-regression to test whether the association was impacted by a range of participant characteristics. In univariate models, there was no association CVD, but they found that the association with composite poor outcome was influenced by prevalence of hypertension (weaker association in populations with greater hypertension prevalence, $p<0.001$). In studies where prevalence of hypertension was $>25\%$, the RR was 1.93 (95% CI 1.48 to 2.52, $I^2=58\%$), compared to 3.06 in studies with prevalence of hypertension $<25\%$ (95% CI 2.19 to 4.26; $I^2=33\%$). However, in multivariable meta-regression including both age and hypertension, the association was attenuated for both hypertension ($p=0.107$, RRs not reported) and age ($p=0.334$) suggesting the observed differences are probably dependent on each other.

The other three reviews provide very little data. Barerra 2020 reports an unadjusted RR from one study of 22 people showing a high point estimate for risk of severe COVID-19 in PWD with hypertension, but due to the small sample size, CIs are very wide (RR 10, 95% CI 0.94 to 105.2).⁽²⁰⁾ Boddu 2020 cites a large UK-cohort study (45) and observes that the relationship between diabetes and COVID-19 mortality is particularly pronounced in older age groups with pre-existing renal or cardiac disease.⁽⁴⁰⁾ They interpret the low absolute risk of in-hospital death with COVID-19 in PWD under 40 years old as indication that co-morbidities may contribute significantly to increased risk of death with COVID-19 in PWD. Of note, in Haddon 2020, adjusting for previous hospital admissions with coronary heart disease, cerebrovascular disease, or heart failure somewhat attenuated the observed increase in risk of death with COVID-19 in PWD, but a clear increase in risk remained for both types of diabetes (type 1 OR 2.86, 95% CI 2.58 to 3.18; type 2 OR 1.80, 95% CI 1.75 to 1.86).⁽⁴⁵⁾

Conclusions:

- Individual studies, including a very large population-based study in the UK, show that type 1 diabetes is associated with higher risks of COVID-19 mortality than type 2 diabetes, but meta-analyses investigating this found no clear evidence of a difference. These meta-analyses were all judged to have multiple critical weaknesses.
- There is no evidence of differences in risk between new-onset and pre-existing diabetes during COVID-19-. Whether COVID-19 causes new-onset diabetes continues to be unclear.
- Higher blood glucose levels, both in the immediate and longer-term, are associated with worse COVID-19 outcomes. As high blood glucose can be caused by infection and/or steroids to treat said infection, it is difficult to determine the causal relationship between worse COVID-19 outcomes and measures of blood glucose control taken when ill with COVID-19. However, general practice and national health services databases using HbA1c measured prior to COVID-19 show a clear association between glucose control and COVID-19 outcomes, with higher HbA1C prior to illness increasing risk from said illness. In the

literature HbA1c of 10% (86 mmol/mol) or 7.5% (58 mmol/mol) are commonly used as cut-offs for defining 'high'.

- Metformin use prior to hospitalisation with COVID-19 was associated with a clinically meaningful reduction in the risk of death with COVID-19, as evidenced in twelve meta-analyses and an overview of reviews. Confounding by indication can not be ruled out and no studies could establish causality.
- The association between DPP4i use and COVID-19 outcomes in people with diabetes is unclear, with conflicting results across reviews.
- Insulin use prior to COVID-19 illness was associated with a clinically meaningful increase in the risk of death with COVID-19, as evidenced in six meta-analyses and an overview of reviews. None included studies which could establish causality.
- There is very little evidence regarding the role of co-morbidities in increasing risk of worse outcomes from COVID-19 in PWD.

Discussion

This overview of reviews provides consistent evidence from multiple meta-analyses and overviews of reviews that diabetes is a risk factor for severe disease and death from COVID-19. There was less data available on ICU admission as an outcome, but where available this data also signalled increased risk in PWD. Within PWD, higher blood glucose levels and insulin use prior to infection were associated with worse COVID-19 outcomes. Data were limited but also suggested co-morbid cardiovascular and/or renal disease increased risk from COVID-19 in PWD. Metformin was associated with improved outcomes; data on DPP4i were inconsistent.

Due to the nature of the review questions, the majority of data contributing to included reviews comes from retrospective observational studies. Reviews varied in the extent to which they assessed risk of bias. In the one high quality review which used the GRADE framework to evaluate certainty, the authors judged the evidence on the association between diabetes and increased risk of worse outcomes and death from COVID-19 to be of high certainty.⁽²⁹⁾ Though the majority of studies contributing to these analyses were judged to be at high risk of bias, results remained consistent when removing studies at high risk of bias and those which did not provide adjusted estimates.

We were unable to reach any firm conclusions on whether PWD were more likely to be infected with SARS-CoV-2. This is unsurprising and reflects limited data, especially a lack of widespread community asymptomatic testing for both SARS-CoV-2 and diabetes. Additionally, other complex issues may be at play which determine whether or not someone is tested. This includes country-level variations in testing capacity but also individual-level considerations. For example, it may be that PWD are more likely to get tested than others (if they feel or are a priori perceived as more vulnerable), but given links between deprivation and diabetes, it may also be that PWD are less likely to be tested, given reports from healthcare providers that some symptomatic patients refused to be tested or isolate at the height of the pandemic because they could not afford to miss work.

There are of course other well-established differences in risks for COVID-19 outcomes beyond those investigated here. It is worth noting that risk factors which exist in the wider population also exist in PWD – e.g., older age, deprivation, obesity, non-white ethnicity, and being male all confer greater risk both within and outside PWD. Some of these risk factors for COVID-19 severity are also risk factors for diabetes. To the extent to which reviews and individual studies have been able to adjust for these, associations have only been somewhat attenuated. In a nationwide analysis in England – arguably the largest study of its type to contribute data on COVID-19 risks in PWD – authors adjusted for age, sex, deprivation, ethnicity and geographic region and still found increased ORs for in-

hospital COVID-19 related death of approximately 2-fold for people with type 2 diabetes and greater than 3-fold for people with type 1 diabetes.(1) As both diabetes and worse COVID-19 outcomes are associated with socioeconomic disadvantage, their intersection will further exacerbate existing health disparities. This warrants urgent attention.

[A note regarding paediatric populations](#)

Age was not a pre-specified characteristic for this review due to clear evidence that COVID-19 risk increases with age. Risk of severe disease in children and adolescents from COVID-19 is low in the general population, and none of the systematic reviews suggested otherwise in children and adolescents with diabetes. However, even though absolute risk may be low, the one review which conducted a separate analysis in a paediatric population found that, when pooling data from four studies, children with diabetes had a higher risk of severe COVID-19 than those without diabetes (RR 2.26, 95% CI 1.95 to 2.62, n=5233, I²=0%).(81) Caution needs to be taken when interpreting this finding, as we judged this review to have significant limitations, and the result was primarily driven by a large American retrospective study finding that children with type 1 diabetes who were hospitalized for COVID-19 developed more severe disease than children without diabetes (adjusted OR 2.38, 95% CI 2.06 to 2.76).(82)

Tables

Table 1. Citations for included reviews

Study ID	Citation
Abdi 2020	Abdi, A.; Jalilian, M.; Sarbarzeh, P. A.; Vlaisavljevic, Z. Diabetes and COVID-19: A systematic review on the current evidences. <i>Diabetes Research & Clinical Practice</i> 2020;166():108347
Abdelhafiz 2021	Abdelhafiz AH, Emmerton D, Sinclair AJ. Diabetes in COVID-19 pandemic-prevalence, patient characteristics and adverse outcomes. <i>International Journal of Clinical Practice</i> . 2021;75(7):e14112.
Aggarwal 2020	Aggarwal, G.; Lippi, G.; Lavie, C. J.; Henry, B. M.; Sanchis-Gomar, F. Diabetes mellitus association with coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. <i>Journal of Diabetes</i> 2020;12(11):851-855
Akbari 2022	Akbari A, Fathabadi A, Razmi M, Zarifian A, Amiri M, Ghodsi A, et al. Characteristics, risk factors, and outcomes associated with readmission in COVID-19 patients: A systematic review and meta-analysis. <i>American Journal of Emergency Medicine</i> . 2022;52:166-73.
Aktar 2021	Aktar S, Talukder A, Ahamad MM, Kamal AHM, Khan JR, Protikuzzaman M, et al. Machine Learning Approaches to Identify Patient Comorbidities and Symptoms That Increased Risk of Mortality in COVID-19. <i>Diagnostics</i> . 2021;11(8):31.
Alhumaid 2021	Alhumaid S, Al Mutair A, Al Alawi Z, Rabaan AA, Alomari MA, Al Salman SA, et al. Diabetic ketoacidosis in patients with SARS-CoV-2: a systematic review and meta-analysis. <i>Diabetology & metabolic syndrome</i> . 2021;13(1):120.
Alireza 2021	Alireza Abdi MJPASZV. Diabetes and COVID-19: A systematic review on the current evidences. <i>Diabetes Research and Clinical Practice</i> . 2021:108347.
Alvez 2021	Alves V, Casemiro F, Araujo B, Lima M, Oliveira R, Fernandes F, et al. Factors Associated with Mortality Among Elderly People in the COVID-19 Pandemic (SARS-CoV-2): A Systematic Review and Meta-Analysis. <i>Preprints.org</i> ; 2021.
Apicella 2020	Apicella, Matteo; Campopiano, Maria Cristina; Mantuano, Michele; Mazoni, Laura; Coppelli, Alberto; Del Prato, Stefano. COVID-19 in people with diabetes: understanding the reasons for worse outcomes. <i>The Lancet Diabetes & endocrinology</i> 2020;8:782–92
Ashktorab 2021	Ashktorab H, Pizuorno A, Fierro NA, Villagrana EDC, Solis MEH, Cardenas G, et al. A Comprehensive Meta-Analysis of COVID-19 in Latin America. <i>Soj Microbiology & Infectious Diseases</i> . 2021;8(1):1-11.
Awortwe 2020	Awortwe, C.; Cascorbi, I. Meta-analysis on outcome-worsening comorbidities of COVID-19 and related potential drug-drug interactions. <i>Pharmacological Research</i> 2020. https://doi.org/10.1016/j.phrs.2020.105250
Badawi 2021	Badawi A, Vasileva D. Comparative profile for COVID-19 cases from China and North America: Clinical symptoms, comorbidities and disease biomarkers. <i>World Journal of Clinical Cases</i> . 2021;9(1):118-32.
Bae 2021	Bae S, Kim SR, Kim MN, Shim WJ, Park SM. Impact of cardiovascular disease and risk factors on fatal outcomes in patients with COVID-19 according to age: a systematic review and meta-analysis. <i>Heart</i> . 2021;107(5):373-80.
Bajgain 2020	Bajgain, K. T.; Badal, S.; Bajgain, B. B.; Santana, M. J. Prevalence of comorbidities among individuals with COVID-19: A rapid review of current literature. <i>American Journal of Infection Control</i> 2020. https://doi.org/10.1016/j.ajic.2020.06.213
Baradaran 2020	Baradaran, A.; Ebrahimzadeh, M. H.; Baradaran, A.; Kachooei, A. R. Prevalence of Comorbidities in COVID-19 Patients: A Systematic Review and Meta-Analysis. <i>Archives of Bone & Joint Surgery</i> 2020;8(Suppl 1):247-255
Barrera 2020	Barrera FJ, Shekhar S, Wurth R, Moreno-Pena PJ, Ponce OJ, Hajdenberg M, Alvarez-Villalobos NA, Hall JE, Schiffrin EL, Eisenhofer G, Porter F, Brito JP, Bornstein SR, Stratakis CA, González-González JG, Rodríguez-Gutiérrez R, Hannah-Shmouni F. Prevalence of Diabetes and Hypertension and Their Associated Risks for Poor Outcomes in Covid-19 Patients. <i>J Endocr Soc</i> . 2020 Jul 21;4(9):bvaa102. doi: 10.1210/jendso/bvaa102. Erratum in: <i>J Endocr Soc</i> . 2020 Nov 07;5(1):bvaa175. PMID: 32885126; PMCID: PMC7454711. Format:
Bennett 2020	Bennett, S.; Tafuro, J.; Mayer, J.; Darlington, D.; Wong, C. W.; Muntean, E. A.; Wong, N.; Mallen, C.; Kwok, C. S. Clinical features and outcomes of adults with coronavirus disease 2019: A systematic review and pooled analysis of the literature. <i>International Journal of Clinical Practice</i> 2020;():e13725

Study ID	Citation
Bepouka 2022	Bepouka B, Odio O, Mangala D, Mayasi N, Mandina M, Longokolo M, et al. Diabetes Mellitus is Associated With Higher COVID-19 Mortality Rates in Sub-Saharan Africa: A Systematic Review and Meta-analysis. <i>Cureus</i> . 2022;14(7):e26877.
Boddu 2020	Boddu, S. K.; Aurangabadkar, G.; Kuchay, M. S. New onset diabetes, type 1 diabetes and COVID-19. <i>Diabetes and Metabolic Syndrome: Clinical Research and Reviews</i> 01 Nov 2020;14(6):2211-2217
Bonora 2021	Bonora BM, Avogaro A, Fadini GP. Disentangling conflicting evidence on DPP-4 inhibitors and outcomes of COVID-19: narrative review and meta-analysis. <i>Journal of Endocrinological Investigation</i> . 2021;44(7):1379-86.
Bradley 2022	Bradley SA, Banach M, Alvarado N, Smokovski I, Bhaskar SMM. Prevalence and impact of diabetes in hospitalized COVID-19 patients: A systematic review and meta-analysis. <i>Journal Of Diabetes</i> . 2022;14(2):144-57.
Carrasco-Sanchez 2022	Carrasco-Sanchez FJ, Carretero-Anibarro E, Gargallo MA, Gomez-Huelgas R, Merino-Torres JF, Orozco-Beltran D, et al. [Executive Summary from Expert consensus on effectiveness and safety of iDPP-4 in the treatment of patients with diabetes and COVID-19]. <i>Endocrinologia Diabetes y Nutricion</i> . 2022;69(3):209-18.
Chen 2020	Chen, J.; Wu, C.; Wang, X.; Yu, J.; Sun, Z. The Impact of COVID-19 on Blood Glucose: A Systematic Review and Meta-Analysis. <i>Frontiers in Endocrinology</i> 2020;11():574541
Chen 2022 (1)	Chen Y, Lv X, Lin S, Arshad M, Dai M. The Association Between Antidiabetic Agents and Clinical Outcomes of COVID-19 Patients With Diabetes: A Bayesian Network Meta-Analysis. <i>Frontiers in Endocrinology</i> . 2022;13:895458.
Chen 2022 (2)	Chen Z, Peng Y, Wu X, Pang B, Yang F, Zheng W, et al. Comorbidities and complications of COVID-19 associated with disease severity, progression, and mortality in China with centralized isolation and hospitalization: A systematic review and meta-analysis. <i>Frontiers in Public Health</i> . 2022;10:923485.
Cheng 2021	Cheng S, Zhao Y, Wang F, Chen Y, Kaminga AC, Xu H. Comorbidities' potential impacts on severe and non-severe patients with COVID-19: A systematic review and meta-analysis. <i>Medicine</i> . 2021;100(12):e24971.
Chidambaram 2020	Chidambaram, V.; Tun, N. L.; Haque, W. Z.; Majella, M. G.; Sivakumar, R. K.; Kumar, A.; Hsu, A. T.; Ishak, I. A.; Nur, A. A.; Ayeh, S. K.; Salia, E. L.; Zil, E. Ali A.; Saeed, M. A.; Sarena, A. P. B.; Seth, B.; Ahmadzada, M.; Haque, E. F.; Neupane, P.; Wang, K. H.; Pu, T. M.; Ali, S. M. H.; Arshad, M. A.; Wang, L.; Baksh, S.; Karakousis, P. C.; Galiatsatos, P. Factors associated with disease severity and mortality among patients with COVID-19: A systematic review and meta-analysis. <i>PLoS ONE [Electronic Resource]</i> 2020;15(11):e0241541
Choi 2022	Choi JH, Choi SH, Yun KW. Risk Factors for Severe COVID-19 in Children: A Systematic Review and Meta-Analysis. <i>Journal of Korean Medical Science</i> . 2022;37(5):e35.
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Zheng 2020	Zheng, Z.; Peng, F.; Xu, B.; Zhao, J.; Liu, H.; Peng, J.; Li, Q.; Jiang, C.; Zhou, Y.; Liu, S.; Ye, C.; Zhang, P.; Xing, Y.; Guo, H.; Tang, W. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. <i>Journal of Infection</i> 2020;81(2):e16-e25
Zhou 2020 (1)	Zhou, X.; Cheng, Z.; Shu, D.; Lin, W.; Ming, Z.; Chen, W.; Hu, Y. Characteristics of mortal COVID-19 cases compared to the survivors. <i>Aging</i> 2020, Vol 12, Advance
Zhou 2020 (2)	Zhou, Y.; Yang, Q.; Chi, J.; Dong, B.; Lv, W.; Shen, L.; Wang, Y. Comorbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: A systematic review and meta-analysis. <i>International Journal of Infectious Diseases</i> 2020;99:47-56
Zhu 2021	Zhu Z, Mao Y, Chen G. Predictive value of HbA1c for in-hospital adverse prognosis in COVID-19: A systematic review and meta-analysis. <i>Primary care diabetes</i> . 2021;15(6):910-7.

Table 2. Key characteristics of included reviews¹

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
Abdi 2020	This study aims to summarize the evidence about diabetes and COVID-19 outbreak through a systematic review and meta-analysis approach.	Studies considered focused on those that reported diabetes in COVID-19 patients.	3 (2020)	Scopus, PubMed, Science direct, and Web of science	Prevalence, discuss severity and mortality narratively in text.	27 studies included overall, 18 for pooled analysis for prevalence of diabetes.	Not reported	Not reported	Majority in China
Aggarwal 2020	We carried out a pooled analysis of current studies for evaluating potential associations between DM and infection severity outcomes in COVID-19 patients.	Studies were included if they fulfilled the following criteria: (1) Report history of DM in COVID-19 patients; (2) report outcomes of interest; (3) sample size >10.	3(2020)	PUBMED, EMBASE and CENTRAL	Severe disease (undefined), death	16 in total 12 reporting on severe vs less severe COVID cases 4 reporting on non-survivors vs survivors	Severe vs non-severe comparison: 2564 Non-survivors vs survivors comparison: 618	Not reported	China
Akbari 2022	We aimed to determine the characteristics, risk factors, and outcomes associated with readmission in COVID-19 patients	All studies comparing characteristics of readmitted and non-readmitted COVID-19 patients were included. We also included articles reporting the reasons for readmission in COVID-19 patients.	8 (2021)	PubMed, Embase, Web of Science, Scopus	Readmission with COVID-19	28	68236 overall (4823 readmitted, 63413 not readmitted for total population)	Hospital	14/28 studies from USA
Aktar 2021	To determine which comorbidities are associated with severe symptoms and mortality would thus greatly	For this study, articles that described the clinical characteristics of COVID-19 patients were included, particularly symptoms and comorbidities, along with their prevalence and	4 (2020)	PubMed (Medline), Web of Science, EMBASE, and Cochrane Library	prevalence, severity and mortality	26 studies	13400 participants	Hospital	24 studies from China, 1 from Italy, 1 from USA

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	assist in COVID-19 care planning and provision.	specific information on the distribution of patients on the basis of severity.							
Alhumaid 2021	To re-evaluate the association of SARS-CoV-2 and development of DKA and analyse the demographic and biochemical parameters and the clinical outcomes in COVID-19 patients with DKA.	Case reports, case series and cohort studies discussing and reporting occurrence of DKA in COVID-19 patients. English language only.	6 (2021)	Proquest, Medline, Embase, Pubmed, Cinahl	prevalence and mortality in subgroups	68 studies	639 DKA patients with confirmed COVID-19	States includes all healthcare settings but mentions hospitalised patients in text	Primarily United States (n = 29), United Kingdom (n = 6), India (n = 6), Peru (n = 5), Saudi Arabia (n = 4),
AlirezaAbdi 2021	To review current evidence and provide guidelines for prevention and treatment of people affected by both COVID-19 and diabetes	Inclusion of publications that were observational studies, such as cohort, case-report and case-control research. Additionally, we included letters, viewpoints, and review studies that provide further advice about diabetes. Studies considered focused on those that reported diabetes in COVID-19 patients.	3 (2020)	Scopus, PubMed, Science direct, and Web of science	prevalence	18 studies in MA	Not reported for MA	Not reported	Primarily China
Alves 2021	The objective of this meta-analysis was to evaluate the factors associated with the mortality of elderly Italians diagnosed with	Primary studies on the mortality of elderly Italians (65 years or more) with a diagnosis of coronavirus were selected, with publications in the English, Italian and Spanish languages included, which	7 (2020)	Pubmed, Embase, Lilacs, Cinahl	mortality	5 studies	Not reported	Hospitalised or living in institutions	Italy

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	coronavirus who resided in institutions or who were hospitalized because of the disease.	carried out quantitative and qualitative analyses.							
Apicella 2020	Not explicitly stated - overall aim (from title) to understand the reasons for worse outcomes in people with diabetes	Not explicitly stated	6 (2020)	PUBMED, and Google Scholar for additional references.	Prevalence, severity, mortality, glycaemic control, DPP4 - all discussed narratively in text	Not reported	Not reported	Not reported	China, UK, France, Italy
Ashktorab 2021	We performed a comparative analysis of the clinical characteristics, mortality, and symptoms of the confirmed COVID-19 cases reported in various Latin American countries that have made pertinent information publicly available.	Confirmed diagnosis of COVID-19 as reported by each country and referenced by WHO or cross-checked via World-Meter or Johns Hopkins University COVID-19 dashboard; No distinction about the number of diagnosed cases; No distinction about sex, age, severity of disease, inpatient or outpatient management, data collection date, treatment and outcome. Excluded studies where the cohort was not Latino or Hispanic, studies where the cases were not confirmed by RT-PCR, and studies with incomplete symptoms or comorbidities' report.	7 (2020)	PubMed, OVID, Scopus, Google Scholar, LANCOVID (Latin America research network on COVID), and other resources from official health organizations of countries in Latin America such as Ministries of Health, National Institutes of Hygiene, or Hospitals	prevalence and mortality	9 studies (8 countries)	728282	Inpatients and outpatients	Peru, Ecuador, Bolivia, Mexico, Chile, Argentina, Venezuela, and Brazil.

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
Awortwe 2020	A meta-analysis on COVID-19 clinical studies which characterized the epidemiological or clinical features of affected patients with comorbidities independent of pharmacological interventions.	Selection criteria for the analysis focused exclusively on clinical studies characterizing the clinical or epidemiological features of COVID-19 patients. O	6 (2020)	PubMed, Medline, Scopus and google scholar	Disease severity, mortality, ICU admission,	24	5586	Not reported	1 Iran, 1 Israel, rest china
Badawi 2021	To analyze and compare the profile of COVID-19 cases between China and North America as two regions that differ in many environmental, host and healthcare factors related to disease risk.	Studies from the Aggregated Dataset of Clinical Outcomes for COVID-19 Patients for China and USA	4 (2020)	Aggregated Dataset of Clinical Outcomes for COVID-19 Patients	prevalence	124 studies (105 from China, 19 from USA	72025	Not reported	China and USA
Bae 2021	We aimed to investigate the impact of cardiovascular disease (CVD) and its risk factors on fatal outcomes according to age in patients with COVID-19.	All observational studies (case series or cohort studies) conducted on in-hospital adult patients with information on clinical outcomes were included.	6 (2020)	PubMed, Embase, medRxiv, Research Square and Lancet preprint database	severe disease and mortality	51 studies	48317 participants	Hospital	37 studies from China, 7 from USA, 6 from Italy, 3 from UK, 3 from Iran
Bajgain 2020	To explore prevalence of comorbidities and	Published primary literature about comorbidities and Covid-	5 (2020)	PubMed, MEDLINE, EMBASE, SCOPUS, google scholar	Prevalence in Covid-19 population,	27	22753	2 studies from long term	China (18 of 27), S Korea,

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	adverse outcomes among individuals with Covid-19	19, studies include patient dataset with major comorbidities including HTN, CVD, COPD, CKD, malignancy and/or diabetes			association with Covid-19 fatality			facilities, rest unclear	Italy, Mexico, US, UK, Iran
Baradaran 2020	Study assessed prevalence of comorbidities in confirmed COVID-19 patients. Found 11% had diabetes mellitus	All studies that reported the prevalence of comorbidities among the confirmed COVID-19 patients were included. There was no language restriction	4 (2020)	EMBASE, PubMed, and google scholar	Prevalence of comorbidities	33 studies extracted (29 studies with data on diabetes prevalence)	9249	Not reported	32 papers from China, 1 paper from Taiwan
Barrera 2020	We systematically assessed the prevalence of diabetes and hypertension in patients with Covid-19 after excluding repeated patients across studies and analysed the associated risks for Covid-19 severity, intensive care unit (ICU) admission and mortality	Observational and interventional studies that reported the frequency of diabetes and/or hypertension in adult population with Covid-19. For our second aim, we included studies that reported exposure-outcome association as univariate or multivariate analysis, with diabetes, hypertension being the exposure, and severe Covid-19 through ICU admissions or mortality being the outcome of interest.	4 (2020)	Ovid Medline In-Process & Other Non-Indexed Citations, Ovid Medline, Ovid Embase, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and Scopus.	Prevalence, severity, ICU admission, mortality, subgrouping diabetes plus HTN	65 studies overall 31 studies looked at prevalence of diabetes	15,794 overall 12,870 looked at prevalence of diabetes	88% inpatient setting	71% from China
Bennett 2020	Determine systematically the evidence from studies of more than 100 adult patients that reported	Studies that report on one or more of: clinical features of patients, comorbidities of patients, radiological findings for patients and outcomes for patients. Sample sizes	4 (2020)	MEDLINE, EMBASE	Prevalence of diabetes in Covid-19 population	45	14358	Hospital admissions	China (42 of 45), US, Europe

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	clinical features and outcomes of those affected by COVID-19.	bigger than 100. laboratory confirmed diagnosis of Covid-19							
Bepouka 2022	to determine the mortality rate of COVID-19 among diabetes patients in sub-Saharan Africa	The analysis excluded commentaries, case reports, family studies, and pediatric studies. Clinical studies that did not clearly state death as a possible consequence were also excluded.	7 (2021)	PubMed, Google Scholar, and Web of Science	Mortality	7 studies	7778 participants	Not reported	Sub Saharan Africa
Boddu 2020	In this review, we explore the mechanisms of hyperglycaemia particularly in relation to COVID 19 illness and also examine the Covid-19 related morbidity and mortality in people with T1DM.	Not explicitly stated	10 (2020)	Medline (PubMed), Scopus, and Google Scholar	Prevalence (new onset), Mortality by HbA1C and by Type 1 and Type 2 diabetes	2 nationwide analyses in the UK (Mortality Type 1 vs Type 2 and by HbA1C) 1 multicentre study in the UK (prevalence of new onset)	Not reported	Not reported	UK
Bonora 2021	We focused on the impact of DPP4i treatment on COVID-19-related outcomes in people with DM. For this purpose, we conducted a systematic review and meta-analysis to summarize the	We included in the analysis all studies reporting separately data for patients with diabetes treated with DPP4i or other GLMs. Published observational (cohort or nested case-control) studies published were included.	12 (2020)	Pub-Med, Scopus and Cochrane Library	association (narrative) and mortality	12 studies (7 in MA)	6022 patients with DM	Not reported	Italy 4 studies, Korea 2 studies, China 2 studies and one from each France, Spain, Singapore, Iraq

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	existing evidence on this topic.								
Bradley 2022	This study sought to determine the prevalence of diabetes in hospitalized COVID-19 patients and investigate the association of diabetes severe COVID-19, rate of acute respiratory distress syndrome (ARDS), mortality, and need for mechanical ventilation by performing a systematic review and meta-analysis.	(a) age \geq 18 years, (b) availability of comparative data between diabetes and non-diabetes groups, (c) patients with a confirmed diagnosis of COVID-19 in a hospital setting, and (d) studies with good methodological design (with appropriate sample size deemed to be >20 patients in each group). Relevant data on diabetes or relevant clinical outcomes reported.	7 (2021)	PubMed, Embase, and Cochrane Central Register of Controlled Trials.	prevalence, severity, mortality	24 studies	10648 patients	hospital	China 9 studies, Iran 3, S Korea 3, USA 2, India 2 and 1 each from France, Saudi Arabia, Qatar, Italy and Singapore
Carrasco-Sanchez 2022	This consensus aims to clarify the role of Dipeptidyl Peptidase-4 inhibitors (iDPP-4) in managing patients with diabetes during the COVID-19 pandemic	Various scientific societies were convened, all of them related to the clinical management of diabetes (Spanish Society of Internal Medicine, Society Española de Diabetes, Spanish Society of Endocrinology and Nutrition, and redGDPS Foundation). They posed clinical questions, reviewed the results of the search and analysed the data narratively informed by CEBM grading criteria. No	2 (2021)	PubMed	risk of infection, ICU admission, mortality	22 studies overall, 8 studies examining DDP4i	For DPP4i - 2 MA (of 9 and 4 studies each) and 6 primary observational studies totalling 7687 patients	Not reported	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
		further details regarding study selection.							
Chamorro-Pareja 2020 (abstract)	To examine the correlation between diabetes and mortality from COVID-19	Observational studies on diabetic adult populations hospitalized for COVID-19 and that assessed possible correlation between diabetes and mortality.	5 (2020)	Medline, Embase, Google Scholar, and medRxiv	Association between diabetes in COVID patients and mortality. Diabetes vs non-diabetes.	14 studies	18,506 patients: 3,713 diabetics (DM group) and 14,793 non-diabetics (no-DM group).	Hospital	USA and others (not specified)
Chen 2020	This meta-analysis aimed to summarize available data on the association between glycaemic parameters and severity of COVID-19	Observational studies investigating blood glucose or glycated haemoglobin A1c (HbA1c) according to the severity of COVID-19 were considered for inclusion.	5 (2020)	PubMed, Embase and the Cochrane Library	Severe COVID (defined as those who required mechanical ventilation, intensive care unit admission or those who died) by blood glucose and HbA1C	3 studies, 1 with 100% diabetes, 2 mixed populations	222 COVID patients (131 severe, 91 mild)	Not reported	China
Chen 2022 (1)	We aimed to systematically review the comorbidities and complications of COVID-19 that are associated with various disease severity, progression, and mortality in China, to provide contemporary and reliable estimates in settings with centralized isolation and hospitalization.	To identify all the related comorbidities and complications of COVID-19, in the China region with centralized isolation and hospitalization, with disease severity, progression, and mortality.	1 (2022)	PubMed, Embase, Cochrane Library, and the Web of Science, and China National Knowledge Infrastructure, Wanfang Data Knowledge Service Platform, VIP information resource integration service platform databases, and Chinese biomedical literature service system	prevalence, ICU admission, progressive disease, comorbidities and complications (including mortality)	187 studies overall	77013 participants	Hospital	China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
Chen 2022 (2)	This study aimed to assess the impact of different antidiabetic agents on individuals with diabetes and COVID-19.	(1) original studies evaluating the clinical outcomes of diabetic COVID-19 patients receiving specific antidiabetic agents at home or in the hospital; (2) study designs including randomized controlled trials (RCT), and observational studies; (3) studies published in English.	10 (2021)	PubMed, Web of Science, Embase, and Cochrane Library databases	Mortality and severe disease (defined as those requiring intensive care unit admission, mechanical ventilation of acute respiratory distress syndrome, disseminated intravascular coagulation, or others described in the individual study as severe disease)	42 overall, 35 studies for pairwise MA, 18 studies for Bayesian network MA	Not reported	Not reported	Italy, USA, Spain, Belgium, Denmark, Austria, China, Turkey, France, UK, Netherlands, S Korea, Brazil, S Africa, Singapore
Cheng 2021	The present study aimed to estimate the association of chronic comorbidities in severe and non-severe cases of COVID-19	(1) studies describing the epidemiological and clinical features of COVID-19; (2) studies providing data of patients with severe and non-severe cases; and (3) studies written in English or Chinese.	4 (2020)	PubMed, Embase, China National Knowledge Infrastructure (CNKI), and Wanfang Database, Chinese Scientific Journals Full-text Database (CQVIP)	prevalence	22 studies overall, 20 studies examining diabetes	3286 patients overall, 3271 for studies examining diabetes	Hospital	China
Chidambaram 2020	Sought to better understand the clinical, laboratory and radiological parameters associated with mortality and disease severity among patients with COVID-19.	Observational studies that included patients with microbiologically confirmed SARS-CoV-2 infection, all studies that reported a direct comparison of clinical, laboratory or radiologic characteristics between a) patients who died and those who survived or b) patients with severe disease and those without severe disease.	5 (2020)	Pubmed, EMBASE, WHO covid database	association with mortality, association with severe disease	108	Risk of mortality: 20296 severity of disease: 17992	Hospital admissions	Risk of mortality: 32 studies China, six United States, two Spain, one UK, one Italy, one Iran and a multi-country study. Severe disease: seventy-one studies China and one study Italy

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
Choi 2022	We performed a systematic review and meta-analysis to identify children at high risk of severe COVID-19, with a focus on comorbidities and age.	1) the rates of intensive care unit (ICU) admission, invasive mechanical ventilation, and/or death among children with COVID-19; 2) the inclusion of different age groups, particularly neonates and infants younger than 3 months of age; and 3) the prevalence of comorbidities including prematurity, obesity, diabetes, genetic disorders, neurologic disease, cardiac disease, lung disease, hemato-oncologic disease, and immunocompromised status.	8 (2021)	PubMed, EMBASE, Scopus and KoreaMed databases	severe disease	17 studies (10 in MA)	not reported	Not reported	USA 9 studies, 1 each from multinational, Europe, UK, Italy, Turkey, UAE, Iran
Chowdhury 2020	This narrative review attempts to address key questions regarding COVID-19 and T1D.	Not explicitly stated	5 (2020)	Pubmed	Risk of infection discussed, mortality, mortality by HbA1C and obesity	2 (with relevant data)	Not reported	Not reported	UK
Chua 2021	This systematic and meta-review aimed to compare clinical presentation, outcomes, and care management among patients with COVID-19 during the early phase of the pandemic.	observational cohort studies or case series with clinical data on patients consecutively admitted for laboratory-confirmed COVID-19. Studies focusing on specific groups of patients (with comorbidities, pregnant women) or only CT outcomes or scores were excluded.	4 (2020)	PubMed, Google Scholar, and Chinese Medical Journal databases.	Prevalence of diabetes in non-severe, severe disease and death from COVID-19	40 studies in MA	4994 participants in MA	hospital	30/40 studies from China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
Corona 2021	The aim of the present work is to provide an overview and a meta-analysis of main predictors and of country differences of SARS-CoV-2) infection-associated mortality rate in hospitalized patients.	All prospective and retrospective observational studies reporting crude overall COVID-19-related MR in hospitalized subjects, without any arbitrary restriction, were included, even if mortality was not the principal endpoint.	7 (2020)	Medline, Embase, Cochrane	Mortality rate	87 studies	35486 patients	hospital	48 from Asia, 21 from Europe, 13 from USA, 4 from other countries
Costa 2020	Providing overview of metabolic changes associated with metabolic syndrome and its relationship with development and worsening of SARS-CoV-2 infection, as well as to review the proposed drugs for the treatment of these patients.	Not stated (just state search terms of obesity, diabetes, liver, NAFLD, hypertension, cardiovascular disease, chloroquine, hydroxychloroquine, antiretroviral drugs, and treatment of coronavirus	6 (2020)	Pubmed, Google Scholar	Prevalence, severity and mortality discussed narratively in text.	Not stated; approximately 5 narratively discussed	Not reported	Not reported	not stated; 1 narratively mentioned Wuhan, China
Damayanthi 2021	This study aimed to systematically review the numerous factors associated with mortality among COVID-19 infected older people.	All clinical studies evaluating factors associated with mortality of older people aged 60 years or over and diagnosed with COVID-19 were included	4 (2021)	PubMed and Science Direct	Mortality	20 studies (10 in MA)	Not reported	13/20 studies in hospitals, 3 in long term care facilities, 4 in other settings	5 from China, 5 from Italy, 2 each from the UK, Spain and Belgium, 1 each from Sweden, Korea,

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
									Switzerland, Brazil
d'Annunzio 2020	The aim of our study was to analyse available data about COVID-19 infections and type 1 diabetes mellitus, and to formulate recommendations for children and adolescents with or who may develop type 1 diabetes mellitus in the time of Covid-19 infection.	Not reported	5 (2020)	Medline and Embase	Risk of infection and severity of outcomes discussed	No studies cited which relate to the review question. One relevant statement not cited. Focus on children and adolescents but papers cited from adults also.	Not reported	Not reported	Not reported
de Almeida-Pititto 2020	The aim of this study is to evaluate the association of diabetes, hypertension, cardiovascular disease and ACEI/ARBs exposure with severity (intensive care unit treatment or mechanical ventilation necessity or O2 saturation < 90%), or mortality	Observational studies that met the following criteria were included: (1) study design (cross-sectional, self-controlled case series or retrospective cohort studies); (2) presence of the following comorbidities (diabetes mellitus, hypertension or cardiovascular disease); (3) use of ACE inhibitors and/or ARB.	5 (2020)	PubMed, Cochrane Library and SciELO	Severity, mortality	18 for severity outcome 10 for mortality outcome	4305 for severity outcome 4247 for mortality outcome	Hospital (only included in-hospital deaths)	35/40 studies (40 is total for HTN, CVD as well as DM) were from China and 5 were from France, Italy, Greece, and the USA.

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	from COVID-19 infection.								
Del Sole 2020	As clinical and laboratory characteristics associated with severe SARS-CoV-2 infection are not completely clarified, we performed a systematic review and meta-analysis of the data so far reported in SARS-CoV-2-infected patients to identify clinical and laboratory variables associated with a high-risk ARDS, ICU or poor survival.	Clinical studies in patients with SARS-CoV-2 infection that reported comorbidities and laboratory analysis of patients distinguished in severe vs non-severe infection	5 (2020)	PubMed, ISI Web of Science, SCOPUS and Cochrane database.	Severity (ARDS, ICU admission, deaths)	12	2794 patients of which 596 had severe disease	Not reported	11/12 studies from China, 1/12 from the Netherlands
Deravi 2020	Therefore, this review aimed to elucidate the role and underlying mechanisms of chronic conditions, including DM and hypertension, in clinical manifestations and disease severity of COVID-	We included all observational studies conducted on diabetic and/or hypertensive adult patients with confirmed COVID-19, SARS, and MERS	3 (2020)	Pubmed, Google Scholar, Excerpta Media Database (EMBASE), Web of Science and ResearchGate	Not reported	Not reported	Not reported	Not reported	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	19, MERS and SARS.								
Desai 2020	The objective of this study was to evaluate the pooled estimate of diabetes prevalence in young (<50 years) versus elderly (>50 years) COVID-19 cohorts.	Literature search until March 2020, all eligible studies reporting frequency of diabetes mellitus were included	3 (2020)	PubMed, Scopus and Web of Science	The overall prevalence of diabetes in studies including COVID-19 patients, in patients with a mean age >50 vs <50	11	2084	Not reported	Not reported
Deshmukh 2020	To summarize the updated epidemiology, causes, clinical manifestation and diagnosis, as well as prevention and control of the novel coronavirus SARS-CoV-2.	Not reported	Not reported	PubMed, Medline, Web of Science, Google Scholar and World Health Organization-WHO	Mortality	Not reported	Not reported	Not reported	Not reported
Dessie 2021	to summarize available findings on the association between comorbidities, complications, smoking status, obesity, gender, age and D-dimer, and risk of	Studies reporting odds ratios (ORs) or hazard ratios (HRs) along with 95% CI for the association between demographic or epidemiological or clinical characteristics and fatal outcome of coronavirus. No language restrictions.	8 (2020)	Google Scholar, Cochrane Library, Web of Sciences, EMBASE, Medline/PubMed, COVID-19 Research Database (WHO), COVID-19 Open Research Dataset Challenge, and Scopus	Mortality	42 studies	423117 patients	hospital	13 were performed in China, 11 in USA, 2 in Spain, 2 in Mexico, 2 in Korea, 3 in Italy, 1 in France, 1 in Australia, 1 in

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	mortality from COVID-19 using a large dataset from a number of studies.								Asia, 1 in Brazil, 1 in UK, 2 in Turkey and 2 mixed region.
Dhar 2021	Not reported	Not reported	NR	Not reported	Severe disease	12 studies	3127 patients	not reported	China, France, Italy and USA
Du 2020	To systematically evaluate the prevalence of diabetes among COVID-19 patients in China and its impact on clinical outcomes, including ICU admission, progression to severe cases, or death.	The inclusion criteria for articles in the meta-analysis included: (1) Cross-sectional studies or cohort studies; and (2) Studies that reported the prevalence of diabetes in COVID-19 patients.	3 (2020)	PubMed, Web of Science, Embase	Prevalence, severity, ICU admission, death	23	49564 COVID-19 patients (1573 with and 47991 without diabetes)	Not reported	China
Du 2021	to screen the risk factors for severe illness and death and provide help for early clinical treatment of the new coronavirus (COVID-19).	studies that explored the cause and risk factors for severe illness and death in COVID-19 patients.	10 (2020)	PubMed, Embase, and Web of Science	Severe diseases and mortality	17 studies	not reported	not reported	16 from China, 1 from Italy
Emami 2020	The current meta-analysis aimed to estimate the prevalence of underlying disorders in hospitalized COVID-19 patients.	Any relevant articles that reported clinical characteristics and epidemiological information on infected patients were included in the analysis.	2 (2020)	PubMed, Scopus, Web of Science, Google scholar, and Embase	Prevalence	10	3403	Hospital	China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
Espinosa 2020	The aim of this meta-analysis was to calculate the prevalence and geographical distribution of comorbidities in all patients admitted to intensive care units (ICUs), and the mortality rate of COVID-19.	This review considered studies that conducted epidemiological and clinical descriptions in patients and in fatal cases from different parts of the world, in order to determine the prevalence and geographic distribution of comorbidities in patients affected by COVID-19.	5 (2020)	Latin American and Caribbean Health Sciences Literature (LILACS), the bibliographic database of the US National of Medicine (Medline), the Elsevier database (EMBASE), Web of Science and SCOPUS.	ICU admission, mortality and prevalence	42, 39 of which were analysed for prevalence	89,238	Not reported	2 Korea, 2 USA, 1 India, 1 Italy, 1 Singapore , the rest China
Fadini 2020	We show results of a meta-analysis of studies reporting the prevalence of diabetes among people infected with the SARS-CoV-2 and its impact on disease severity or progression.	Not reported	3 (2020)	Not reported	Prevalence, severity (severe, progressed, ICU admission, death)	12	2108	Hospital (8/12)	China
Faghir-Gangi 2020	The present study estimated the pooled prevalence of diabetes in patients with COVID-19.	All cross-sectional studies reporting prevalence of diabetes in patients with COVID-19 were eligible for the study. There was no limitation in the time and language of the published papers.	4 (2020)	Web of Science, Scopus and PubMed	Prevalence	20	5515 COVID-19 patients, 578 with diabetes	Not reported	12/20 from Wuhan, 6/20 rest of China, 2 elsewhere (France, USA)
Fang 2020	A systematic review and meta-analysis were conducted,	Studies were eligible for inclusion in this meta-analysis if they met the following criteria: (data	4 (2020)	PubMed, medRxiv and bioRxiv	Severity of COVID-19 Death ICU Admission ARDS	69 in qualitative analysis 61 in	Not stated	Hospital	China (with 1 study in Singapore)

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	seeking to collect and comprehensively evaluate the associations of epidemiological, co-morbidity factors with the severity and prognosis of COVID-19	published in a peer reviewed journal in English or Chinese); (2) the study is a case-control, cohort or cross-sectional design in human beings; (3) the studies provide sufficient information for epidemiological, comorbidity factors with severity or prognosis of COVID-19			Invasive Ventilation Disease Progression	quantitative analysis			
Fathi 2021	to provide additional data regarding the clinical characteristics of the patients diagnosed with COVID-19, and in particular to analyze the factors associated with disease severity, lack of improvement, and mortality.	All studies evaluating the clinical risk factors, underlying diseases, and comorbidities of COVID-19 have been reviewed. For our final analysis, the studies selected should report data on the prevalence of each of the risk factors for the severity of COVID-19 and its comorbidities in patients with COVID-19 infection, including hypertension, chronic kidney disease, diabetes, cardiovascular and cerebrovascular diseases, and coronary heart disease. English language only.	9 (2020)	PubMed, Scopus, Web of Science, and Embase	Prevalence	102 studies	121,437 participants	not reported	Most of the studies were conducted in China, while 11 were conducted in the United States, 6 in Italy, 4 in the UK, 2 in Korea, 1 in Spain, 1 in Belgium, 1 in Greece, 1 in Bolivia, and 1 in Singapore.
Figliozi 2020	We reviewed available evidence and provided pooled estimates on predictors of	We included published peer-reviewed, pre-proof articles and papers published ahead of print which reported Covid-19	4 (2020)	PubMed/Medline and Scopus	Severity (composite), mortality	49	20211	Not reported	Multiple

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	clinical outcomes in patients with COVID-19	cases along with pre infection comorbidities and demographical, laboratory, and clinical information.							
Flaherty 2020	This narrative review article will focus on the issues facing adults with predisposing medical conditions, especially cardiorespiratory and metabolic, in an effort to provide greater clarity to the travelling public and guidance to their healthcare providers.	The final reference list was agreed by all authors on the basis of its relevance to the topics covered in this review, with the aim of exploring the clinical presentation and complications of COVID-19 in patients with co-morbid conditions.	6 (2020)	PubMed	Severity, death, and by obesity and glycaemia	130 relevant publications (looking at a number of different comorbidities)	Not reported	Not reported	Not reported
Gaba 2022	We carried out a meta-analytic synthesis to evaluate the association between diabetes mellitus and related clinical outcomes, co-morbidities, their risk factors and resource utilization in patients with COVID-19.	(i) studied subjects were diabetic and non-diabetic exposed to COVID-19; (ii) outcome of interest reported comorbidities and clinical manifestations of COVID-19; and (iii) studies reporting observational study design (retrospective cohort, case-control, prospective cohort, and cross-sectional studies). English language only.	1 (2021)	MEDLINE or PubMed, Web of Science, Google Scholar	ICU and mechanical ventilation, mortality and subgroups for comorbidity	14 studies	5697 patients	not reported	12 were conducted in China, one in the USA, and one in the UK

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
Gallo Marin 2020	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Ganesh 2022	to perform a systematic review and meta-analysis to investigate whether the use of metformin in COVID-19 patients with new or pre-existing diabetes mellitus affects outcomes such as mortality and severity of the disease	Studies reporting data on metformin use in COVID-19 patients with DM. i. The studies should be published in English language in all databases. ii. All participants should be adult patients (>18 y) diagnosed with COVID-19 and diabetes mellitus. iii. randomised controlled trials (RCTs) or observational studies that looked at patients taking metformin vs. patients not taking metformin which reported at least 1 outcome (mortality or composite endpoint) and an OR, risk ratio or hazards ratio in either adjusted and/or nonadjusted forms. iv. The studies should have at least 70 patients with COVID-19 and diabetes mellitus.	4 (2021)	PubMed, Scopus, Web of Science, EMBASE, Clinicaltrials.gov and Cochrane library	Mortality by metformin use	32 studies	2,916,231 participants	not reported	11 were from China; 6, USA; 6, UK; 4, South Korea; 2, France; 1, Spain; 1, Italy; and 1, Belgium
Giri 2021	The aim of this analysis was to assess the prevalence of clinical features, comorbidities, complications and treatment options in the patients with COVID-19	All studies comparing clinical data of severe and non-severe patients of COVID-19 were included. The inclusion criteria were as follows: (a) study population: studies with patients diagnosed with COVID-19; (b) comparative studies:	7 (2020)	PubMed, Embase, Scopus and Web of Sciences	prevalence, severity	12 studies	3046 participants	Not reported	China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	and compare incidence of these clinical data in severe and non-severe patients.	studies that compare severe and non-severe cases of COVID-19; and(c) the studies reporting parameters of clinical features, comorbidities, complications and treatment. English language only and adult or mixed populations, paediatric only studies excluded.							
Giri 2021	to compare the clinical characteristics, comorbidities, complications, and treatment modalities among severe and non-severe COVID-19 patients, in order to obtain clear picture of risk factors of severe cases.	(a) Studies with patients diagnosed with COVID-19, (b) Studies involving the severe cases or ICU cases and non-severe or non-ICU cases, (c) at least one outcomes reported among clinical features, comorbidities, complications, and treatment options in severe and non-severe patients.	11 (2020)	PubMed, Scopus, Embase, and Web of Sciences	prevalence, severity	41 studies	16,495 participants	Not reported	Most studies were from China (n = 26), followed by United States (n = 5),
Goel 2021	In our review, clinical characteristics and laboratory parameters of COVID-19 patients were compiled systematically, with special reference to pregnant women in order to	identified target population; included cases with diagnosed COVID-19; and provided detailed accounts of clinical features and related laboratory parameters.	5 (2020)	PubMed, Google Scholar, Embase, and Web of Science	prevalence	7 studies	3231 participants	Not reported	China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	understand the disease course.								
Gold 2020	In this systematic review, we aimed to assess the epidemiological characteristics of comorbidities in patients infected with SARS-CoV-2. Furthermore, we aimed to evaluate comorbidities associated with severe COVID-19 disease/mortality.	(1) Studies with patients of all ages with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. (2) Prospective and retrospective case series, retrospective cohort studies, and epidemiological governmental situation reports.	4 (2020)	PubMed and EmBase	Prevalence, severity and mortality.	33	29,096	Not reported	China, 1 Europe, 1 Singapore, 3 USA, 2 Korea, 1 India, 1 Australia, 1 Netherlands
Guler 2020	In this review, we have aimed to focus on the most common co-morbidities in patients with COVID-19 and their possible roles in disease progression	We included case reports, retrospective studies, systematic reviews, meta-analyses, clinical guidelines and recommendations	5 (2020)	Pubmed and Google Scholar	Labratory Measures Prevalence Case-fatality	Not stated	Not stated	Not stated	Not stated
Guo 2020	Diabetes mellitus has been reported to be one of the most prevalent comorbidity inpatients with Coronavirus Disease 2019 (COVID-19). We aimed to assess the association of	All research articles in adult patients diagnosed with COVID-19; with direct or indirect information on the outcome of disease severity or mortality grouped by comorbid diabetes; conducted in Mainland China and published between January 01 and May 30, 2020.	5 (2020)	PubMed, Web of Knowledge, medRxiv, and bioRxiv for English-language literatures, the China National Knowledge infrastructure (CNKI) and the Wanfang database for Chinese-language publications.	Disease severity or death (8/9 studies report severity, 1/9 reports deaths)	9	8807 COVID patients, 1070 patients with diabetes	Not reported	China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	comorbid diabetes with COVID-19 severity or mortality in China.								
Gupta 2021	The present systematic review and meta-analysis aimed to determine the overall mortality and diabetes-associated mortality in COVID-19 patients.	We included case-control/cohort studies conducted on COVID-19 patients, as well as the studies representing the data of COVID-19 mortality and diabetes-associated mortality.	12 (2020)	Pubmed, Embase, MEDLINE, Web of Science, Google Scholar, and DOAJ databases.	prevalence and mortality	35 studies	25,934 participants	Not reported	23 studies from China, 12 from outside China
Han 2022	This study was performed to clarify anti-inflammatory effects of anti-diabetic agents on COVID-19 in patients with diabetes.	a) Observational study including cohort and retrospective cohort study; b) Patients were older than 18 years of age and diagnosed with both diabetes and COVID-19; c) Home use or in-hospital use of specific anti-diabetic agents vs. drugs or therapy except specific anti-diabetic agents; d) Clinically validated definition of death, poor composite outcomes including intubation ventilation, Acute Respiratory Distress Syndrome (ARDS), Disseminated intravascular coagulation(DIC), intensive care unit (ICU) admission,	4 (2021)	China National Knowledge Infrastructure (CNKI), Wanfang Data Knowledge Service Platform, Chinese periodical service platform VIP Database, China Biology Medicine (CBM, Sinomed), MedRxiv, PubMed, ScienceDirect, Web of Science, Ovid Databases (LWW), Springer Link, Wiley Online Library, Oxford Academic, Nature Press Group, Cochrane Library, and BMJ Evidence-Based Medicine	Mortality and poor composite outcomes with metformin and DPP4i use	31 studies	66914 patients	Home and hospital use of medications	Europe, North America, Asia

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
		disease progression, or other adverse outcomes.							
Hariyanto 2020	This study aims to analyse the potential association between metformin use and the mortality rate from COVID-19 infection.	All articles identified that matched the search criteria were assessed, and those reporting the rate of metformin use in COVID-19 patients with a clinically validated definition of “mortality” were included in this meta-analysis.	9 (2020)	Google Scholar	Mortality by metformin	5	6937	Not reported	USA and China
Hariyanto 2021	This study aims to analyze the potential association between DPP-4 inhibitor and the composite poor outcome of COVID-19.	representation for clinical questions (P: patients with diabetes who have positive/confirmed cases of COVID-19; I: a group of patients with DPP-4 inhibitor as their medication; C: a group of patients without DPP-4 inhibitor usage; O: severe COVID-19 and mortality, type of study was a randomized control trial, cohort, clinical trial, case-cohort, and cross-over design, and if the full-text article was available.	11 (2020)	PubMed and Europe PMC database	Severity and mortality and DPP4i use	10 studies	7012 patients	Not reported	Europe and E Asia
Hartmann-Boyce 2020	To consider direct and indirect risks posed to PWD by COVID-19 and management considerations for PWD both with and without	Not reported	Not reported	Not reported	Prevalence, disease severity, outcomes by blood glucose	Three SRs and 2 primary studies report on prevalence Four SRs, 6 cohorts report on severity 5 primary studies report	Not reported for all studies	Not reported for all studies although majority from hospital settings	Multiple

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	COVID-19 infection.					on glucose and outcomes			
Hoang 2021	This study aimed to compare the contribution of comorbidities in the development of critical conditions in coronavirus disease 2019 (COVID-19) patients.	all published case series, retrospective or prospective observational studies, and clinical trials that compare the prevalence of comorbidities between critical and non-critical patients admitted owing to COVID-19. The pre-specified underlying diseases were chronic obstructive pulmonary disease (COPD), cardiovascular disease (CVD), cerebrovascular accident (CVA), hypertension, diabetes, chronic liver disease, chronic kidney disease, and malignancy. The pre-specified severity outcomes were severe infection, intensive care unit (ICU) admission, acute respiratory distress syndrome (ARDS), cardiac injury, and liver injury.	4 (2020)	PubMed, EMBASE, and the Cochrane Library	Severity and ICU	18 studies	5179 patients	Not reported	China
Honardoost 2021	This meta-analysis aimed to assess the association between all underlying comorbidities in COVID-19 infection severity.	We included all relevant articles reporting clinical characteristics and epidemiological information on COVID-19 patients separately in a severe and non-severe group. The criteria for	NR	Not reported - can't find supplement with search strategy which may have details.	Severity	28 studies	6270 participants	Not reported	Majority from China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
		severe disease include ICU admission, acute respiratory distress syndrome, need for supplemental oxygen or O ₂ saturation <93%, critically ill cases, and severe outcome							
Hu 2020	To evaluate the risk factors of COVID-19. Aim was to "describe epidemiological, clinical characteristics, complications, and outcomes of patients confirmed to have 2019-nCoV infection, and to compare the severity between diabetes or hypertension and non-diabetes or non-hypertension patients"	Randomized controlled trial, clinical trials, and series cases; patients who were of either sex and had been diagnosed with COVID-19; all patients with laboratory-identified SARS-CoV-2 infection; clear description of the clinical characteristics such as comorbidities; clear description of the outcomes including	3 (2020)	Medline, Sino Med, EMBASE, and Cochrane Library databases	Most prevalent clinical symptoms. Prevalence of comorbidities Risks of severity and mortality rates. Percentage of severe cases in patients with diabetes and hypertension	21 included in qualitative and quantitative synthesis	47,344 patients (24,419 male and 22,925 females)	Not reported	Singapore and China
Hu 2021	We aim to investigate the clinical characteristics and risk factors for the severe cases of coronavirus disease 2019 (COVID-19) in	The studies on observation of clinical characteristics in severe and non-severe patients with COVID-19 were included.	7 (2020)	PubMed, EMBASE, Web of Science, and CNKI	Severity and ICU	30 studies	6685 patients	Not reported	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	comparison with the non-severe patients.								
Huang 2020	We conducted a systematic review and meta-analysis in order to investigate the association between DM and poor outcome in patients with COVID-19 pneumonia.	adult patients diagnosed with COVID-19 with information on DM and clinical grouping or outcome of the clinically validated definition of mortality, severe COVID-19, ARDS, ICU care, and disease progression.	4 (2020)	PubMed and EuropePMC, MEDLINE	Mortality, severe COVID, ICU care, composite poor outcome	30	6452	Not reported	Not reported
Hussain 2020	We aimed to briefly review the general characteristics of the novel coronavirus (SARS-CoV-2) and provide a better understanding of the coronavirus disease (COVID-19) in people with diabetes, and its management	Not reported	4 (2020)	PubMed and Google Scholar	Prevalence, severe COVID, mortality	Not reported	Not reported	Not reported	Not reported
Hussain 2020	Evidence suggests diabetes to be a risk factor for the progression and poor prognosis of COVID-19. Therefore, we aimed to understand the	We selected all those studies that reported the prevalence of diabetes and associated outcomes (mortality, ICU admission) in confirmed COVID-19 patients. We included only published peer-reviewed studies that had presented	4 (2020)	PubMed, MEDLINE	Prevalence, ICU admission, mortality	43	23007 overall. Detail for each included study in Table 1.	Not reported	Detail for each included study in Table 1.

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	pooled prevalence of diabetes in patients infected with COVID-19. We also aimed to compute the risk of mortality and ICU admissions in COVID-19 patients with and without diabetes.	their findings on at least ten confirmed COVID-19 patients.							
Izcovich 2020	The objective of our systematic review is to identify prognostic factors that may be used in decision-making related to the care of patients infected with COVID-19	We included studies that assessed patients with confirmed or suspected SARS-CoV-2 infectious disease and examined one or more prognostic factors for mortality or disease severity.	4 (2020)	n PubMed/MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL) and Embase.	Diabetes Mortality in COVID and prevalence of diabetes in severe COVID	207	75607	Not reported	12 different countries (China, USA, Canada, Spain, France, Turkey, Korea, Japan, Italy, Germany, India and Singapore).
Javanmardi 2020	The aim of current study is evaluating the prevalence of underlying disease in died people with COVID-19.	Included criteria were defined as follow: any articles about death related to COVID-19, studies which reported underlying diseases in died patients.	6 (2020)	International database including PubMed, Scopus, Web of Science, Cochrane and google scholar	Severity of disease and high mortality rate	32	2431	Not reported	Majority in China
Jindal 2022	This study aimed to estimate the prevalence of co morbidities among COVID 19 patients in the Indian population and their association with mortality.	Studies conducted in India in English language published online that reported detailed epidemiological characteristics, prevalence of co-morbidities and in-hospital mortality were included. Also, studies that	5 (2021)	PubMed, Google Scholar, and World Health Organization website	prevalence and mortality	34 studies	23,034 patients	Not reported	India

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
		reported the prevalence of co-morbidities without mortality were included only for the meta-analysis of prevalence.							
Kaminska 2021	This systematic review and meta-analysis aim to summarize and synthesize the evidence published about the impact of diabetes mellitus on in-hospital mortality in patients with COVID-19.	The prespecified criteria for studies included in the meta-analysis were original papers of RCTs or cohort studies with minimum 10 patients in each group of (P) participants, adult patients with diabetes mellitus; (E) COVID-19 disease; (C) patients without diabetes mellitus; (O) outcomes, detailed information for survival, complications and length of hospital stay	12 (2020)	MEDLINE, EMBASE, Web of Science, Scopus, Cochrane	severe disease, mortality	19 studies	10,801 patients	Hospital	10 studies were performed in China, two in USA, two in France, two in Korea, one in each of the UK, Qatar and South Korea.
Kan 2021	To assess various antidiabetic agents' association with mortality in patients with T2D who have COVID-19	Inclusion criteria were as follows: study type, published studies regarding associations between antidiabetic agents and patients with T2DM who had COVID-19; exposure intervention, patients with T2DM who had COVID-19 received antidiabetic agents (e.g., metformin, sulfonylurea, glucagon-like peptide 1 [GLP-1] receptor agonists, dipeptidyl peptidase 4 [DPP-4] inhibitors, sodium-glucose cotransporter 2 [SGLT2])	2 (2021)	PubMed, Web of Science, Embase, and Cochrane Library	Mortality by subgroup	18 studies	17338 participants	Not reported	7 from China, 2 from USA, 1 from S Korea, 2 from UK, 3 from Italy, 3 from France

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
		inhibitors, a-glucosidase inhibitors, and/or insulin); and outcome indicator, quantitative assessment of associations between antidiabetic agent use and patient mortality, including odds ratios (ORs) and 95% confidence intervals (CIs).							
Kandil 2021	We, therefore, combined the results of the published studies via a meta-analysis to precisely detect the excess risk of COVID-19 mortality attributed to diabetes.	The study was considered eligible if 1) it was published in English, 2) the exposure was COVID-19 patients with diabetes in comparison with COVID-19 patients without diabetes, 3) the outcome was COVID-19 mortality, and 4) the number of COVID-19 patients with diabetes is 50 or more.	5 (2020)	MEDLINE (PubMed), Web of Science, and Scopus	mortality	15 studies	75,200	Not reported	10 studies were from China, 3 from USA and 1 each from Iran and Mexico
Kubjane 2020	The primary objective is to assess the association between diabetes and severe COVID-19 clinical course in patients hospitalized due to COVID-19. The secondary objective is to assess the prevalence of diabetes in patients	Observational cohort and case-control studies that compare exposure with outcomes between different groups. The study population included children, adolescents, and adults who were hospitalized due to suspected, probable, or confirmed COVID-19. To be eligible for inclusion, studies must have compared outcomes in a group of exposed individuals (people with	5 (2020)	Medline and Embase	Severe disease (composite measure of any of the following - mortality, ICU admission, requirement for IMV, or clinically diagnosed with refractory, progressive, severe or critical disease according to WHO criteria)	45 studies	22091 participants	Hospital	The majority of the studies were set in China (n = 40), with the remainder in Korea (n = 1), USA (n = 2), and France (n = 2).

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	hospitalized due to COVID-19. The exploratory objective is to report putative prognostic factors as identified in studies with hospitalized patients living with diabetes who developed severe COVID-19 clinical course.	diabetes) with a group of unexposed individuals (people without diabetes). Only peer-reviewed, published studies were included. Non-English language studies were excluded.							
Kumar 2021	We aimed to pool and analyse two or more co-morbid factors, such as smoking, diabetes, hypertension and cardiovascular disease. In addition, an appraisal of their cumulative risk associated with clinical outcomes in terms of severity, morbidity and mortality of hospitalized COVID-19 patients has been reviewed.	All case studies of COVID-19, all confirmed positive cases with laboratory-identified SARS-CoV-2 infection by real-time reverse-transcriptase polymerase chain reaction (RT-PCR), demographic data, clinical symptoms and treatments.	6 (2020)	PubMed, Scopus, and Google Scholar	severity	19 studies	12,037 participants	Not reported	China, USA, Europe
Kaur 2020	The primary aim of this study was	Peer-reviewed published articles that reported cases	4 (2020)	PubMed	Prevalence	50	6635	Not reported	Multiple

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	to evaluate the epidemiological and clinical characteristics of COVID-19 patients while also highlighting the comorbidities and radiological findings.	with confirmed SARS-CoV-2 infection and have details on demographics, clinical symptoms, imaging features, and coexisting comorbidities. All studies that had information on above mentioned characteristics in COVID-19 patients were included							
Khan 2020	This study aimed to assess the prevalence of pre-existing comorbidities among COVID-19 patients and their mortality risks with each category of pre-existing comorbidity.	(i) conducted for the hospitalized patients infected with COVID-19 with or without pre-existing comorbidities, (ii) presented survivor and non-survivor counts following COVID-19 among patients with or without pre-existing morbidity or presented hazard/risk/odds ratio of deaths or survival following COVID-19 with the types of morbidities, and (iii) published in the English language.	5 (2020)	Medline, Web of Science, Scopus, and CINAHL	Prevalence and mortality	41	27,670	not reported	Majority in China
Khateri 2020	The aim of this study was to determine the prevalence of underlying diseases and associated comorbidities in COVID-19 patients using a systematic	In this study, full-text articles published as original research in scientific journals were selected in the first step.	7 (2020)	PubMed (including Medline), Web of Science, Scopus, CINAHL and Embase	Prevalence	12	2393	Not reported	China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	review and meta-analysis.								
Kow 2020	We performed a meta-analysis of the current studies to explore whether the use of metformin was associated with decreased mortality in COVID-19 patients.	Cohort or case-control design, included patients with confirmed COVID-19, and with data available to compare the risk of mortality among metformin users compared to non-metformin users in adjusted analyses.	8 (2020)	PubMed, Scopus, Goggle Scholar, medRxiv	Mortality by metformin use	5	8121	States hospitalised for COVID-19	2 USA, 2 China, 1 France
Kumar 2020 (1)	This meta-analysis was conducted with the primary objective of exploring the relationship between underlying diabetes and severity and mortality of COVID-19 disease; and with the secondary objective of determining the prevalence of diabetes inpatients with COVID-19.	(1) The studies should be in English language in the PubMed database. (2) The study design should be case-control and should have categorized the patients into two or more groups depending on the severity, clinical course, or mortality of the patients with COVID-19 (i.e. composite endpoint). Studies without this categorization were not included. The study should have data of diabetes mellitus in each group. (3) The study should be observational (4) The study should have included at least 100 patients of COVID-19.(5) The participants should be adult patients	4 (2020)	PubMed only	Prevalence, severe disease, mortality	33	16003	Reported for individual studies in table 1	Reported for individual studies in table 1

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
Kumar 2020 (2)	This systematic review and meta-analysis were conducted with following objectives: (1) to study the demographic, clinical and laboratory manifestations of COVID-19; and (2) to determine the factors associated with severe clinical course of COVID-19	(1) The studies should be in English language; (2) The studies should be published in full (3) the study design should be retrospective or prospective observational or case control study (4) the participants should be adult patients with COVID-19 disease.	3 (2020)	PubMed	Association of co-morbidities with severe clinical course	58	6892	Not reported	China, Hong Kong, Singapore, South Korea, Australia and Europe - NB 97.5% of patients included were from mainland china
Lee 2020	This meta-analysis aims to determine if hyperglycaemia may be associated with an increased severity of COVID-19.	Original articles that examined the severity of COVID-19 in hyperglycaemic patients, determined by variables such as mortality and ICU admissions were included.	Not reported	PubMed, Embase and China National Knowledge Infrastructure	ICU admission and mortality by hyperglycaemia	8	681 with diabetes and hyperglycaemia	Not reported	Not reported
Li 2020 (1)	The aim of this systematic review and meta-analysis aims to elucidate regional variations in baseline clinical characteristics, presentation and factors associated with outcomes in COVID-19 patients including sub-group analysis by	Original research articles were included if they fulfilled the following criteria: (1) laboratory confirmed COVID-19 and (2) if the study provided information about clinical features and outcomes of COVID-19.	4 (2020)	PubMed, Embase, Scopus, the Cochrane library, the Chinese Medical Journal, BioRxiv, MedRxiv	Association of co-morbidities with severe clinical course Association of co-morbidities with mortality from COVID-19	212	281,461	Hospital/Tertiary Care	Mainland China 180, USA 8, South Korea 6, Singapore 3, Italy 3, Taiwan 3, UK 2, Hong Kong 2, Canada 1, Japan 1, Vietnam 1, and more than one

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	country/region and by disease severity								country/region 2
Li 2020 (2)	The current study performed a systematic review and meta-analysis to comprehensively compare the burden and key clinical features of hospitalized patients between the 2009 influenza and COVID-19 pandemic	Studies were included if they met the following criteria: i) they contained clinical characteristics of SARS-CoV-2-confirmed patients and ii) they contained clinical characteristics of 2009 pandemic H1N1 influenza-confirmed patients	Not reported	Medline, Embase, Web of Science, Cochrane CENTRAL, and Google scholar	Prevalence of diabetes as a co-morbidity in hospitalised COVID patients	113 - others were regarding influenza as opposed to COVID-19	36,422	Hospital	Not stated
Li 2020 (3)	The aim of this analysis is to determine the association of cardiovascular metabolic diseases with the development of COVID-19.	(1) comparative studies: randomised controlled trials RCTs or non-RCTs published in English; (2) study population: more than ten participants (3) patients in the studies should be confirmed to have been infected by 2019 novel coronavirus; (4) parameters: the comorbidities of cardiovascular metabolic diseases and the outcome of cardiac injury should be given	2 (2020)	EMBASE and PubMed	Proportions of diabetics in COVID-19 patients as well as the incidence of diabetes in severe/ICU cases vs non-icu/non-severe cases	6	1527	Not reported	China
Li 2020 (4)	We aimed to investigate the relationship between clinical	(1) cohort studies or case-control studies reporting the clinical characteristics of patients with SARS-	4 (2020)	PubMed, Embase, and Cochrane Library	Severity of COVID	12	2,445	Not reported	China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	characteristics, outcomes and the severity of severe acute respiratory syndrome coronavirus 2 pneumonia.	CoV2infection; (2) one or more clinical features were analysed, including epidemiology, clinical symptoms, laboratory findings, comorbidities, treatment, complications, and outcomes; and (3) patients were grouped according to the severity of disease, for example, severe and non-severe groups or ICU and non-ICU groups.							
Li 2021 (1)	We aimed to systematically identify the possible risk factors responsible for severe cases.	Inclusion criteria:(1) case-control studies or cohort studies; (2) articles reporting the clinical characteristics and the severity of disease in patients diagnosed with COVID-19; (3) articles reporting the severity of COVID-19 and details of related factors; (4) articles reporting the specific grading standards of the severity of COVID-19. The definition of severe disease was based on clinical symptoms, i.e., patients having severe dyspnea, extremely low oxygen saturation, respiratory distress or requiring mechanical ventilation, ICU admission or death.	2 (2021)	PubMed, Embase, Web of science and Cochrane Library	severe disease	41 studies	21,060 participants	Not reported	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
Li 2021 (2)	We aimed to critically appraise and synthesise published evidence on the risk factors for poor outcomes in hospitalised COVID-19 patients.	<ul style="list-style-type: none"> • Reported data for hospitalised COVID-19 infected patients; AND • Reported data for demographic and/or clinical factors associated with the following poor outcome measures: mortality, ICU admission, and IMV; AND • Case identification was confirmed by: PCR, nucleic acid test, molecular testing, “laboratory diagnosed/confirmed”; AND • Reported adjusted OR/RR/HR, with age and sex being considered for adjustment as a minimum; AND • Used clearly defined demographic and/or clinical factors. 	5 (2020)	PubMed, medRxiv and the WHO COVID-19 literature database	ICU, mechanical ventilation, mortality	40 studies	Not reported	Hospital	95% from China, Europe, USA
Li 2021 (3)	This study aimed to assess the benefits and risks of metformin in COVID-19 patients.	Observational studies assessing the association between metformin use and the outcomes of COVID-19 patients were included. Studies were included if they: (1) were designed as cohort, cross-sectional, case-control studies; (2) compared the rates of death, risk of intubation, disease deterioration, hospitalization, acute	2 (2021)	PubMed, Embase, Cochrane Library, and Chinese Biomedical Literature Database	mortality	28 studies, 19 in MA	2,910,462 overall	Not reported	14 from Asia, 7 from USA, 7 from Europe

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
		respiratory distress syndrome (ARDS), acidosis, and heart failure in COVID-19 patients with and without using metformin, and (3) reported the effect size including odds ratios (ORs), relative risks (RRs), or hazard ratios (HRs) and their 95% confidence intervals (CIs).							
Liu 2020 (1)	This present study was aimed to provide a systematic evaluation and detailed estimate on the prevalence and effects of pre-existing chronic conditions in COVID-19 patients. This assessment may aid the public health sector while developing policies for surveillance, preparedness, and response to COVID-19 and its severe outcomes.	Articles describing the epidemiological, demographic, clinical features, outcomes and reporting the prevalence of chronic diseases in COVID-19 patient	4 (2020)	PubMed, Ovid MEDLINE, EMBASE, CDC, and NIH databases later an additional eight reports were identified from a search of the bibliographies of previously obtained articles and other sources such as Google, Google Scholar,	incidence of comorbid disease in patients with covid-19, association between pre-existing chronic diseases and clinical outcomes (disease severity, admittance to ICU and mortality rate) in patients with COVID-19	24	10948	Not reported	Among them, 20 studies were from China, 2 from United States, 1 from Italy, and 1 from France.
Liu 2020 (2)	The present study was undertaken to provide a systematic	Articles were eligible for inclusion if they met the following criteria: (1) those that were clinical studies or	4 (2020)	MEDLINE via PubMed, Embase, Web of Science, and the Cochrane Library	Prevalence	12 for COVID-19	51268 for COVID-19	Not reported	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	evaluation and detailed estimate of the prevalence of cardiovascular comorbidities (hypertension, cardiac disease, and diabetes mellitus) in SARS, MERS and COVID-19 cases.	consecutive cases about human; (2) required clinical data could be extracted from articles; and (3) at least 3 cases were reported in an article.							
Lu 2020	Coronavirus Disease 2019 (COVID-19) is a pandemic. This systematic review compares mortality risk factors including clinical, demographic and laboratory features of COVID-19, Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). The aim is to provide new strategies for COVID-19 prevention and treatment	(I) Studies included patients infected by SARS-CoV-2, SARS-CoV, and MERS-CoV. (II) Patients in the studies had clinical outcomes including death. (III) Studies reported demographic characteristics, clinical manifestations, laboratory indicators and imaging. (IV) Articles were written in either Chinese or English.	4 (2020)	MEDLINE, EPISTEMONIKOS, COCHRANE, China National Knowledge Infrastructure and WANFANG STATA	mortality	28 studies (including SARS and MERS only and studies only looking at lab indicators) 5 studies regarding diabetes	11818 COVID patients (looking at lab indicators as well, patients looking only at diabetes- 2307	Not reported	Beijing, Guangdong, Shanxi, Hong Kong and Taiwan in China, and Toronto
Lukito 2020	In light of paucity regarding high-	primarily observational studies (cross-sectional,	9 (2020)	Pubmed, EuropePMC, EBSCOhost, Proquest,	Mortality by metformin	9	10233	Hospital	3 from USA, 2 from UK, 2

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	quality data of metformin consumption and mortality in COVID-19 patients, we want to explore the state-of-the-art evidence regarding this critical topic through this systematic review and meta-analysis.	case-control, retrospective/prospective cohort studies) that reported the odds ratios (ORs) or hazard ratios (HRs) in adjusted and non-adjusted forms regarding patients who consume metformin vs who did not.		Cochrane library. preprint.org and Medrxiv					from China, 1 from South Korea, 1 from France
Luo 2020	In this study, we conducted a systematic review of available studies to assess the association between underlying comorbidities and acute cardiac injury and the severity or the prognosis in COVID-19 patients. The underlying comorbidities and cardiac injury may be associated with the prognosis in COVID-19 patients	Eligible studies should be written in English, and describe the relationship between age, gender, comorbidities and the prognosis of adult COVID-19 patients. The number of enrolled patients is more than ten.	7 (2020)	PubMed, EMBASE (by Ovidsp), Web of Science and The Cochrane Library	COVID-19 severity, survivors vs non survivors	124			Asia, the minority was from the USA, Italy, Spain and other countries

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
Maddaloni 2021	We conducted a systematic review and meta-analysis of studies reporting clinical outcomes of subjects hospitalized for Covid-19 with and without history of cardiovascular disease. We secondarily aimed to investigate whether cardiovascular disease further increases the risk of poor Covid-19 outcomes in the high-risk group of people with diabetes mellitus, which may be considered a cardiovascular equivalent.	Observational studies published in English language, reporting original clinical data about history of cardiovascular disease in Covid-19 inpatients aged > 18 years old with and without at least one outcome among death, mechanical ventilation, admission in an intensive care unit (ICU), or a composite outcome with at least one of the above.	10 (2020)	PubMed	mortality (subgroup of patients with CVD and diabetes)	33 studies (4 relevant to review Q)	52857 participants	Hospital	China (n = 11, 33.3%), Italy (n = 6, 18.2%) and United States (n = 5, 15.2%). The remaining studies were from United Kingdom (n = 3), Korea (n = 2), Spain (n = 2), France (n = 1), Greece (n = 1), Poland (n = 1) and Brazil (n = 1).
Mahumud 2020	The main purpose of this study was to examine the overall distribution of chronic comorbidities in coronavirus disease-19 (COVID-19)	Eligible studies were included if they 1) were original articles; 2) published between January 2020 and April 9th, 2020; focused on 3) epidemiological perspective, 4) reported clinical characteristics of the COVID-19 among	4 (2020)	PubMed, Scopus, EBSCOhost (CINAHL, Medline), Web of Science, and the first 20 pages of Google Scholar.	Mortality	23 studies (21 reporting on diabetes)	202005	Not reported	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	infected populations and the risk of the underlying burden of disease in terms of the case fatality ratio (CFR).	infected people, and 5) reported the prevalence of chronic comorbid conditions in infected patients.							
Mair 2020	The objective of this meta-analysis was to look at the pooled prevalence of symptoms, laboratory tests, and imaging of all COVID-19 infected patients.	Not reported	5 (2020)	PubMed, EMBASE, and Ovid	Pooled prevalence and hospitalisation	67	8302	Not reported	Predominantly China, but also Europe, Singapore, Australia, India, Iran and Japan.
Mantovani 2020	We have carried out an updated and comprehensive systematic review and meta-analysis of observational studies that have estimated the global prevalence of pre-existing diabetes in patients admitted to hospital with laboratory-confirmed SARS-CoV-2 infection. We also examined whether there is an association between presence	(1) observational studies examining the clinical and biochemical characteristics of hospitalized patients with laboratory-confirmed COVID-19; and (2) all studies that reported data on presence of established diabetes among hospitalized patients with COVID-19. Study participants included in the meta-analysis were adult individuals (aged>18 years) of either sex without any restriction in terms of age, race, ethnicity or comorbidities.	5 (2020)	PubMed, Scopus and Web of Science	Prevalence, severity, mortality	83	78874	Hospital	Multiple - sixty-two studies were conducted in Asian countries, mostly in China, and 21 studies were conducted in Europe

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	of pre-existing diabetes and severity of COVID-19 illness or risk of in-hospital mortality amongst infected patients.								
Matsushita 2020	To identify whether cardiovascular disease (CVD) and its traditional risk factors predict severe coronavirus disease 2019 (COVID-19)	Not reported	4 (2020)	PubMed and Embase	Severe COVID	25	76,638	Not reported	China (21/25)
Mattey-Mora 2022	to determine the background characteristics and pre-existing comorbidities associated with hospitalisation for COVID-19 patients. This will help identify the most vulnerable populations for severe COVID-19 infections that would require hospitalisation.	Cross-sectional, cohort (retrospective/prospective), and case-series studies with laboratory-confirmed diagnoses for COVID-19 (according to World Health Organisation guidance), which examined patient demographic factors such as ethnicity/race, sex, smoking status, and pre-existing comorbidities including cardiovascular diseases, diabetes mellitus, hypertension, obesity, renal chronic disease, and respiratory diseases	12 (2020)	PubMed, Web of Science, and Cochrane Library	risk of hospitalisation	40 studies	1002006 participants	Hospital and outpatients	Majority in United States (27 studies), Mexico, United Kingdom, Spain (2 studies conducted in each country)
Mehraeen 2020	The aim of this study was to systematically review the	The English-written peer-reviewed original papers published from January 1,	6 (2020)	PubMed, Scopus, Embase, Google Scholar, and Web of Science	Mortality	114	310494	Hospital	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	assessment of risk and model the predictors of mortality in COVID-19 patients.	2020, to June 27, were included.							
Meng 2020	To conduct a meta-analysis to investigate the relationship between severe COVID-19 and underlying CHD, hypertension and diabetes	Not reported	7 (2020)	PubMed, Cochrane, Web of Science, WanFang Data and CNKI	the association between diabetes and severe COVID-19 (pooled OR)	32	8170	Not reported	Majority Asia (China, South Korea), also US, Australia, Italy, France, Poland
Meng 2021	To effectively predict the progression of COVID-19 via patients' clinical features at an early stage, the prevalence of these clinical factors and their relationships with severe illness were assessed.	Without limiting the language of the articles, including those describing the epidemiological and clinical characteristics of COVID-19 cases	4 (2020)	PubMed, Embase, Web of Science, and Chinese databases	prevalence and progression to severe disease	24 studies	3547 participants	Not reported	China
Mesas 2020	Risk factors for in-hospital mortality in confirmed COVID-19 patients have been summarized in numerous meta-analyses, but it is still unclear	(i) participants—100 and more patients with confirmed COVID-19; (ii) design—observational studies (prospective or retrospective) with primary individual data for each mortality outcome group, i.e., non-survivors and	7 (2020)	e MEDLINE (via PubMed), Scopus and Web of Science	mortality	60	51,225	Not reported	Predominantly china

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	whether they vary according to the age, sex and health conditions of the studied populations. This study explored these variables as potential mortality predictors.	survivors; (iii) exposure variables (iv) outcome—all patients followed up to definitive hospital discharge or COVID-19 mortality.							
Miller 2020	The purpose of this systematic review with meta-analysis was to determine the mortality rate of hospitalized patients with Covid-19 in China and to identify factors that may potentially influence this rate.	Observational studies that reported the mortality rate of hospitalized patients in China with a confirmed diagnosis of Covid-19.	3 (2020)	Medline, Embase, and the Cochrane Central Register of Controlled Trials, the Directory of Open Access Journals, Google Scholar,	Mortality	16	1832	Hospital	China
Minh 2021	to systematically review the published literature on the Covid-19 to estimate the frequency of clinical symptoms by comparing different clinical presentations based on the severity and living	all possible case reports, case series, and epidemiological observational studies containing any medical information or clinical investigation of confirmed SARS-CoV-2 cases, regardless of the country and time of examination. We also included non-English articles that were written in Chinese.	3 (2020)	PubMed, EMBASE, SCOPUS, Web of Science (WoS), Google Scholar, Cochrane Library and WHO Global Health Library (WHO GHL)	mortality	171 studies (148 in MA)	62909 participants	Not reported	Primarily China (n = 146), South Korea (n = 6), Singapore (n = 3).

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	status of the cases.								
Mirjalili 2021	Currently, the number of patients with SARS-COV-2 infection has increased rapidly in Iran, but the risk and mortality of SARS-COV-2 infection in Iranian patients with diabetes mellitus (DM), chronic kidney disease (CKD), hypertension and cardiovascular diseases (CVDs) still not clear. The aim of this meta-analysis was to estimate the proportion and mortality of SARS-COV-2 in these patients.	(1) primary case series and case-control publications; (2) studies evaluated clinical characteristics and outcome of SARS-CoV-2 infection Iranian patients with diabetes mellitus, chronic kidney disease, hypertension and cardiovascular disease; (3) studies reported mortality of SARS-CoV-2 infection Iranian patients with diabetes mellitus, chronic kidney disease, hypertension and cardiovascular disease; and (4) sufficient data were presented to calculate the odds ratio (OR) with 95 % confidence interval (CI).	1 (2021)	PubMed/MEDLINE, Google Scholar, EMBASE, Cochrane Library database, SciELO, Springer Link, Chinese Biomedical Database (CBD), China National Knowledge Infrastructure (CNKI) platforms, VIP, Chinese literature (Wan Fang) and China Science and Technology Journal database and Egyptian Knowledge Bank (EKB) Journals	prevalence and mortality	10 studies	11,755 participants	Not reported	Iran
Mishra 2021	We aim to assess the association of CVD with the severity and mortality of COVID-19.	The studies assessing comorbid CVD according to disease severity were included. We included observational studies that includes case-control, cross-sectional, and both retrospective and prospective cohort designs.	9 (2020)	PubMed, Cochrane Library, Google Scholar	severity and mortality	19 studies	6872 participants	Not reported	17 from China, 1 each from US and Iran

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
		We also included case series with sample size ≥ 30 patients as the disease we are trying to study is new.							
Moula 2020	The aim of this meta-analysis is to quantify the risk of mortality in coronavirus disease 2019 (COVID-19) patients. A meta-analysis was conducted analysing the impact of (1) sex, (2) age, (3) CVD with coronary artery disease (CAD), (4) CAD alone, (5) CVD without CAD, (6) hypertension, (7) cerebrovascular diseases, and (8) diabetes on mortality.	The articles were selected based on the following inclusion criteria: (1) human studies; (2) full articles about COVID-19 disease containing separate data for patients that survived and patients that did not; (3) analyses of fatality cases; (4) studies including at least 10 patients; (5) articles published from December 2019 and (6) articles in English language.	5 (2020)	Pubmed	Mortality	26	8497	Not reported	Twenty papers from China, two papers from Italy, two papers from Korea, one from Iran and one from the United States of America.
Mudatsir 2020	To identify the predictors associated with poor clinical outcomes in patients with COVID-19	Ssessed the clinical manifestations and laboratory findings of patients with mild to severe COVID-19; (2) provided adequate data for the calculation of OR and 95% CI.	4 (2020)	PubMed, Embase, Cochrane, and Web of Science	COVID-19 severity	19	3578	Hospital	China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
Nandy 2020	To evaluate the impact of various morbidities on serious events in COVID 19.	We included only human studies and articles with clearly defined clinical outcome measures.	4 (2020)	PubMed, Cochrane Central Register of Clinical Trials	Mortality, serious events and mortality	16	3994	Not reported	China
Ng 2021	To evaluate the correlation between comorbidities and their role in the exacerbation of disease in COVID-19 patients leading to fatal outcomes.	1. Only studies reporting comorbidities and patient's outcome were included. 2. Only peer-reviewed journals were included.	09 (2020)	MEDLINE, Scopus, Web of Science, and EMBASE	Mortality	53	375,859	Not reported	Across 14 countries
Ng 2022	Quantified the impact of DM, HTN, IHD and myocardial injury on six adverse COVID-19 outcomes in unvaccinated individuals	(i) patients ≥ 18 years of age with suspected or confirmed SARS-CoV-2 infection (COVID-19); (ii) pre-existing CV risk factors, specifically HTN and DM, IHD, or evidence of myocardial injury (defined as serum troponin level above the 99th percentile upper reference limit); and (iii) COVID-19 related outcomes, in particular all-cause mortality, ARDS, IMV, admission to intensive care (ITUadm), AKI, and study-defined severe COVID-19 disease (SCoV)	07 (2020)	MEDLINE, CINAHL, Embase, EMCARE, British Nursing Index) and pre-print (medRxiv)	Mortality, ARDS, invasive mechanical ventilation (IMV), admission to ICU, AKI and severe COVID-19 disease	110	49,017	In- and out-patients	Reported based on comorbidities
Nguyen 2022	(1) summarized the effects of every single antidiabetic	RCTs, non-RCTs and observational studies, including prospective and retrospective cohort	11 (2021)	PubMed/MEDLINE, EMBASE, Scopus, and Web of Science	Mortality	61	3,061,584	Not reported	Reported for individual outcomes

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	medication on the mortality of patients with COVID-19 having diabetes and (2) evaluated the dose-responsiveness of the impacts of medications on mortality.	studies and case-control studies							
Noor 2020	The main aim of this study was to find the prevalence of mortality among hospitalized COVID-19 infected patients and associated risk factors for death.	We included the articles assessing the association between age, gender, comorbidities and mortality risk factors from COVID-19 infection as the major outcomes of interest. Articles that reported SARS-CoV-2 infected patients confirmed by real time reverse transcriptase polymerase chain reaction (RT-PCR) were included.	8 (2020)	PubMed, Science Direct and Google Scholar	Mortality	58	122,191	Not reported	Majority: China 26, 8 in USA, 7 in Italy.
Ogungbe 2021	To quantify the association between biomarkers of myocardial injury (troponin), myocardial stretch (NT-proBNP, Gal-3), coagulation (D-Dimer), inflammation (CRP, IL-6) and severe COVID-19	1) study type: retrospective, prospective, observational, or case-control studies, reporting on cardiac biomarkers (specifically Troponin I or T, NT-proBNP, CRP, IL-6, and Gal-3); 2) population: adult patients diagnosed with COVID-19; 3) exposure/intervention: confirmed COVID 19 infection; 4) outcome	01 (2021)	MEDLINE (PubMed), Embase, CINAHL, Cochrane, Web of Science, and Scopus	Myocardial injury, severe or critical clinical status, and death	62	41,013	Not reported	Most studies were conducted in China (50%), Italy (14%), the United States (12%)

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	or death in hospitalized patients. We also calculated pooled proportions of underlying co-morbidities (hypertension, CAD, diabetes, COPD, and cancer)	indicators: myocardial injury, severe or critical clinical status, and death.							
Pal 2020	The aim of the study was to provide a comprehensive systematic literature review of DKA and combined DKA/HHS in patients with confirmed COVID-19 in order to analyse the demographic and biochemical parameters and the clinical outcomes.	To identify studies reporting COVID-19 patients with DKA and combined DKA/HHS - no further details.	8	PubMed, Scopus, Embase, and Google Scholar	Mortality	19	110 patients 91 (83%) patients had DKA alone while 19 (17%) patients had combined DKA/HHS	Hospital	Not reported
Pal 2021	To provide a precise summary and collate the effect of DPP4i use (preadmission or in-hospital) on mortality in COVID-19 patients	Observational studies including COVID-19 patients with diabetes mellitus, a proportion who must have been taking DPP4i before hospitalization. Studies reporting in-hospital DPP4i use in COVID-19 patients. Studies should report the	01 (2021)	PubMed and Google Scholar	Mortality	9	7008	Hospital	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	with diabetes mellitus	data comparing the rate of occurrence of mortality among DPP4i users compared to DPP4i non-users. studies reporting the adjusted odds ratio (OR) of mortality in DPP4i users compared to DPP4i non-users							
Palaiodimos 2020	The aim of this study was to systematically review and conduct a meta-analysis of the available observational studies reporting the effect of diabetes on mortality among hospitalized patients with COVID-19.	The pre-specified inclusion criteria were as follows: (i) studies which included adult patients hospitalized for COVID-19 and (ii) studies that provided data on any kind of association between diabetes and mortality in the aforementioned population.	5 (2020)	Medline, Embase, Google Scholar, and medRxiv	mortality	14	18506, 3713 diabetics, 14793 non-diabetics	Hospital	Multiple - 5 USA, 2 UK, 1 Spain, 1 Italy, 2 Iran, 3 China
Papadopoulos 2021	To identify all sources reporting mortality rate data regarding COVID-19-related acute metabolic emergencies and summarize their results.	(1) refer to COVID-19 patients who had developed either DKA, or HHS, or combined DKA/HHS, or EDKA, (2) are case reports reporting data regarding both primary (survival/discharge vs. death) and secondary (type of metabolic emergency) outcome); (3) are either case report series or cross-sectional studies or meta-	01 (2021)	EMBASE and PubMed/Medline	Mortality, severity	41	71	Hospital	Reported in individual outcomes

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
		analyses of case reports that report mortality rates or enough data to compute it as well as a relevant measure of statistical significance							
Parohan 2020	We aimed to systematically review the present evidence on the association between age, gender, hypertension, diabetes, chronic obstructive pulmonary disease (COPD), cardiovascular diseases (CVDs) and risk of death from COVID-19 infection, and to summarize the available findings in a meta-analysis	(1) all studies assessing the association between age, gender, comorbidities and mortality risk from COVID-19 infection as the major outcomes of interest; (2) observational studies with retrospective design; (3) those that reported hazard ratios (HRs), odds ratios (ORs) or relative risks (RRs) along with 95% confidence intervals (CIs) for the relationship between risk factors and COVID-19 mortality	5 (2020)	Web of Science, PubMed, Scopus, Cochrane Library and Google scholar	Associations between age, gender, comorbidities and risk of death from COVID-19	14	29,909	Not reported	China (12 studies), Italy (1), Iran (1)
Parveen 2020	The aim of the meta-analysis was to assess the association of diabetes and hypertension with severity of disease.	The studies describing the prevalence of diabetes and hypertension according to disease severity were included.	3 (2020)	PubMed, Medline and Cochrane, Google Scholar	ICU care, severity (defined as having respiratory distress, RR>30 beats/minute in a resting state, a mean oxygen saturation of <93%, and an arterial blood oxygen partial pressure (PaO2)/oxygen	7	2018	Not reported	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
					concentration (FiO2)<300 mmHg), mortality				
Patel 2020 (1)	We aimed to evaluate epidemiological characteristics, needs of resources, outcomes, and global burden of the disease	Original observational studies that described any details on epidemiological characteristics on patients with COVID-19	3 (2020)	PubMed	Prevalence of diabetes as a co-morbidity in COVID patients	21	2747	Not stated	China, Singapore, Europe, Australia, USA
Patel 2020 (2)	The objective of this study was to evaluate the risk factors including comorbidities, and complications associated with the poor outcomes amongst COVID-19 patients	All studies describing epidemiology of COVID-19 were included.	5 (2020)	PubMed, Web of Science, Scopus, and medRxiv	Risk factors associated with poor outcomes: Prevalence, coexisting comorbidities, complications. Meta-regression on invasive mechanical ventilation (IMV) utilisation and mortality	29	12,258	Hospitalized patients	China mostly, also includes Singapore, Europe (1 study), Australia, USA (5)
Patoulas 2021	To update the previously published meta-analyses.	RCTs or observational studies enrolling adult patients with T2DM with prior use of DPP-4 inhibitors versus other antidiabetic drug classes, with confirmed COVID-19 infection	NR	PubMed and Cochrane Library	Mortality	10	7133	In- and out-patient	Europe 7, Asia 3
Pinedo-Torres 2020	We aimed to determine the pooled prevalence of DM and its associated unfavourable	The inclusion criteria were: (1) available data of more than 10 patients; (2) adult patients; (3) number of participants with confirmed diagnosis of	4 (2020)	Pubmed/Medline, Scopus, Web of Science, Cochrane, and Scielo	Prevalence, ICU admission, death	15 studies reporting on SARS-Cov-2	3758	Not reported	13/15 studies from China, 1 Italy, 1 Singapore

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	health outcomes in patients with acute respiratory syndromes for coronavirus disease according to virus type.	DM type I or II; and (4) confirmed diagnosis of coronavirus infection.							
Pinto 2020	We aimed to investigate the magnitude of this risk (of diabetes on disease severity) and its dependency on age.	We performed a systematic search and meta-analysis for clinical reports of COVID-19 infection which included detailed descriptions of patients' clinical profile – specifically, reporting information about the presence of diabetes at admission.	Not reported	Not reported	Severity - ICU admission, O2 sat<90%	7	1592	Hospital	China
Plasencia-Urizarri 2020	To evaluate the risk of severe clinical presentation of COVID-19 in patients with comorbidities.	Not reported	3 (2020)	PubMed, EBSCO, Clinicalkey, Scopus, Embase and HighWire	Severe vs Non-severe patients	13	99817	Not reported	Not reported
Poly 2021	To investigate the association between metformin and the risk of mortality among diabetes patients with COVID-19.	Study were included if they: (a) were restricted to epidemiological studies and evaluated the risk of mortality among COVID-19 patients with or with metformin, (b) included at least 15 participants to calculate the effect size, (c) provided clear inclusion and exclusion criteria of COVID-19 patients and metformin exposure.	06 (2021)	PubMed, Scopus, Embase, and Web of Science	Mortality, severity	16	Not reported	Not reported	Europe 5, Asia 5, N. America 6

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
Poly 2021b	To investigate relevant epidemiological studies for evaluating the association between obesity and mortality of COVID-19 patients.	Articles were included if they (a) were peer-reviewed, (b) were published in English, (c) were cohort or comparison design, (d) included patients with more than 20, (e) and reported effect size as odds ratio (OR), risk ratio (RR) or hazard ratio (HR).	08 (2020)	Scopus, PubMed, EMBASE, and Web of Science.	Mortality	17	543,399	Not reported	Europe 4, N. America 11, Mixed 1
Prattichizzo 2022	To explore whether glycaemic control, as measured by HbA1c, is a relevant prognostic factor for acute COVID-19 mortality or worsening of symptoms in patients with DM.	(1) enrolling patients with any form of pre-existing DM and hospitalized for COVID-19 (laboratory confirmed or clinically assigned) and (2) reporting data regarding HbA1c values at hospital admission or before infection in relation to COVID-19 mortality or a composite outcome including mortality with any follow-up duration,	12 (2020)	PubMed, Embase and Scopus	Mortality, severity	7	4,985,063	Not reported	Not reported
Puri 2022	To compare comorbidities among severe and non-severe COVID-19 patients in Asian versus non-Asian populations.	(1) Study population: Studies with patients diagnosed with COVID-19; (2) Comparative studies: Studies that compared severe or ICU (elevated troponin T (TnT) level as the second choice if severe or ICU data were not given) and non-severe or non-ICU (normal TnT level as the second choice if non-severe or non-ICU data was not	03 (2021)	PubMed, Embase, Scopus and Web of Science	Severity	66	Not reported	Not reported	Asia 39, non-Asian 27

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
		given) cases of COVID-19; and (3) The studies reporting parameters of comorbidities such as hypertension, diabetes, cardiovascular disease, cancer, chronic obstructive pulmonary disease and chronic kidney disease.							
Qui 2020	The current meta-analysis aimed to find risk factors for the COVID-19-related death, helping to enhance the efficacy and reduce the mortality of COVID-1	1) The cases in each study were patient diagnosed with COVID-19; 2) Involving the death group or non-survivor group and the survivor group; 3) At least one outcome reported among demographical characteristics, comorbidities and clinical manifestations of COVID-19 deceased	4 (2020)	PubMed, Embase, medRxiv and Cochrane Library	The pooled prevalence of diabetes in COVID-19 death patients	15	2401	Not reported	China, Korea
Radwan 2020	To determine the association between comorbidities and the severity of the disease among COVID-19 patients.	The inclusion criteria comprised hospitalized patients diagnosed with COVID-19 according to WHO guidance	Not reported	Cochrane, Medline, Trip, and EMBASE databases	severity of COVID-19-related illness namely, intensive care unit (ICU) admission, mechanical ventilation and death.	7	1885	Hospital	China
Rahman 2021	To estimate the prevalence of all reported symptoms and comorbidities, and then identified the risk factors associated with	Clinical investigations or consecutive cases; focused on infected patients; reported at least ten cases and considered all age-groups from any countries	04 (2020)	PubMed, SCOPUS, EMBASE, WHO, Semantic Scholar	Prevalence	29	4884	Not reported	5 studies each conducted in USA, India, Spain, and South Korea

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	age of COVID-19 infected patients								
Rahman 2021a	To identify some demographic and clinical characteristics which can be appraised as risk factors for the severity of COVID-19	(a) bivariate data available for the severity (death/ICU (Intensive Care Unit)/severe state/others) of COVID-19 patients, (b) multiple factors available for the severity of the disease, (c) full-text access to the article, (d) information presented in English language, (e) peer-reviewed accepted/published articles	04 (2020)	PubMed, Google Scholar, EMBASE and Cochrane Library	Severity	10	2272	Hospitals	China
Rahmati 2022	To summarize studies on the prevalence of childhood T1D during COVID-19	Studies that evaluated pediatrics' new-onset T1D during the COVID-19 pandemic in 2020 and during the same periods in 2019 which have reported at least one of the following outcomes: the number of children with new-onset T1D, the number of DKA among newly diagnosed children with T1D, and the number of severe DKA among newly diagnosed children with T1D.	03 (2022)	MEDLINE/PubMed, CINAHL, Scopus, and EMBASE	Prevalence, severity (DKA)	26	Not reported	Not reported	Mixed: Europe, Asia, N. America, Australia
Rakhmat 2021	To synthesize evidence on dipeptidyl peptidase-4 (DPP-4) inhibitor and mortality in COVID-19 patients	1) observational studies or randomized controlled trials that reported COVID-19 patients, 2) reporting DPP-4 inhibitor use, 3) mortality, and 4) mortality	03 (2021)	PubMed, Scopus, and Embase	Mortality	9	4,477	Not reported	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	and factors affecting it.	based on DPP-4 inhibitor use.							
Rico-Martin 2021	To investigate the relationship between metabolic syndrome (MetS) and its components with SARS and mortality in COVID-19 patients	Primary observational longitudinal studies that reported the association between MetS and its components with SARS and/or mortality in COVID-19 patients.	09 (2021)	Web of Science (WOS), Scopus and PubMed	Mortality, severity	5	>2400	Not reported	Europe 1, Asia 2, USA 2
Rod 2020	evaluating the risk factors for covid-19 disease severity with a two-fold purpose: (i) to provide healthcare and public health professionals with a reference list of the consistency of risk factors for covid-19 severity, and (ii) to inform researchers about the consistency of reporting in the available literature.	Do not list inclusion criteria. They state "Articles were selected for the review if they included a comparison between non-severe and CSF cases according to the categorization of severity in each article." CSF = composite outcome of disease severity-fatality	Not reported	PubMed, Scopus and MedRxiv	Not reported	Not reported	Not reported	Not reported	Not reported
Roncon 2020	To assess the risk of ICU admission and mortality risk in diabetic COVID-19 patients.	Not reported	3 (2020)	MEDLINE, Scopus and Web of Science.	ICU admission, deaths	8	1382	Not reported	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
Sacks 2020	(1) To characterise the outcomes of COVID-19 for people with diabetes and (2) add value to current recommendations for healthcare providers and people with diabetes to encourage optimal management.	Recommendations were summarised in addition to expert guidance based on the following topic areas: diabetes specific, general prevention and logistical considerations.	Not reported	We undertook a search of PubMed, MEDLINE, EMBASE, Google Scholar	incidence of diabetes in covid; severity of infection in PWD; mortality in PWD; effect of diabetes control on covid-19 disease outcome; consequences of Covid-19 for PWD	Not reported	Not reported	Not reported	China, Australia
Saha 2021	To quantify the prevalence of mortality among (1) diabetic and (2) non-diabetic, and (3) the prevalence of DM, in hospitalized COVID-19 patients.	Observational, experimental, or case-series studies of hospitalized COVID-19 patients with confirmed disease regardless of age or gender.	06 (2020)	PubMed, Embase, and Scopus	Prevalence, mortality	22	45,775	Hospital	Europe, Asia and USA
Sahni 2021	To highlight the impact of cardio-metabolic comorbidities on COVID-19 severity and mortality.	(1) cohort studies, case-control studies and case series studies; (2) the study population included patients with laboratory confirmed SARS-CoV-2 infection; and (3) the primary outcome being reported as fatal or critical case (cases requiring ICU admission or developing ARDS or requiring invasive mechanical ventilatory	10 (2020)	Medline (PubMed) and EMBASE	Mortality, severity	33	20,475	Not reported	Europe, Asia (mostly), USA

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
		support or cases labelled as “severe COVID” as per local or national classification criteria) versus non-critical case(s) amongst patients with or without various comorbidities.							
Sahu 2021	To investigate the clinical characteristics that can predict COVID-19 disease severity	Studies that focused on individual symptoms and comorbidities of laboratory-confirmed COVID-19 patients and reported the data according to disease severity or ICU admission.	05 (2020)	PubMed, Embase, and Web of Science	Severity	22	4380	Not reported	Europe 3, Asia 16, USA 3
Saleh 2021	To investigate the association between diabetes, hypertension, BMI or smoking with the risk of death in patients with COVID-19 and to estimate the proportion of deaths attributable to these conditions	Observational studies (cohort studies and cross-sectional) that reported relative risk estimates (such as (HRs), RR or ORs) with the 95% CIs with or without adjustment for potential confounders	11 (2020)	PubMed (MEDLINE), Cochrane library and Embase databases	Mortality	86	1 304 587	Not reported	Europe 58, Asia 60, N. America 58, S. America 6, Africa 4
Sales-Peres 2020	This systematic review asked the following questions: (i) “Is obesity associated with higher levels of COVID-19 incidence, prevalence, and	Our eligibility criteria included case reports, case series, clinical trials, and randomized controlled trials published in English, Portuguese, and Spanish in peer-reviewed journals. The studies must that have addressed epidemiological	5 (2020)	MEDLINE, EMBASE, Web of Science, BVS/LILACS, SCI-ELO, SCOPUS, and Google Scholar	Severity - composite outcome (severe COVID infection, ICU admission, mechanical ventilation, mortality)	9	6577	Not reported	3 USA, 2 China, 2 France, 1 Spain, 1 Italy

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	risk factors?"; and (ii) "Is obesity associated with higher levels of severe medical complications and does it lead to critical illness and ICU admission?".	and clinical features of COVID-19 and its association with obesity.							
Sanyaolu 2020	To review these comorbidities, given that most patients with severe COVID-19 cases had comorbidity. Furthermore, we would like to examine specific comorbidities in relation to the COVID-19 disease progression and outcomes based on the literature report since the outbreak	An article was selected if it included keywords such as coronavirus, COVID-19, SARS-CoV-2, clinical features, comorbidity, diabetes, and hypertension. Articles were then reviewed and included based on the applicability to the topic	4 (2020)	PubMed, Google Scholar, EBSCOhost, Mendeley and Medline Plus	Reporting from other meta-analysis: Prevalence of Diabetes in COVID-19 patients	Not reported	Not reported	Not reported	Not reported
Sathish 2020	We performed a systematic review and meta- analysis to examine the proportion of newly diagnosed diabetes in COVID-19 patients.	Observational studies providing data on the number or proportion of COVID-19 patients (laboratory-confirmed or clinically diagnosed) with newly diagnosed diabetes	7 (2020)	PubMed, MEDLINE, Embase, and Scopus databases and preprint servers (medRxiv and Research Square)	Pooled proportion of covid-19 patients with newly diagnosed diabetes	8	3711	Hospital	China, USA, Italy
Sathish 2021	Is newly diagnosed diabetes as	Observational studies providing data on the	11 (2020)	PubMed, MEDLINE, Embase and Scopus databases and	Prevalence	6	617	Hospitals	Largely China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	frequent as preexisting diabetes in COVID-19 patients?	number or proportion of COVID-19 patients (laboratory confirmed or clinically diagnosed) with newly diagnosed diabetes		preprint servers (medRxiv and Research Square)					
Sayed 2020	In this review, the possible polymorphisms involved in susceptibility or resistance towards viral entry along with rise of telemedicine are investigated	Not reported	8 (2020)	Pubmed, EMBASE	Mortality and morbidity among COVID-19 patients with existing diabetes; deaths in patient with T1D; t1D and deprivation	Not reported	Not reported	Not reported	China, Europe, USA, Israel, England,
Schlesinger 2021	To identify high-risk phenotypes of diabetes associated with COVID-19 severity and death.	Studies of any design that reported risk estimates for associations between phenotypes and death and severity of COVID-19 in individuals with diabetes and WHO-defined confirmed SARS-CoV-2 infection	10 (2020)	PubMed, Web of Science (www.webofknowledge.com), Epistemonikos and the COVID-19 Research Database (WHO)	Severity of COVID-19	22	17,687	Largely hospital	Europe 3, Asia 14, N. America 5
Sepandi 2020	We investigated the possible risk factors of death in patients with COVID-19, and determined the features that may predict mortality.	written in English and reporting factors associated with COVID-19 mortality	3 (2020)	Med-line/PubMed, Scopus, and Google scholar.	Mortality	13 studies (9 reporting on diabetes)	Not reported	Not reported	China
Shafiee 2022	To compare T1D and T2D in terms of disease severity	1) confirmed COVID-19 patients; 2) patients diagnosed with T1D and T2D; 3) studies evaluating outcomes relevant to this	02 (2022)	Pubmed/MEDLINE, Scopus, Web of Science, Cochrane library, and Clinicaltrials.gov	All cause mortality, hospitalization, and ICU admission rates	11	7690415	Not reported	Europe 9, USA 2

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
		topic; and 4) studies reporting both T1D and T2D infected with SARS-CoV-2.							
Shang 2020	In this study, we aimed to assess whether diabetes mellitus (DM) would increase the risk of severe infection and death inpatients with COVID-19.	Only those research articles that reported data of DM and at least one outcome of interest were included in this meta-analysis. The primary outcomes were the pooled severe infection and mortality risk in COVID-19 patients with DM.	7 (2020)	PubMed, Web of Science, MedRxiv and COVID-19 academic research communication platform	Severity, mortality	76	31067	Hospital	Majority from China
Shoar 2020	to identify original cohorts comparing data between survivors and non-survivors from COVID-19.	Original studies in adult patients with COVID-19 comparing the demographics, clinical characteristics, radiologic findings, or laboratory parameters between survivors and non-survivors were eligible for inclusion if available in English language full-text.	Not reported	PubMed	survivor vs non-survivor	12	3257	Not reported	Wuhan, China
Shrestha 2021	To analyze the rate of new-onset diabetes in COVID-19 patients and compare their clinical outcomes with those of other COVID-19 patients who had normal or increased blood sugar levels or a pre-existing	(1) Study type(s): Observational studies with a comparison of outcomes among individuals with new onset diabetes, pre-existing diabetes, hyperglycemic and non-diabetics with COVID-19 were included in this review; (2) Study participant(s): Individuals of any age, gender, or nationality diagnosed with	06 (2020)	PubMed, PubMed Central, Scopus, Embase, and Google Scholar	Mortality, mechanical ventilation/intubation, and ICU admission	10 (7 included in MA)	Only reported for individual studies	Not reported	Europe 2, Asia 6, USA 2

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	diagnosis of diabetes	COVID-19 and new-onset DM							
Silverio 2021	To investigate the burden of cardiovascular risk factors and the rate of fatal outcome in patients infected by SARS-CoV-2, and to explore their relationship during hospitalization.	Observational studies were included if they met the following pre-specified criteria: (I) inclusion of patients hospitalized for COVID-19; (II) data on in-hospital mortality; (III) data on baseline cardiovascular risk factors.	04 (2020)	MEDLINE, Cochrane, Web of Science, and SCOPUS	Occurrence of death during hospitalization.	45	18,300	Not reported	Not reported
Singh 2020 (1)	We aimed to evaluate the outcome in hypertensive patients with COVID-19 and its relation to the use of renin-angiotensin system blockers (RASB)	We have retrieved all the available literature published in English language on COVID-19, that reported the outcomes in different co-morbidities	3 (2020)	PubMed	Prevalence of diabetes in COVID-19 patients	Not reported	Not reported	Not reported	Not reported
Singh 2020 (2)	This review aims to estimate the prevalence of both cardiometabolic and other co-morbidities in patients with COVID-19 infection, and to estimate the increased risk of severity and	We retrieved all studies conducted in patients with COVID-19 that explicitly reported the detailed epidemiological characteristics, prevalence of comorbidities, severity of the disease, and in-hospital death outcomes	4 (2020)	Medline, Scopus and the World Health Organisation website	COVID-19 severity, In-hospital mortality	18	14558	17 studies were based on in-patients, whilst one study used data from infectious diseases registries	16 were based in China, 1 was from the USA, and 1 was from Italy

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	mortality in people with co-morbidities.								
Singh 2020 (3)	This review aims to collate currently available data about diabetes and COVID-19 infection. It specifically looks at the relation between diabetes and COVID-19 in terms of epidemiology, pathophysiology and therapeutics.	Not reported	4 (2020)	PubMed database and Google Scholar	Association of diabetes in COVID-19 patients, morbidity and mortality	Not reported	Not reported	Not reported	Not reported
Singhal 2021	To comprehensively describe the clinical presentation, co-morbidities, severity of disease and outcomes in older adults infected with COVID-19.	Observational studies that included older patients (\geq 60 years) with confirmed COVID-19 infection and reported comorbidities, clinical characteristics, severity of illness or outcome	05 (2020)	PubMed and Scopus	Severity of illness defined as specified in included studies) and outcomes (death, discharge) in older patients with COVID-19 infection.	46	13624	Not reported	Europe 5, Asia 30, USA 8, Mixed 2, Cruise ship 1
Ssentongo 2020	estimated the association of major pre-existing chronic conditions, including cardiovascular diseases,	1. studies involving patients hospitalized for COVID-19, regardless of age. 2.Exposure: any of the 11 comorbidities 3.Comparison: Hospitalized patients with COVID-19 without the above	7 (2020)	PubMed (MEDLINE), OVID (MEDLINE, HEALTHSTAR), SCOPUS, Joana Briggs International EBP, Cochrane Library databases, Google Scholar and Medrxiv.	Mortality	25 studies	65484	Hospital	21/25 from China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	hypertension, diabetes, congestive heart failure, cerebrovascular disease, chronic kidney disease, chronic liver disease, cancer, chronic obstructive pulmonary disease, asthma, and HIV/AIDS, and the risk of mortality from COVID-19.	mentioned pre-existing comorbidities 4. The primary outcome was the mortality in hospitalized patients with COVID-19 5. randomized controlled trials, cohort, and case-control studies.							
Subramaniam 2021	To investigate the incidence, characteristics and outcomes of patients who were readmitted to hospital emergency departments or required rehospitalisation following an index hospitalisation with a diagnosis of COVID-19	Studies reporting on the incidence, characteristics and outcomes of consecutive patients with COVID-19 who represent or require hospital admission	12 (2020)	PubMed, EMBASE, MedRxiv, and BioRxiv	Readmission	6	547	Hospitals	Europe 3, Asia 1, USA 2
Tadic 2020	The aim of this review article was to summarize the current knowledge about the	Not reported	4 (2020)	PubMed, Scopus, Web of Science, Google Scholar	narrative report of prevalence and mortality of people with DM in covid19 patients,	Not reported	Not reported	Not reported	China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	relationship between diabetes and COVID-19 and its role in outcome in these patients.								
Tan 2020	The objective of this systematic review and meta-analysis was to provide a contemporary and global assessment of the point estimate of death and risk factors for severe disease in patients admitted to an ICU with COVID-19	(1) Design that included randomized controlled trials, non-randomized controlled trials(case control or controlled cohort), observational studies and case series, (2) Study population that included adult patients(18 years old) admitted to an ICU or high dependency unit, which included studies that compared ICU and non-ICU cohorts (3) Disease that confirmed COVID-19 or SARS-CoV-2 (4) Outcome that reported in-hospital mortality rates.	8 (2020)	Medline, Embase and Cochrane Library	Prevalence of diabetes in severe COVID-19 patients (i.e. those that were admitted to HDU/ICU)	35 referenced diabetes mellitus)	3345	Hospital (ICU/HDU)	Kuwait, Israel, USA, Spain, Portugal, China, Italy, Greece, France, England, Oman, Netherlands, Switzerland, Canada, Denmark and United Kingdom
Taylor 2021	To determine factors associated with mortality among adults with COVID-19 admitted to intensive care	Adult patients with COVID-19 admitted to ICU, reporting mortality or survival outcomes stratified by patient factors, risk scores and haematological results of interest	12 (2020)	MEDLINE, Embase, the Cochrane Library, Africa-Wide Information via EBSCOhost and SciELO Citation Index via Web of Science	Mortality	58	44,305	Hospital/ICU	Reported in supplementary file - appendix s3
Thakur 2021	To determine the differences in the prevalence of major comorbidities associated with COVID-19 and the	(1) originally published in the English language; (2) included confirmed diagnosis of COVID-19 through laboratory examination; (3) conducted on human patients; (4)	07 (2020)	PubMed, Scopus, and EMBASE	Mortality, severity	120	125,446	Hospital	Across 19 countries

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	severity and mortality of COVID-19 associated with each of the comorbidities according to the geographical regions.	provided information about comorbidities; (5) contained information on the disease outcomes: severity or mortality within comorbidity; and (6) published as an original investigation							
Tian 2020	To conduct a systematic meta-analysis of published articles to comprehensively elucidate predictors of mortality in hospitalized COVID-19 patients	NOT STATED EXPLICITLY ("eligibility criteria" mentioned but not detailed). Studies looking at clinical predictors of mortality in hospitalised COVID-19 patients, with death from COVID-19 as a clear outcome	4 (2020)	PubMed, Google scholar, Web of Science, and China National Knowledge Infrastructure (CNKI)	Prevalence of diabetes between mortality vs survival group, associations between mortality from COVID-19 and diabetes i.e. mortality in diabetes vs non-diabetes	14, 12 used for DM	In total, 4659 patients. 4315 used for DM. 3212 survived of which 682(21.2%) had DM.	Hospitals	China
Treskova-Schwarzbach 2021	To summarise the global evidence on the risk of severe COVID-19 outcomes in patients with pre-existing health conditions	SR had to investigate the association between at least one pre-existing health condition, and at least one of the following severe health outcomes due to COVID-19: hospitalisation, admission to ICU, ventilation (intubation) or death	12 (2020)	PubMed and Embase (including Medline), supplemented by hand searches on ArRxiv, BioRxiv, ChemRxiv, MedRxiv, Preprints.org, ResearchSquare and SSRN	Hospitalisation, admission to ICU, ventilation (intubation) or death	160	Not reported	Not reported	Not reported
Vardavas 2022	To investigate the role of underlying medical conditions as prognostic factors for adverse outcomes due to severe acute	Only cohort studies conducted in Europe, including EU/EEA countries provided 1) they evaluated patients with clinically diagnosed or laboratory-confirmed COVID-19 in one	06 (2021)	Medline (Ovid) and Embase (Ovid)	Mortality, severity, hospitalisations, ICU admission	88	6 653 207	Community, hospital and ICU	Europe

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	respiratory syndrome coronavirus 2 (SARS-CoV-2)	of three settings (community, hospital or ICU) and 2) they assessed the associations between underlying clinical conditions (as risk factors) and primary adverse outcomes of COVID-19							
Varikasuvu 2020	We aim to evaluate the risk of disease severity and mortality in association with diabetes in COVID-19 patients.	Studies reporting diabetic proportions in sub- groups of COVID-19 patients (Severe vs. Non-severe & Mortal vs. Survival) were included.	5	Pubmed, Cochrane, medRxiv, "other databases"	Severity and mortality	47	PWD 1009/3773 and 1360/9495 in severe/mortal and non-severe/survival groups of COVID-19 cases, respectively.	Not reported	Majority China; also Italy, France, USA,
Venkata 2020	Not reported	Not reported	Not reported	PubMed, Embase, and Google Scholar	Prevalence	22 studies	>11,000	Hospital	8 countries
Wang 2020 (1)	We performed a systematic review and meta-analysis in order to identify risk factors associated with the severity and mortality rate among COVID-19 patients.	(1) The study was a clinical observation in humans; (2) the study included COVID-19 patient information; and (3) the study included information regarding comorbidity and/or organ injury.	4 (2020)	PubMed, Embase, Web of Science, medRxiv, and bioRxiv	Clinical characteristics associated with increased disease severity and mortality among patients with COVID-19; the association between preexisting diabetes and COVID-19 severity i.e. diabetics vs non-diabetics.	34, 31 used for DM (counted from figure 6)	A total of 6,263 COVID-19 cases	Not reported	China
Wang 2020 (2)	We performed a meta-analysis of the available studies to explore relationship between	(1) Types of Studies: published studies reported the relationship between comorbidity and patients with COVID-19; (2) Subjects: diagnosed	3 (2020)	PubMed (Medline), EMBASE, Springer, Web of Science, and Cochrane Library databases	Association between diabetes in COVID patients and severe disease (severity sub-grouped into ICU admission and clinical	6, 6 used for DM. 2 studies used whether patients experienced ICU care to	For DM, 324 severe group cases and 1234 non-severe group cases (1558 in total)	Not reported	China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	comorbidity and patients with COVID-19.	patients with COVID-19; (3) Exposure intervention: COVID-19 patients with comorbidity included: hypertension, diabetes, chronic obstructive pulmonary disease (COPD), liver disease, malignancy, renal disease, cardiovascular disease, cerebrovascular disease; (4) Outcome indicator: the odds ratios (OR) with 95% confidence intervals (CI) for each comorbidity.			symptoms). Diabetes vs non-diabetes.	judge the severity of the disease, and the other 4 studies used clinical symptoms to judge the severity of the disease.			
Wang 2020 (3)	The aim of this research was to systematically assess the prevalence of diabetes mellitus among 2019-nCoV.	The inclusion criteria were as follows: (1) the studies were published in English; (2) 2019-nCoV diagnosed depending on World Health Organization interim guidance; (3) those were clinical studies; (4) clinical information can be collected from the articles.	2 (2020)	PubMed, Embase, Web of Science, and Medline	Prevalence of diabetes overall and in moderate and severe COVID patients	9	2007	Not reported	China
Wang 2022	To review observational studies on the effect of insulin use and mortality in patients with COVID-19 and diabetes	Patients confirmed to have or were clinically diagnosed with COVID-19 and diabetes, and data regarding the risk of death between insulin and noninsulin users were available	12 (2020)	PubMed, EMBASE, Medline, and Cochrane Library databases	Mortality	6	1338	Not reported	Europe 3, China 2, USA 1
Wicaksana 2020	This article aims to review the current evidence on diabetes	We conducted a scoping review in PubMed, Science Direct, DOAJ and Microsoft Academics databases from	4 (2020)	PubMed, Science Direct, DOAJ and Microsoft Academics databases	ICU admission, mortality	7	Not reported	Not reported	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	management and specific considerations during the COVID-19 pandemic for people living with diabetes.	January 1 to April 17, 2020. Searching terms included "COVID-19", "severe acute respiratory syndrome coronavirus 2", and "Diabetes Mellitus" were used. Only scientific articles discussing diabetes management and specific considerations were selected and extracted.							
Wu 2020	This meta-analysis first aims to explore the possible clinical mortality between diabetes and COVID-19, analyse if diabetes patients infected with SARS-CoV-2 are exposed to the worst clinical prognostic risk, and to evaluate the reliability of the evidence.	Primitive studies were carefully examined, and there were no nation restrictions in our study. The inclusion criteria were as follows: (1) all studies reporting data on COVID-19 non-survivors, survivors, and laboratory-confirmed COVID-19 patients; (2) studies limited to mankind, contained original data, published in English and appeared in the form of either abstract or full-text.	4 (2020)	Medline via PubMed, EMBASE, and Web of Science	Mortality	9 studies	1471	Hospital	China
Wu 2021	To evaluate the in-hospital mortality and risk factors of death in COVID-19 patients	All eligible studies should report the mortality and/or risk factors for death in COVID-19 patients	05 (2020)	PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), VIP, and Wanfang databases	Mortality	80	Not reported	Hospitals	Europe 11, Asia 61, N. America 8
Xiang 2021	To summarize clinical, laboratory,	(I) hospitalized patients with confirmed COVID-19; (II) reported	06 (2020)	PubMed, EMBASE and Cochrane	Mortality	20	15408	Not reported	Europe 4, Asia 13, USA 1, mixed 1

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	radiological features, and complications of non-survivors with confirmed COVID-19.	demographical, clinical feature, laboratory values, chest CT findings, treatment or outcomes of survivors and non-survivors respectively; (III) the risk factor of mortality; (IV) cross-sectional studies and (V) article language was English and/or Chinese							
Xie 2021	To summarize the characteristics of COVID-19 patients in the early stage of the pandemic and explore the risk factors of disease progression	Studies that reported more than 50 cases of SARS-CoV-2 infection confirmed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) with demographical, clinical, laboratory, and image characteristics	03 (2020)	PubMed, Chinese medical journal network, and CNKI	Severity	90	16526	Not reported	88 (97.8%) were from China
Xu 2020	To systematically review evidence for the risk factors of COVID-19 patients progressing to critical illness.	(i) Prospective or retrospective original reports; (ii) All of the patients were diagnosed with COVID-19; (iii) Characteristics of severe and mild cases were documented; and (iv) Complete medical records were available for data extraction.	3 (2020)	Chinese and English electronic bibliographic databases, including China National Knowledge Infrastructure (CNKI), Wanfang Database, Weipu Database, Chinese Biomedicine Literature Database (CBM-SinoMed), PubMed, Embase, Cochrane Central Register and Web of Science	Not explicit, but association between diabetes in COVID patients and diseases severity, grouped into severe and non-severe disease.	20, 10 used for DM	1083 for diabetes	Not reported	China
Yanai 2020	I systematically reviewed a possible association of metabolic syndrome with the	Not reported	Not reported	Not reported	Severity (undefined)	12 studies	Not reported	Not reported	Not reported

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# participants	Setting(s)	Country(s)
	susceptibility to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and severity of COVID-19 by literature search.								
Yang 2020	We will provide a systematic evaluation and detail, which will not only estimate the prevalence of comorbidities in all patients, but also assess the risk of underlying diseases in severe patients compared to non-severe patients.	Eligible were those that described the epidemiological, clinical features of COVID-19, and the prevalence of chronic diseases in infected patients".	2 (2020)	PubMed, EMBASE, and Web of Science databases	The association between presence of diabetes and severe and non-severe diseaseAlso, prevalence of diabetes in COVID-19 patients.	7 in total. Between severe group and non-severe group for DM used 4.	1576 participants in total, of which 9.7% had diabetes in the pooled analysis.	Hospitals	China
Yang 2021 (1)	To detect the overall effects of metformin on COVID-19 patients with diabetes	(1) evaluation on the effect of metformin on COVID-19 patients with diabetes; (2) inclusion of sufficient data or the data can be acquired from the manuscript or supplementary materials to calculate ORs and 95% CIs; and (3) the study was published in English	06 (2021)	PubMed, Embase and CNKI (China National Knowledge Infrastructure) databases	Mortality, severity	17	20719	Not reported	Europe 4, Asia 9, USA 4
Yang 2021 (2)	To determine the association between insulin	(1) population: the subjects were patients with both COVID-19 and diabetes; (2)	02 (2021)	PubMed, Cochrane Library, EMBASE and Web of Science	Mortality, Severe/Critical Complications	18	12277	Not reported	Europe 6, Asia 7, USA 5

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	injection and the outcomes of COVID-19	intervention: insulin treatment; (3) comparator/control: the control group involved non-insulin treatment; (4) outcomes refer to the mortality and other complications of COVID-19, and the form of the outcomes must be original data of COVID-19 deaths and complications or calculated adjusted/unadjusted odds ratios (ORs) or risk ratios (RRs); and (5) study design: clinical studies							
Yang 2021 (3)	To systematically describe the relationship between the use of DPP-4is and the mortality of COVID-19	(1) they contained information on DPP-4is and the outcomes of COVID-19, including mortality and the development of severe COVID-19; and (2) the subjects were patients with both COVID-19 and T2DM	10 (2020)	PubMed, Cochrane Library, EMBASE and Web of Science	Mortality	4	1933	Not reported	Europe
Yifan 2020	We have systematically reviewed the single-centre or multicentre observational studies of older patients with COVID-19 and comprehensively dissected the true impact of age as a	Eligibility criteria are as follows: (a) research types: descriptive studies including case-control studies, retrospective cross-sectional studies, cohort studies, and case series; (b) research subjects: patients with laboratory-confirmed COVID-19; (c) studies comparing clinical characteristics, laboratory	8 (2020)	PubMed, EMBASE, Cochrane Library, Scopus, and Web of Science databases	Association between diabetes in COVID patients and age (adult vs elderly). Diabetes vs non-diabetes.	4	2047 patients confirmed with COVID-19. 195 had diabetes	Not reported	China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	complex variable on COVID-19 disease.	findings, and outcomes for the elderly and young.							
Yin 2021	To assess the role of comorbidity in COVID-19 progression	(1) Designed studies published online. (2) Studies contained well-recorded clinical characteristics and epidemiological information of patients diagnosed with COVID-19, including age, gender, symptoms, date of hospitalization, and comorbidities. (3) Participants in the study must be stratified into different groups according to severity or disease progression, in the form of either mild/ moderate/ severe/critical illness based on clinical symptoms or ICU/non-ICU based on admission care	01 (2021)	PubMed and Web of Science, and the Chinese database CNKI	Prevalence	41	12,526	Not reported	China
Zaki 2020	To undertake a review and critical appraisal of published/preprint reports that offer methods of determining the effects of hypertension, diabetes, stroke, cancer, kidney issues, and high-	Not reported	Not reported	COVID-19 Open Research Dataset (CORD-19), PubMed, Google Scholar	Prevalence, mortality	11 on diabetes	Not reported	Hospital	Majority from China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	cholesterol on COVID-19 disease severity.								
Zangiabadian 2021	To summarize the available evidence on the potential mechanism of action and the efficacy of metformin in COVID-19 patients with DM	Not reported	07 (2020)	PubMed/Medline, EMBASE, the Cochrane Controlled Register of Trials (CENTRAL), and Web of Science	duration of hospitalization, the effect on in-hospital death, and effect on poor prognosis	14 - 3 on effect of metformin on outcomes	Not reported - 3 studies reported 6,659 participants	Not reported	Not reported
Zein 2022	To synthesize the latest evidence on the effect of dipeptidyl peptidase-4 (DPP-IV) inhibitor in patients with COVID-19	prospective or retrospective observational studies or case series or randomized controlled trials (RCTs) reporting DPP-IV inhibitor use in patients with COVID-19 and mortality	07 (2021)	PubMed, Scopus, Embase, and Clinicaltrials.gov	Mortality	11	5950	Not reported	Europe 7, Asia 3, N. America 1
Zeng-HongWu 2021	To explore the possible clinical mortality between diabetes and COVID-19, analyze if diabetes patients infected with SARS-CoV-2 are exposed to the worst clinical prognostic risk, and to evaluate the reliability of the evidence	(1) all studies reporting data on COVID-19 nonsurvivors, survivors, and laboratory-confirmed COVID-19 patients; (2) studies limited to mankind, contained original data, published in English and appeared in the form of either abstract or full-text	04 (2020)	Medline via PubMed, EMBASE, and Web of Science	Mortality	9	926	ICU, isolation wards	China
Zhao 2020 (1)	The aim of our study is to perform a	Inclusion criteria were as follows: (1) any study that gives information about the	2	PubMed, Embase, Cochrane, the Web of Science Core Collection (Clarivate	Severity, mortality	30 studies overall (10	53,000 (2511 relevant for diabetes)	Not reported	Majority from China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	systematic review and meta-analysis of clinical characteristics to explore the risk factors of COVID-19-associated severe illness and death, and first time to compare the differences of those predictors between COVID-19, SARS and MERS.	clinical characteristics or demographic or outcome of the infectious disease, (2) restriction language to English only, and (3) studies that allowed us to stratify the risk of severe or fatal COVID-19 by demographic or medical condition were preferred.		Analytics), and MedRxiv databases		relevant for diabetes)			
Zhao 2020 (2)	This study aimed to compare the epidemiological and clinical features between ICU patients and non-ICU patients in order to find the risk factors for exacerbation prediction of Novel Coronavirus Infected Pneumonia (NICP) patients, which was very valuable to identify the development, treatment and prognosis of NCIP patients.	(i) patients were diagnosed with NCIP; (ii) study design was the cohort study comparing ICU patients with non-ICU patients.	2	PubMed, Embase and Google scholar	Association between diabetes in COVID patients and ICU admission. Diabetes vs non-diabetes.	2 studies	179	1 from a single centre, 1 from a hospital	Wuhan, China

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
Zheng 2020	analysed the clinical characteristics of COVID-19 patients with critical/mortal illness and non-critical illness in 13 literatures with 3027 patients, to identify the risk factors for COVID-19 patients to develop critical disease or death, in order to effectively predict the progression of the disease, make early treatment response and allocate medical resources in a better way.	(1) groups involving critical illness or death and non-critical illness; (2) patients should be confirmed to have been infected by 2019 novel coronavirus; (3) study designs included randomized controlled trials, nonrandomized controlled trials, case-control studies, cohort studies, cross-sectional studies, and also case reports; (4) at least one outcome reported among demographical characteristics, comorbidities, clinical manifestations or laboratory examinations; (5) study sample was larger than 20.	3	Pubmed, Embase, Web of Science, and CNKI	Association between diabetes in COVID patients and critical/mortal patients	13 studies, 11 for DM	A total number of 3027 patients. Of those with diabetes - 460 critical/mortal, 2119 non-critical	Not reported	China
Zhou 2020 (1)	We conducted this meta-analysis to provide a comprehensive understanding of the characteristics of COVID-19-related deaths and compare them with those of survivors to enable better investigations of	(1) patients should be confirmed to have been infected with SARS-CoV-2; (2) each study should consist of a death group; (3) the full text of each article should be available; and (4) at least one outcome was reported among demographical characteristics, comorbidities, clinical characteristics, laboratory	8	PubMed, EMBASE, CNKI	Association between diabetes in COVID patients and mortality. Diabetes vs non-diabetes.	19, of which 18 were included in the diabetes pooling - 6 China, 12 other.	Not reported	Not reported	Asia, Europe, America

Study ID	Review objective as stated by authors	Inclusion criteria as stated by authors	Search month (year)	Databases searched	Outcomes reported	# included studies	# part-icipants	Setting(s)	Country(s)
	the prognostic factors of COVID-19 in infected individuals.	examinations, or image examinations							
Zhou 2020 (2)	The aim of this study was to integrate recent advances and present an updated meta-analysis of the relationships between comorbidities and severe or fatal outcomes associated with COVID-19.	(1) published studies reporting the relationship between comorbidities and patients with COVID-19 written in English; and (2) the inclusion of data on the prevalence of comorbidities in COVID-19 patients who had severe manifestations, or were admitted to an ICU, or died	4	PubMed, Embase, and Cochrane Library databases	The primary outcome measure was overall prevalence of comorbidities in severe or fatal COVID-19 and to	34. 25 used for diabetes, 17 with clinical symptoms as outcome, 4 with ICU admission and 4 with death	16110	Not reported	China, the USA, the UK, Italy, France, Spain, Australia, Singapore, and Korea
Zhu 2021	To estimate if higher HbA1c levels are associated with adverse prognosis of COVID-19 patients	(a) peer-reviewed prospective or retrospective original reports; (b) all patients were diagnosed as COVID-19; (c) outcome indicators were adverse prognosis (fatal and/or critical outcomes).	11 (2020)	Wanfang Database, China National Knowledge Infrastructure (CNKI), Chinese Biomedicine Literature Database (CBM-SinoMed), Weipu Database, Embase, Cochrane Central Register, PubMed and Web of Science	fatal and/or critical outcomes	9	2577	Not reported	Europe 3, USA 2, Asia 4

1 18 citations are not listed in the above table. This includes 16 reviews which were borderline for inclusion, as they did not contain any meta-analyses on the main outcomes for this review and did not have data on our subgroups of interest (Abdelhafiz 2021; Boden 2022; Huang 2021; Justino 2022; Khanal 2022; Leretter 2022; Mason 2021; Nassar 2021; Nikoloski 2021; Pandey 2022; Pellicori 2021; Peterfi 2022; Pizuorno 2021; Tisminesky 2022; Wingert 2021; Yin 2021). All relevant content in these reviews was consistent with findings from our other included reviews. A further two umbrella reviews are synthesised narratively in the text.

Table 3. Summary of AMSTAR-2 judgements by domain²

Domain	No	Partial yes	Yes
Protocol registered in advance (item 2)	147	8	48
Adequacy of search (item 4)	18	137	49
Justification for excluding individual studies (item 7)	169	11	24
Risk of bias from individual studies being included in the review (item 9)	75	48	81
Appropriateness of meta-analytical methods (item 11) (Note, 26 did not conduct meta-analysis)	11	65	101
Consideration of risk of bias when interpreting the results of the review (item 13)	119	42	43
Assessment of presence and likely impact of publication bias (item 15)	81	37	86

Table 4. AMSTAR-2 critical domain judgements for included reviews

	Protocol registered before commencement of the review (item 2)	Adequacy of the literature search (item 4)	Justification for excluding individual studies (item 7)	Risk of bias from individual studies being included in the review (item 9)	Appropriateness of meta-analytical methods (item 11)	Consideration of risk of bias when interpreting the results of the review (item 13)	Assessment of presence and likely impact of publication bias (item 15)	Total yes/ partial yes
Abdi 2020	Yes	Yes	No	No	Partial yes	No	Yes	4
Aggarwal 2020	No	Partial yes	No	No	Partial yes	No	No	2
Akbari 2022	No	Partial yes	No	Partial yes	Partial yes	Partial yes	Partial yes	5
Aktar 2021	No	Partial yes	No	No	Partial yes	No	Partial yes	3
Alhumaid 2021	No	Partial yes	No	Partial yes	No	Partial yes	No	3
AlirezaAbdi 2021	Partial yes	Partial yes	No	Partial yes	Partial yes	No	Partial yes	5
Alves 2021	Partial yes	Partial yes	No	No	Partial yes	No	No	3
Apicella 2020	No	Yes	No	No	n/a	No	No	1
Ashktorab 2021	No	Partial yes	No	No	No	No	No	1
Awortwe 2020	No	Partial yes	No	No	Partial yes	No	Yes	3
Badawi 2021	No	No	No	No	Partial yes	No	Partial yes	2
Bae 2021	Yes	Partial yes	No	Yes	Partial yes	No	No	4
Bajgain 2020	No	Partial yes	No	Yes	No	No	No	2
Baradaran 2020	No	Partial yes	No	No	Partial yes	No	No	2
Barrera 2020	Yes	Yes	No	Yes	Yes	Yes	No	5
Bennett 2020	No	Partial yes	No	Yes	No	No	No	2
Bepouka 2022	No	Partial yes	No	Partial yes	Partial yes	No	Partial yes	4
Boddu 2020	No	Partial yes	No	No	n/a	No	No	1
Bonora 2021	No	Partial yes	No	No	Partial yes	No	No	2
Bradley 2022	No	Partial yes	No	No	Partial yes	No	No	2
Carrasco-Sanchez 2022	No	No	No	Partial yes	No MA	Partial yes	No	2

² Assessed as per standard AMSTAR-2 guidance set out in Shea 2017. 18 citations are not listed in the above table. This includes 16 reviews which were borderline for inclusion, as they did not contain any meta-analyses on the main outcomes for this review and did not have data on our subgroups of interest (Abdelhafiz 2021; Boden 2022; Huang 2021; Justino 2022; Khanal 2022; Leretter 2022; Mason 2021; Nassar 2021; Nikoloski 2021; Pandey 2022; Pellicori 2021; Peterfi 2022; Pizuorno 2021; Tisminesky 2022; Wingert 2021; Yin 2021) and the two umbrella reviews.

Total yes/ partial yes	Assessment of presence and likely impact of publication bias (item 15)	Consideration of risk of bias when interpreting the results of the review (item 13)	Appropriateness of meta-analytical methods (item 11)	Risk of bias from individual studies being included in the review (item 9)	Justification for excluding individual studies (item 7)	Adequacy of the literature search (item 4)	Protocol registered before commencement of the review (item 2)	
3	Partial yes	No	Partial yes	No	No	Partial yes	No	Chamorro-Pareja 2020 (abstract)
3	No	No	Yes	Yes	No	Yes	No	Chen 2020
4	No	No	Partial yes	Partial yes	No	Partial yes	Yes	Chen 2022
6	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	Yes	Chen 2022
5	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	No	Cheng 2021
3	yes	No	no	Yes	No	Partial yes	no	Chidambaram 2020
3	No	No	Partial yes	Partial yes	No	Partial yes	No	Choi 2022
0	No	No	n/a	No	No	No	No	Chowdhury 2020
4	Partial yes	No	Partial yes	Partial yes	No	Partial yes	No	Chua 2021
6	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	Yes	Corona 2021
1	No	No	n/a	No	No	Partial yes	no	Costa 2020
1	No	No	n/a	No	No	Partial yes	No	d'Annunzio 2020
4	No	No	Partial yes	Partial yes	No	Partial yes	Yes	Damayanathi 2021
4	Yes	No	Yes	No	No	Yes	Yes	de Almeida-Pititto 2020
2	No	No	Yes	No	No	Yes	No	Del Sole 2020
2	No	No	n/a	No	Partial yes	Yes	no	Deravi 2020
2	No	No	Partial yes	No	No	Partial yes	no	Desai 2020
1	No	No	n/a	No	No	Partial yes	no	Deshmukh 2020
5	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	No	Dessie 2021
2	Partial yes	No	Partial yes	No	No	No	No	Dhar 2021
5	Yes	Yes	Yes	Yes	No	Yes	No	Du 2020
5	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	No	Du 2021
4	Yes	No	Yes	Yes	No	Yes	No	Emami 2020
7	Yes	Yes	Yes	Yes	yes	Yes	yes	Espinosa 2020
1	No	No	Yes	No	No	No	No	Fadini 2020
4	Yes	No	Yes	Yes	No	Partial yes	No	Faghir-Gangi 2020
6	Yes	Yes	Partial yes	No	Yes	Partial yes	Yes	Fang 2020
4	Partial yes	No	Partial yes	Partial yes	No	Partial yes	No	Fathi 2021
6	Yes	Yes	Yes	Yes	No	Partial yes	Yes	Figliozi 2020
0	No	No	n/a	No	No	No	No	Flaherty 2020
6	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	Yes	Gaba 2022
0	No	No	n/a	No	No	No	No	Gallo Marin 2020
6	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	Yes	Ganesh 2022
4	No	Partial yes	Partial yes	Partial yes	No	Partial yes	No	Giri 2021
4	No	Partial yes	Partial yes	Partial yes	No	Partial yes	No	Giri 2021
1	No	No	No	No	No	Partial yes	No	Goel 2021 (see comment)
2	No	No	Partial yes	No	No	Partial yes	no	Gold 2020
1	No	No	n/a	No	No	Partial yes	No	Guler 2020

Total yes/ partial yes	Assessment of presence and likely impact of publication bias (item 15)	Consideration of risk of bias when interpreting the results of the review (item 13)	Appropriateness of meta-analytical methods (item 11)	Risk of bias from individual studies being included in the review (item 9)	Justification for excluding individual studies (item 7)	Adequacy of the literature search (item 4)	Protocol registered before commencement of the review (item 2)	
Guo 2020	Yes	No	Yes	No	No	Yes	No	3
Gupta 2021	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	No	5
Han 2022	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	Yes	6
Hariyanto 2020	No	No	Yes	No	No	Partial yes	No	2
Hariyanto 2021	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	No	5
Hartmann-Boyce 2020	No	Partial yes	n/a	No	No	No	No	1
Hoang 2021	Partial yes	No	Partial yes	No	No	Partial yes	No	3
Honardoost 2021	Partial yes	No	Partial yes	Partial yes	No	No	No	3
Hu 2020	Yes	No	Yes	Yes	No	Yes	No	4
Hu 2021	Partial yes	No	Partial yes	No	No	Partial yes	No	3
Huang 2020	Yes	No	Yes	No	No	Partial yes	No	3
Hussain 2020	No	No	n/a	No	No	Yes	No	1
Hussain 2020	No	No	Yes	Yes	No	Yes	No	3
Izcovich 2020	Yes	Yes	Yes	Yes	yes	Yes	yes	7
Javanmardi 2020	Yes	No	Yes	Yes	yes	Partial yes	no	5
Jindal 2022	Partial yes	No	Partial yes	Partial yes	No	Partial yes	No	4
Kaminska 2021	No	No	Partial yes	Partial yes	No	Partial yes	No	3
Kan 2021	Partial yes	Partial yes	Partial yes	Yes	No	Partial yes	No	5
Kandil 2021	Partial yes	No	Partial yes	Partial yes	No	Partial yes	No	4
Kaur 2020	No	No	No	No	No	No	No	0
Khan 2020	Yes	No	Partial yes	Yes	yes	Yes	no	5
Khateri 2020	yes	Yes	Yes	Yes	Partial yes	Yes	no	6
Kow 2020	No	Partial yes	Yes	No	Yes	Partial yes	No	4
Kubjane 2020	Partial yes	Partial yes	Yes	Partial yes	Yes	Partial yes	Partial yes	7
Kumar 2020 (1)	Yes	Partial yes	Yes	Yes	No	Partial yes	Yes	6
Kumar 2020 (2)	No	No	Yes	No	Yes	No	Yes	3
Kumar 2021	Partial yes	No	Partial yes	No	No	Partial yes	No	3
Lee 2020	No	No	Yes	No	No	Partial yes	Yes	3
Li 2020 (1)	Yes	Yes	No	Yes	No	Partial Yes	Partial Yes	5
Li 2020 (2)	No	Yes	Yes	Partial Yes	No	Partial yes	Partial Yes	5
Li 2020 (3)	No	No	Yes	Yes	yes	Yes	no	4
Li 2020 (4)	No	No	No	Yes	yes	Partial yes	no	3
Li 2021	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	No	5
Li 2021	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	Yes	6
Li 2021	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	Yes	6
Liu 2020 (1)	Yes	No	Yes	Yes	yes	Yes	no	5
Liu 2020 (2)	Yes	Yes	Yes	Yes	No	Partial yes	No	5
Lu 2020	Partial yes	No	n/a	Yes	yes	Partial yes	Yes	5
Lukito 2020	Yes	Yes	Yes	Yes	No	Yes	No	5
Luo 2020	Yes	Yes	Yes	Yes	yes	Partial yes	no	6
Maddaloni 2021	Partial yes	No	Partial yes	No	No	No	No	2
Mahumud 2020	Yes	No	Yes	Yes	No	Yes	No	4
Mair 2020	No	Yes	Yes	Yes	No	Yes	no	4

Total yes/ partial yes	Assessment of presence and likely impact of publication bias (item 15)	Consideration of risk of bias when interpreting the results of the review (item 13)	Appropriateness of meta-analytical methods (item 11)	Risk of bias from individual studies being included in the review (item 9)	Justification for excluding individual studies (item 7)	Adequacy of the literature search (item 4)	Protocol registered before commencement of the review (item 2)	
5	Yes	Partial yes	Yes	Yes	No	Yes	No	Mantovani 2020
5	yes	No	Yes	Yes	No	Yes	yes	Matsushita 2020
6	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	Yes	Mattey-Mora 2022
2	No	No	n/a	Yes	No	Partial yes	No	Mehraeen 2020
6	Yes	Partial yes	Yes	Yes	Partial yes	Yes	no	Meng 2020
3	Partial yes	No	Partial yes	No	No	Partial yes	No	Meng 2021
7	yes	Yes	Yes	Yes	yes	Partial yes	yes	Mesas 2020
4	Yes	No	Yes	No	No	Yes	Yes	Miller 2020
4	No	No	Partial yes	Partial yes	No	Partial yes	Yes	Minh 2021
5	Partial yes	Partial yes	Partial yes	Partial yes	No	Partial yes	No	Mirjalili 2021
3	No	No	Partial yes	Partial yes	No	Partial yes	No	Mishra 2021
5	yes	Yes	Yes	Yes	No	Partial yes	No	Moula 2020
6	Yes	Yes	Yes	Yes	yes	Partial yes	no	Mudatsir 2020
2	No	No	No	Yes	No	Partial yes	No	Nandy 2020
2	No	No	Yes	No	No	Partial yes	No	Ng 2021
7	Yes	Yes	Yes	Yes	Yes	Partial yes	Yes	Ng 2022
6	Yes	Yes	Yes	Partial yes	No	Partial yes	Yes	Nguyen 2022
4	yes	No	Yes	Yes	No	Partial yes	no	Noor 2020
6	Yes	Yes	Yes	Yes	No	Partial yes	Yes	Ogungbe 2021
1	No	No	n/a	No	No	Partial yes	No	Pal 2020
4	No	Partial yes	Yes	Yes	No	Partial yes	No	Pal 2021
4	Yes	No	Yes	Yes	No	Yes	No	Palaodimos 2020
6	Yes	Yes	Yes	Yes	No	Yes	Yes	Papadopoulos 2021
4	Yes	No	Yes	Yes	No	Yes	No	Parohan 2020
3	No	No	Yes	Yes	No	Yes	No	Parveen 2020
1	No	No	n/a	No	No	No	Partial Yes	Patel 2020 (1)
4	No	Yes	Yes	Yes	No	Yes	No	Patel 2020 (2)
2	No	No	Yes	No	No	Partial yes	No	Patoulas 2021
6	Yes	Partial yes	Yes	Yes	No	Yes	Yes	Pinedo-Torres 2020
1	No	No	Yes	No	No	No	No	Pinto 2020
6	Yes	Yes	Yes	Yes	yes	Yes	No	Plasencia-Urizarri 2020
3	Yes	No	Yes	No	No	Partial yes	No	Poly 2021
5	Yes	Yes	Yes	Yes	No	Partial yes	No	Poly 2021b
6	Yes	Yes	Yes	Partial yes	Yes	Partial yes	No	Prattichizzo 2022
4	No	Partial yes	Yes	Partial yes	No	Partial yes	No	Puri 2022
5	Yes	Yes	Yes	No	No	Partial Yes	Partial Yes	Qui 2020
5	No	Yes	Yes	Yes	yes	Partial yes	no	Radwan 2020
5	Yes	No	Yes	Partial yes	No	Partial yes	Yes	Rahman 2021
2	No	No	Yes	No	No	Partial yes	No	Rahman 2021a
5	Yes	Yes	Yes	Yes	No	Partial yes	No	Rahmati 2022

Total yes/ partial yes	Assessment of presence and likely impact of publication bias (item 15)	Consideration of risk of bias when interpreting the results of the review (item 13)	Appropriateness of meta-analytical methods (item 11)	Risk of bias from individual studies being included in the review (item 9)	Justification for excluding individual studies (item 7)	Adequacy of the literature search (item 4)	Protocol registered before commencement of the review (item 2)	
5	Yes	No	Yes	Partial yes	No	Partial yes	Yes	Rakhmat 2021
5	Yes	Yes	Yes	Partial yes	No	Partial yes	No	Rico-Martin 2021
1	No	No	Partial yes	No	No	No	No	Rod 2020
5	Yes	Partial yes	Yes	Yes	No	Yes	No	Roncon 2020
2	No	Partial yes	n/a	No	No	Yes	no	Sacks 2020
6	Yes	Yes	Yes	Partial yes	No	Partial yes	Yes	Saha 2021
3	Yes	No	Yes	No	No	Partial yes	No	Sahni 2021
5	Yes	Partial yes	Yes	Partial yes	No	Partial yes	No	Sahu 2021
6	Yes	Partial yes	Yes	Yes	No	Partial yes	Yes	Saleh 2021
5	Yes	No	Yes	Yes	No	Yes	Yes	Sales-Peres 2020
1	No	No	n/a	No	No	Partial yes	No	Sanyaolu 2020
7	Partial yes	Yes	Yes	Yes	Partial yes	Yes	yes	Sathish 2020
4	No	No	Yes	Partial yes	No	Partial yes	Yes	Sathish 2021
1	No	No	n/a	No	No	Partial yes	no	Sayed 2020
4	Yes	No	Yes	Yes	No	Partial yes	No	Schlesinger 2021
5	Yes	Partial yes	Yes	Yes	No	Yes	No	Sepandi 2020
6	Yes	Yes	Yes	Yes	No	Partial yes	Yes	Shafiee 2022
5	Yes	Yes	Yes	Yes	No	Yes	No	Shang 2020
3	No	No	Partial yes	No	yes	Partial yes	no	Shoar 2020
5	Yes	No	Yes	Yes	No	Partial yes	Yes	Shrestha 2021
4	Yes	No	Yes	Yes	No	Partial yes	No	Silverio 2021
0	No	No	n/a	No	No	No	No	Singh 2020 (1)
6	Yes	No	Yes	Yes	yes	Partial yes	Yes	Singh 2020 (2)
1	No	No	n/a	No	No	Yes	no	Singh 2020 (3)
5	Yes	Yes	Yes	Partial yes	No	Partial yes	No	Singhal 2021
6	Yes	Yes	Yes	Yes	No	Yes	Yes	Ssentongo 2020
3	No	No	Yes	Yes	No	Partial yes	No	Subramaniam 2021
1	No	No	n/a	No	No	Partial yes	no	Tadic 2020
7	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Tan 2020
4	Yes	No	Yes	Yes	No	Partial yes	No	Taylor 2021
4	Yes	No	Yes	Partial yes	No	Partial yes	No	Thakur 2021
3	No	No	Partial yes	Yes	No	Partial yes	No	Tian 2020
7	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Treskova-Schwarzbach 2021
5	Yes	Yes	Yes	Yes	No	Partial yes	No	Vardavas 2022
6	Yes	Partial yes	Partial yes	Yes	No	Yes	Yes	Varikasuvu 2020
2	No	No	Yes	No	No	Partial yes	No	Venkata 2020
4	Yes	No	Partial yes	No	Partial yes	Yes	No	Wang 2020 (1)
6	Yes	Partial yes	Partial yes	Yes	Partial yes	Partial yes	No	Wang 2020 (2)
3	Yes	No	Yes	No	No	Yes	No	Wang 2020 (3)
4	Yes	Yes	Yes	No	No	Partial yes	No	Wang 2022
1	No	No	n/a	No	No	Partial yes	No	Wicaksana 2020

Total yes/ partial yes	Assessment of presence and likely impact of publication bias (item 15)	Consideration of risk of bias when interpreting the results of the review (item 13)	Appropriateness of meta-analytical methods (item 11)	Risk of bias from individual studies being included in the review (item 9)	Justification for excluding individual studies (item 7)	Adequacy of the literature search (item 4)	Protocol registered before commencement of the review (item 2)	
2	No	No	Partial yes	No	No	Yes	No	Wu 2020
6	Yes	Yes	Yes	Yes	No	Partial yes	Yes	Wu 2021
5	Yes	No	Yes	Yes	No	Yes	Yes	Xiang 2021
5	Yes	Partial yes	Yes	Partial yes	No	Partial yes	No	Xie 2021
5	Yes	Yes	Partial yes	Yes	Partial yes	No	No	Xu 2020
0	No	No	n/a	No	No	No	No	Yanai 2020
3	No	No	Partial yes	No	Partial yes	Partial yes	No	Yang 2020
5	Yes	Partial yes	Yes	Partial yes	No	Partial yes	No	Yang 2021
5	Yes	Partial yes	Yes	Yes	No	Partial yes	No	Yang 2021
5	Yes	Yes	Yes	Yes	No	Partial yes	No	Yang 2021
5	Partial yes	No	Partial yes	Yes	Partial yes	Yes	No	Yifan 2020
4	Yes	No	Yes	No	No	Partial yes	Yes	Yin 2021
1	No	No	n/a	No	No	Partial yes	No	Zaki 2020
1	No	No	No MA	No	No	Partial yes	No	Zangiabadian 2021
5	Yes	Partial yes	Yes	Yes	No	Partial yes	No	Zein 2022
4	Yes	No	Yes	Yes	No	Partial yes	No	Zeng-HongWu 2021
4	Yes	No	Yes	Yes	No	Partial yes	No	Zhao 2020 (1)
2	No	Yes	No	No	No	Partial yes	No	Zhao 2020 (2)
5	No	Yes	Yes	Yes	Partial yes	Partial yes	No	Zheng 2020
4	Yes	No	Partial yes	No	Yes	Partial yes	No	Zhou 2020 (1)
6	Yes	Partial yes	Partial yes	No	Partial yes	Partial yes	Partial yes	Zhou 2020 (2)
4	Yes	No	Yes	Yes	No	Partial yes	No	Zhu 2021

Table 5. Prevalence of diabetes in people with COVID-19³

First author/Year	Prevalence
Abdi 2020	14.5% (95% CI 10.4 to 19.9)
Aktar 2021	11.8% (95% CI 8.3 to 19.1)
AlirezaAbdi 2021	14.5% (95% CI 10.4 to 19.9)
Ashktorab 2021	8.3% (Range 0.6 to 20.6%)
Badawi 2021	11.8% (95% CI 10.9 to 12.6) (China only)
Bae 2021	15.16% (95% CI 12.9 to 17.8)
Bajgain 2020	17.40%
Baradaran 2020	10%
Barrera 2020	Across all studies: 12% (95% CI 10, 15), N=1414/12870, 31 studies Severe COVID-19 only: 18% (95% CI 16 to 20, n = 1099)
Bennett 2020	9.2% in hospitalised patients
Bradley 2022	31% (95% CI 25 to 38)
Chen 2022	Overall 12.78% (95%CI 11.93, 13.63) Prevalence in mild disease: 7.84% (5.78, 10.54) Prevalence in moderate disease: 8.59% (7.25, 10.16) Prevalence in severe disease: 17.99% (16.29, 19.84) Prevalence in critical disease: 22.68% (19.93, 25.69)
Chua 2021	Overall prevalence 19.5% (95% CI 15.9, 23.4) Prevalence in non-severe disease - 5.9% (2.58, 10.14)
Del Sole 2020	10.1%
Desai 2020	Overall prevalence of diabetes in COVID-19 patients with a mean age>50 years was 13.2% [95% CI 9.7%-17.1%, I ² =53%]; studies with relatively younger patients (mean age <50 years) had a pooled prevalence of 9.0% [95% CI 5.1%-13.5%, I ² =63%]
Du 2020	The pooled prevalence of diabetes was 10% [95% confidence interval (CI): 7%-15%] in COVID-19 patients. The prevalence of diabetes was higher in severe patients (17%; 95%CI: 14%-20%) than in non-severe patients (6%; 95%CI: 5%-8%), and in dead patients (30%; 95%CI: 13%-46%) than in survivors (8%; 95%CI: 2%-15%). Both funnel plot and Egger's test showed publication bias on the pooled prevalence of diabetes (P < 0.001)
Emami 2020	Pooled prevalence for diabetes 7.87% (95% CI 6.57, 9.28)
Espinosa 2020**	22% (95% CI: 21-23)
Fadini 2020	Pooled prevalence for diabetes 10.3% (For comparison, the nationwide prevalence of diabetes in China in 2013 was 10.9% overall and 12.3% among people aged 40–59)
Faghir-Gangi 2020	Pooled prevalence 14% (95% CI 11, 17), I ² =93.4%, random effects model.
Fathi 2021	14.29% (95% CI 11.88, 16.87), I ² 99.1%
Giri 2021	11.5% (95%CI 9.0, 14.1), I ² =66%
Giri 2021	17.1% (95%CI 14.0, 20.3)
Goel 2021	9.96%
Gold 2020	9.65% (95%CI: 6.83%- 13.48%)
Guler 2020	7.7%
Gupta 2021	16.8%

³ ** considered higher quality (judged as yes or partial yes for at least 6 of 7 critical AMSTAR-2 domains)

First author/Year	Prevalence
Hartmann-Boyce 2020	Systematic reviews primarily consisting of data from China have estimated rates of 8% (95% CI 6–11%) (2), 7.87% (95% CI 6.57–9.28%) (3), and 9.7% (95% CI 6.9–12.5%) of diabetes in people hospitalized with COVID-19. The percentage hospitalization appears higher in the U.S., where from February 12 to 28 March 2020, PWD accounted for 10.9% of all COVID-19 patients (similar to the proportion of the U.S. population with diabetes), 24% of hospitalized cases (non-intensive care unit [ICU]), and 32% of ICU admissions. A recent (preprint) U.K. study found uncomplicated diabetes to be the second most common comorbidity (19%) in patients hospitalized with COVID-19; complicated diabetes is reported in a figure only, but prevalence looks to be approximately 6.5%
Honardoost 2021	9.96%
Hu 2020	7.7 % (95% CI 6.1–9.3 %)
Hu 2021	Severe disease prevalence of diabetes 15% (95%CI 12, 19), I ² 52.2% ICU prevalence of diabetes 31% (19, 43), I ² 82.8%
Hussain 2020	Primary studies included in this meta-analysis reported diabetes prevalence in COVID-19 patients within the range of 2.66% to 40% with a pooled prevalence of 15% (95% CI: 12% to 18%), p<0.0001. Prevalence was computed using a random-effect model because of the presence of significant heterogeneity(I ² =97.47%). When the prevalence was stratified based on the country, we found a prevalence of 21% (95% CI: 6% to 35%) in the U.S. and 14% (95% CI: 12% to 16%) in China. The single studies from Korea, Spain, and India reported a prevalence of 35%, 19%, and 14% respectively.
Jindal 2022	17.7% (95% CI 12.2, 25.1), I ² =99%
Kaur 2020	12.80%
Khan 2020	25.2%
Khateri 2020 **	14% (pooled)
Kumar 2020 (1) **	The pooled prevalence of diabetes was calculated to be 11.2% (95% CI: 9.5%-13.0%). Heterogeneity was high at 92%. The results of meta-regression showed that proportion of diabetes in patients with COVID-19 was influenced by age (with studies with higher patient age having higher proportion of diabetes, p<0.001), type of composite endpoint (with studies reporting mortality endpoint having higher proportion of diabetes, p=0.004), and country of study (with studies outside of China having higher proportion of diabetes, p=0.006). There was no influence of number of patients in studies or quality score of studies.
Liu 2020 (1)	10.0% (95% CI 8.0% to 12.0%)
Liu 2020 (2)	8.5% (95% CI 5.5, 11.4), I ² 96.2
Mair 2020	8% hospitalised; 4% non-hospitalised
Mantovani 2020	The pooled prevalence of established diabetes in the overall population of confirmed COVID-19 cases (n=83 studies included) was 14.34% (95% confidence intervals [CI] 12.62-16.06%). The high heterogeneity observed in the overall primary analysis of these studies (I ² =97.8%) likely reflects differences in the characteristics of study populations (mostly age and country). Indeed, the pooled prevalence of pre-existing diabetes was remarkably greater amongst COVID-19 patients aged>60 years than amongst those aged<60 years (23.30% [95%CI19.65-26.94] vs. 8.79% [95%CI 7.56-10.02]; p<0.0001). Furthermore, the pooled prevalence of diabetes was also significantly greater in non-Asian countries than in Asian countries (23.34% [95%CI 16.40-30.28] vs. 11.06% [95%CI 9.73-12.39]; p=0.001), possibly reflecting the marked differences in median age values of the study populations between the two countries.
Matsushita 2020	The prevalence of diabetes ranged from 5% to 58%

First author/Year	Prevalence
Meng 2020 **	The incidences of diabetes in all the included patients were 12.55%. The incidences of diabetes in severe patients were 20.50%
Meng 2021	9% (95% CI 15, 23), $I^2=56\%$
Miller 2020	14.40%
Minh 2021	Prevalence in severe to critical disease: 19% (95% CI 16, 22) Prevalence in non-survivors: 23% (95% CI 16, 33)
Mirjalili 2021	16.3% (95% CI 8.5, 29.1)
Nandy 2020	The pooled prevalence of Diabetes mellitus (DM) in COVID-19 infection from 8 studies with 1895 patients was 13% (95%CI, 10%–17%). We did a heterogeneity test between 13 studies with a result of $I^2 = 81\%$, $p < 0.01$
Ogungbe 2021	21% (95% CI 18%–23%), range 8% to 44%.
Patel 2020 (1)	10%
Patel 2020 (2)	Diabetes 15.4% (95% CI: 12–19.4%; $p < 0.001$; 2897/11680)
Pinedo-Torres 2020 **	10.8% (95% CI 5.9, 16.6)
Sacks 2020	The incidence of diabetes in COVID-19 cases in China has varied from 5% to 20% however large-scale data suggest incidence may be in the order of 5.3–7.4% (15–21). These discrepancies may be attributed to incomplete data due to lack of testing and comorbid analysis of cases of death. In comparison, diabetes was reported in approximately 10.9% of the Chinese population prior to COVID-19. Therefore, based on early prevalence studies in China, it appears that people with diabetes are not significantly more likely to be infected with COVID-19.
Sales-Peres 2020	30.3% in people who also had obesity
Sanyaolu 2020	9.4% to 23.8%
Sathish 2021	Preexisting diabetes 14.8% (95% CI 8.1–23.0%); newly diagnosed diabetes 14.4%, (95% CI 5.9–25.8%)
Sayed 2020	1.7% to 39.7%
Shrestha 2021	New-onset diabetes 19.70% (CI: 10.93-32.91, $I^2= 96.71\%$)
Tadic 2020	3% to 21%
Thakur 2021	18% (15-20%)
Tian 2020	23.80%
Venkata 2020	23%
Wang 2020 (3)	Overall pooled prevalence 9% (95% CI 6, 12), $I^2 65\%$ Pooled prevalence in moderately severe COVID patients: 7% (4, 10), $I^2 58.7\%$ Pooled prevalence in severe COVID patients: 17% (13, 21), $O^2 0\%$
Zaki 2020	12% to 22%
Zhou 2020 (2) **	Meta-analysis of the proportions of comorbidities in severe or fatal COVID-19 cases showed diabetes had a prevalence of 17%, 95% CI 15–20%.

Table 6. Association between diabetes and severe outcomes with COVID-19⁴

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
Abdi 2020	NR		Death rate higher among patients with both diabetes and COVID-19. No pooled data.		Severe symptoms higher among patients with both diabetes and COVID-19. No pooled data.	
Aggarwal 2020	NR		Diabetes in people not surviving COVID-19 versus those surviving COVID-19: OR: 2.03 [95%CI: 1.29-3.20] 4 studies, 307/618 died of which 96 (15.5%) had DM. I ² =0%	↑↑	Diabetes in COVID-19 patients with or without severe disease: OR: 2.60 [95% CI: 1.96 to 3.45] . 12 studies. 754/2564 severe cases where 265 (10.3%) have DM. I ² =56% and not explored/explained.	↑↑
Aktar 2021	NR		NR		Composite severe disease/ICU admission/death: OR 2.08 (95% CI 1.39, 3.1) I ² 46%, p value on Effer test 0.95, 11 studies, 2693 patients	↑↑
Alves 2021	NR		RR 1.9 (95%CI 1.53, 2.37) I ² =62.7%	↑↑	NR	
Apicella 2020	Reports estimates from 3 other reviews, all of which are included here. No new data.		Reports data from 2 other reviews, both of which are included here. No new data. Also reports data from large primary studies in type 1 and 2 diabetes (Barron et al): N=23804, 32% T2D, OR 2.03 (1.97, 2.09); 1.5% T1D, OR 3.5 (3.15, 3.89)		NR	
Ashkortab 2021	NR		"multiple regression analysis showed that diabetes was significantly associated with mortality (r=0.91, p=0.01)"	↑↑	NR	
Awortwe 2020	Risk difference for ICU vs non-ICU 0.01 (-.33;0.34) , p value 0.98, I ² =84.8 (n studies/participants NR)	↑	Risk difference for surviving COVID-19 vs. not surviving: 0.14 [0.08; 0.19] , p value (<00000.1), I ² =21%. (n studies/participants NR)	↑↑	Risk difference for severe v mild (not defined): 0.08 (0.02 to 0.14) , p=0.002, I ² =56. (n studies/participants NR)	↑↑

⁴ NR not reported. ** higher quality (6 or 7 yes or partial yes on AMSTAR-2). Bold=pooled estimates. ↑ increased risk in PWD, not statistically significant; ↑↑ statistically significant increased risk in PWD; ↓ lower risk in PWD, not statistically significant

⁵ Severity as per definitions of individual study authors unless otherwise specified

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
Bae 2021	NR		OR 2.11 (95% CI 1.63, 2.73)	↑↑	“severe disease” OR 2.47 (95% CI 1.86, 3.27)	↑↑
Bajgain 2020	NR		66 fatal, 172 non-fatal with diabetes. In studies showing only fatal cases: 33.2% fatality for diabetes and Covid-19		NR	
Barrera 2020	Unadjusted RR, 3 studies, N=8890, RR 1.96 (1.19, 3.22) , I ² =80%	↑↑	Unadjusted RR, 4 studies, N=2058, RR 2.78 (1.39, 5.58) , I ² =75%	↑↑	Unadjusted RR for severe COVID-19 (not defined): 1.50, 95% CI 0.90 to 2.50 . I ² =74%, 6 studies, n=1991	↑
Bepouka 2022	NR		OR 1.39 (95% CI 1.02, 1.76) , I ² =0.3%	↑↑	NR	
Bradley 2022	NR		OR 2.44 (95% CI 1.93, 3.09) , I ² =54.6%	↑↑	‘Severity’ OR 3.39 (95% CI 2.14, 5.37) , I ² =77.6%	↑↑
Chen 2022 (1)	OR 2.2 (95%CI 1.35, 3.59), I ² =58.7%, 10 studies, 3003 patients	↑↑	NR		NR	
Cheng 2021	NR		NR		Severity: OR 1.64 (95% CI 1.3, 2.08) , I ² 60.4%	↑↑
Chidambaram 2020	NR		PWD in those who died versus those who survived: RR 1.59 [1.41–1.78] . 27 studies, n=16263, I ² =23	↑↑	PWD in severe versus non severe cases: OR 2.09, 95% CI 1.66 to 2.64 , I ² =40%, 36 studies, n=7552	↑↑
Choi 2022	NR		NR		RR for severe disease (ICU/death) 2.26 (95%CI 1.95, 2.62) , I ² =0%, 4 studies, 5233 patients Separate analysis in children with diabetes: children with diabetes had a higher risk of severe COVID-19 than those without diabetes (RR, 2.26; 95% CI, 1.95–2.62)	↑↑
Chowdhury 2020	NR		Only reports data from Barron et al primary studies: 3.50 (3.15–3.89) odds of dying in hospital with COVID-19 in PWD compared with those without diabetes which was attenuated to 2.86 when also adjusted for previous hospital admissions with coronary		NR	

First author/Year	ICU admission and direction of effect	Mortality and direction of effect	Other measures of severity ⁵ and direction of effect
		heart disease, cerebrovascular disease, or heart failure	
Corona 2021	NR	OR 1.85 (95% CI 1.36, 2.51) “For DM the adjusted relationship endpoint with mortality rate was $r=0.187$, $p=0.001$ (adjusted by age, sex, associated morbidities)”	↑↑ NR
Costa 2020	NR	Report results from 3 individual studies (no synthesis), all of which show greater risk in PWD. Cite Chinese CFR of 7.3% in PWD compared to 2.3% in total population.	NR
Damayanthi 2021	NR	OR 1.31 (95% CI 0.22, 7.83) , $I^2=96\%$, 3 studies, 10059 older people with COVID-19	↑ NR
de Almeida-Pititto 2020	NR	10 studies, 4247 patients, 532 PWD. Compared diabetes rate in people who died versus people who survived. OR 2.50 (95% CI 1.74–3.59) . Random effects model ($I^2=50.72$; $p=0.032$). No publication bias was detected.	↑↑ Severity (defined as ICU admission or need for mechanical ventilation or low O ₂ saturation < 90%): 18 studies, 4305 patients, 564 PWD. Compared diabetes rate in severe v non-severe. OR 2.35 (95% CI 1.80–3.06) , Random effects model ($I^2=34.78$; $p=0.073$), with no significant publication bias
Del Sole 2020	NR	NR	Severity (ARDS, ICU admission, death): OR 2.78 (95% CI 2.09 to 7.72) , 10 studies, $n=2794$. I^2 NR
Deravi 2020	NR	NR	Individuals with diabetes mellitus and hypertension are reported to be at higher risks for the late viral clearance of the coronavirus, and the worsened prognosis in SARS, MERS and COVID-19 infections.

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
Deshmukh 2020	NR		Narrative only. "These reports indicate that severe or critically ill COVID-19 patients with concurrent hypertension, diabetes and cardiovascular disease have a significantly higher risk of mortality and require special attention during their hospitalization."		NR	
Dessie 2021	NR		OR 1.52 (95%CI 1.36, 1.69) , I ² =78.9%, 13 studies	↑↑	NR	
Dhar 2021	NR		NR		'Severe disease' RR 1.52 (95% CI 1.25, 1.85) , I ² 86.6%, Egger test p=0.0017	↑↑
Du 2020	Diabetes was not found to be significantly associated with admission to ICU (RR = 1.16, 95%CI: 0.15-9.11). 2 studies, n=1631. I ² =78%. Suspected publication bias.	↑	Compared with patients without diabetes, the risk of death (RR = 3.16, 95%CI: 2.64-3.78 , I ² = 34%) was higher in COVID-19 patients with diabetes. No evidence of publication bias. 4 studies, n=46,654	↑↑	Compared with patients without diabetes, the risks of severe cases [risk ratio (RR) = 2.13, 95%CI: 1.76-2.56 , I ² = 49%] was higher in COVID-19 patients with diabetes. No evidence of publication bias. 7 studies, n=2662	↑↑
Du 2021	NR		OR 2.6 (95% CI 2.03, 3.34) , I ² =9%, 9 studies	↑↑	"Severe disease" OR 3.27 (95% CI 2.24, 4.79) , I ² =57%, 10 studies	↑↑
Espinosa 2020**	NR		19% prevalence of PWD within deaths with COVID-19, 95% CI (16-22), number of studies NS, no comparisons made		17% prevalence of PWD within ICU admission with COVID-19, 95% CI (15-19), number of studies NS, no comparisons made	
Fadini 2020	NR		NR		Based on these data, we conclude that diabetes may not increase the risk of SARS-CoV-2 infection but can worsen the outcome of this new coronavirus disease.	
Fang 2020**	5 studies, with 3747 total cases, RR 1.88 (1.10-3.23) , I ² =51%. Calculated as rates of diabetes in people in ICU versus those not in ICU.	↑↑	Using 10 studies, with 4748 cases, the RR of death with COVID-19 and co-morbid diabetes is as follows: RR 1.75 (1.27-2.41) , I ² =23%	↑↑	Severity (American Thoracic Society guidelines for community-acquired pneumonia or the New Coronavirus Pneumonia Prevention and Control Guidelines of China): RR 1.95 (1.60 to 2.36) . Data from 23 studies, n=7739, I ² =43%. Statistically and clinically significant increases in	↑↑

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
					risk for ARDS and invasive ventilation also found in pooled data.	
Figliozi 2020**	NR		NR		“Adverse prognosis” composite (death, severe COVID-19 infection, hospitalization in ICU and/or use of mechanical ventilation and progression of the disease): OR 2.34, 95% CI 1.64 to 3.33 , I ² =80%, n=15953, 34 studies.	↑↑
Flaherty 2020	NR		NR		Narrative only. “Patients with diabetes have up to a 50% greater chance of a fatal outcome from COVID-19 than non-diabetic infected individuals”	
Gaba 2022**	OR 2.79 (95% CI 1.79, 4.34), I ² =0%, 5 studies, n=611	↑↑	OR 2.46 (95% CI 1.68, 3.58) , I ² =62%, 12 studies	↑↑	NR	
Giri 2021	NR		NR		‘Severe disease’ OR 3.15 (95% CI 2.39, 4.15) , I ² 49%, 10 studies	↑↑
Giri 2022	NR		NR		‘Severe disease’ OR 2.04 (95% CI 1.67, 2.5) , I ² 55%, 37 studies	↑↑
Gold 2020	NR		Diabetes was more prevalent among fatal cases [24.89% (95%CI: 18.80%, 32.16%)] compared to total cases [9.65% (95%CI: 6.83%, 13.48%)]		NR	
Guler 2020	NR		Narrative only, discusses increased risk as per Costa 2020 (cite increased CFR in PWD)		NR	
Gupta 2021	NR		OR 1.83 (95% CI 1.61, 2.05)	↑↑	NR	
Guo 2020	NR		NR		Severity (indication of respiratory rate >30 breaths/min, or SpO ₂ <93% on room air, or PaO ₂ /FiO ₂ ≤300 mmHg, or critical complication (respiratory failure, septic shock, and or multiple organ dysfunction/failure) or death). Nine studies, 1070/8807 with diabetes,	↑↑

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
					pooled RR 2.96 (95% CI: 2.31–3.79) ; $p < 0.001$), I ² 23%. No evidence of publication bias	
Hartmann-Boyce 2020			Narrative only, cite data showing higher risk of death across individual studies		"...current data suggest that COVID-19 is associated with worse outcomes in PWD."	
Hoang 2021	RR 2.44, 95% CI 1.66 to 3.6 , I ² =45%, 4 studies	↑↑	NR		'Severe infection': RR 2.01 (1.7, 2.39) , I ² 51.1%, 13 studies	↑↑
Honardoost 2021	NR		NR		'Severity': OR 2.61 (95% CI 2.02, 3.3) , I ² 30.5%, 26 studies	↑↑
Hu 2020	NR		No comparisons. Within PWD, the risks of severity and mortality rate ranged from 12.6 to 23.5% and from 2.0 to 4.4%, with pooled estimates at 18.0 and 3.2%, respectively.		No comparisons. The percentage of severe cases (not defined but includes ARDS and acute cardiac injury) in diabetes was 44.5% (95CI 27.0–61.9 %)	
Hu 2021	OR 1.61 (1.043, 1.043) ⁶ , I ² 76.8% (number of studies and n not reported)	↑↑	NR		NR	
Huang 2020	RR 1.47 [0.38, 5.67] , $p=0.57$; I ² =63%. 10 studies, n=1985	↑	RR 2.12 [1.44, 3.11] , $p<0.001$; I ² : 72%. 10 studies, n=1985	↑↑	<i>Severe COVID</i> ((1) respiratory distress (>30 breaths per min); (2) oxygen saturation at rest <93%; (3) ratio of partial pressure of arterial oxygen (PaO ₂) to fractional concentration of oxygen inspired air (fiO ₂) <300 mmHg; or (4) critical complication (respiratory failure, septic shock, and or multiple organ dysfunction/failure): (RR 2.45 [1.79, 3.35]) , $p<0.001$; I ² : 45%, 13 studies, n=3561) <i>Composite poor outcome</i> (including mortality, severe COVID-19, acute respiratory distress syndrome (ARDS), need for intensive care unit (ICU) care, and disease progression): RR 2.38 [1.88, 3.03] , $p<0.001$; I ² : 62%, $p<0.001$). The funnel-plot analysis showed a qualitatively	↑↑

⁶ Note apparent error in CI reported in paper

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
					symmetrical inverted funnel-plot for the association between DM and composite poor outcome.	
Hussain 2020	The risk of ICU admission rate was significantly higher in COVID-19 patients with diabetes as compared to COVID-19 patients without diabetes with a pooled risk ratio of 1.88 (1.20- 2.93) . 5 studies, n=7484, I ² =75%.	↑↑	Mortality risk was found to be significantly higher in COVID-19 patients with diabetes as compared to COVID-19 patients without diabetes with a pooled risk ratio of 1.61 (95% CI: 1.16-2.25) . I ² =93%. 11 studies, n=7093.	↑↑	NR	
Izcovich 2020**	NR		13.6% with diabetes, 7.9% without. OR 1.84 (1.61-2.1) . n=30303, 52 studies, I ² 33%. High certainty evidence according to GRADE. Estimated absolute risks: 5.6% increase in mortality. Between 4.3% more and 7% more.	↑↑	“Severe COVID-19 disease” (severity as reported by primary study authors, or ICU requirement, invasive mechanical ventilation, or ARDs): OR 2.51 (2.2-2.87) . n=21381, 97 studies. I ² = 32%. High certainty evidence according to GRADE. Estimated absolute risks: 13.2% increase severe COVID-19 disease. Between 11% more and 15.5% more	↑↑
Javanmardi 2020	NR		No comparison. 26% (21-31%) of diabetes in those dying with COVID-19.		NR	
Jindal 2022	NR		OR 3.7 (95% CI 2.6, 5.28) , I ² =62.6%, 10 studies	↑↑	NR	
Kaminska 2021	NR		OR 2.39 (95%CI 1.65, 3.64) , I ² =62%, 14 studies	↑↑	Severe disease OR 1.43 (95% CI 0.82, 2.5) , I ² =85%, 6 studies	↑
Kandil 2021	NR		OR 1.87 (95%CI 1.51, 2.31) , I ² =77.9%, 15 studies	↑↑		
Khan 2020	NR		Not calculated for diabetes specifically. For all immune and metabolic disorders (OR = 2.46, 95% CI = 2.03-2.85)		NR	

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
Kumar 2020 (1)**	NR		Presence of diabetes was found to be significantly associated with mortality due to COVID-19 (pooled odds ratio 1.90 [95% CI: 1.37-2.64; p<0.01]). Heterogeneity among the studies was low (I ² =32%). 9 studies, total n not reported.	↑↑	Severity of disease: 24 studies. Endpoints: Pre-defined criteria (16 studies); ICU requirement versus no requirement (2 studies); invasive ventilation requirement versus no requirement (2 studies); progressive disease versus stable disease (2 studies); refractory disease versus responsive disease (1 study); and ARDS versus no ARDS (1 study). Presence of diabetes was found to be significantly associated with severe COVID-19 (pooled odds ratio 2.75[95% CI: 2.09-3.62; p<0.01]) Heterogeneity - I ² 63%. Total n not provided	↑↑
Kumar 2020 (2)	NR		NR		Composite: 'severe clinical course': (1. requiring ICU care; or 2. developing ARDS, shock, respiratory failure, or those requiring mechanical ventilation; 3. categorized as severe or critical groups according to the diagnostic and treatment guideline for SARS-CoV-2 issued by the National Health Commission of the People's Republic of China (version 3-5); or 4. not surviving.). OR 3.11 (95% CI: 1.99-4.88) . I ² of 48%; 14 studies.	↑↑
Kumar 2021	NR		NR		"Severe/critical disease" RR 2.06 (95% CI 1.52, 2.79) , I ² 76.9%, 19 studies	↑↑
Li 2020 (1)	NR		Non-survivors of COVID-19 were significantly more likely to have diabetes than survivors (24.8%, 95% CI 18.7-32.0 vs. 13.9%, 95 % CI 10.5-18.1, p=0.003)		NR	
Li 2020 (3)	Diabetes accounted for 11.7% of ICU/severe cases, but 4.0% of non-ICU/severe cases		NR		"The result indicated a higher proportion of diabetes in ICU/severe patients but without statistical significance RR = 2.21, 95% CI (0.88, 5.57) . I ² =67%. 5 studies, n=1514	↑

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
Li 2021 (1)	NR		NR		'Severe disease' OR 2.4 (95% CI 1.98, 2.91) , I2 55.6%, 39 studies. "No evidence of publication bias"	↑↑
Li 2021 (2)**	ICU admission diabetes versus non diabetes: OR 2.24 (0.84, 5.95), I2 91%, n not reported, 3 studies	↑	OR 1.25 (95% CI 1.11, 1.4) , I2=16.4%, 11 studies	↑↑	NR	
Liu 2020 (1)	NR		NR		"Increased risk of disease severity": OR 2.61, 95% CI 1.93 to 3.52 , I2=26.7%; 10 studies, n not reported	↑↑
Lu 2020	NR		OR 2.63, 95% CI 1.45, 4.76 . 5 studies, n=2307. I2 NR	↑↑	NR	
Luo 2020**	NR		In-hospital mortality OR 2.09, 95% CI: 1.80-2.42 (do not report total n, studies, or I2 for this analysis as part of larger analysis (124 studies))	↑↑	OR 2.54, 95% CI: 1.89-3.41 (do not report total n, studies, or I2 for this analysis as part of larger analysis (124 studies))	↑↑
Mahumud 2020	NR		NR		Chronic comorbid conditions (e.g., hypertension, diabetes mellitus, cardiovascular disease, respiratory disease, and other chronic diseases) were identified as high risk factors.	
Mantovani 2020	NR		Pre-existing diabetes was significantly associated with a ~three-fold greater risk of in-hospital mortality associated with COVID-19 (n=15 studies included random-effects OR 2.68, 95% CI 2.09-3.44 ; I2=46.7%). Publication bias unlikely	↑↑	Severe disease: Patients with established diabetes had an approximate two-fold greater risk of severe/critical COVID-19 illness compared to their counterparts without diabetes (n=22 studies included; random-effects odds ratio 2.10, 95%CI 1.71-2.57 ; I2=41.5%). Publication bias judged unlikely	↑↑
Mehraeen 2020	NR		OR 1.34; 95% CI: 1.10–1.64 (114 studies, 310,494 participants, I2 NR)	↑↑	NR	
Meng 2021	NR		NR		"Patients with diabetes (pooled positive likelihood 2.82, 95% CI: 1.95, 4.1) exhibited increased probability of progressing to severe illness."	↑↑

First author/Year	ICU admission and direction of effect	Mortality and direction of effect	Other measures of severity ⁵ and direction of effect
Mesas 2020**	NR	OR 2.12 (1.79, 2.52)), p value <0.001 and I2 77.9. 38 studies, n=25498	↑↑ NR
Miller 2020	NR	We subsequently undertook a meta-regression analysis to identify possible sources of study-to-study variability in this [mortality] rate. Among the demographics, risk factors, and symptoms, the only variable that statistically significantly influenced the mortality rate was the prevalence of DM, where each 1% increase in DM prevalence was associated with a 1.5% absolute increase in the mortality rate (P<.001)	NR
Mirjalli 2021	NR	OR 5.49 (95%CI 4.48, 6.71) , I2=0%, 8 studies	↑↑ NR
Mishra 2021	NR	OR 1.9 (95%CI 1.5, 2.42) , I2=0%, 13 studies, 4110 patients	↑↑ 'Severe disease' OR 2.07 (95%CI 1.44, 2.97) , I2=39.5%, 13 studies, 2762 patients
Moula 2020	NR	Patients with diabetes had 1.59-fold higher chance of dying than patients without diabetes (RR: 1.59 [95% CI: 1.25, 2.02] , p < 0.0001; 28 studies, total n not reported, I2 not reported)	↑↑ NR
Mudatsir 2020**	NR	NR	OR 2.10; 95% CI: 1.33, 3.34 (severity not defined). 17 studies, n=3120, I2=63%
Nandy 2020	NR	Patients with diabetes mellitus had a higher risk of mortality than non-diabetic patients (OR 2.28 95 CI 1.40 to 5.55) (p = 0.004).	↑↑ NR
Ng 2021	NR	HR 1.94 (95% CI, 1.54 to 2.46)	↑↑ NR
Ng 2022**	NR	OR 2.16 (95% CI 1.97–2.36) , 40 studies, 18,979 patients, 3,791 with DM	↑↑ NR

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
Noor 2020	NR		The prevalence of mortality among COVID-19 patients with diabetes was 49%. Pooled risk ratio 1.87 (1.23–2.84) , test for overall affect 2.03, p value <0.001	↑↑	NR	
Pal 2020	NR		The in-hospital mortality rate was 45% in PWD		NR	
Palaiodimos 2020	NR		In our meta-analysis of 14 studies, we found that patients with diabetes were associated with a higher risk of death compared with patients without diabetes, but with significant heterogeneity (OR 1.65; 95% CI 1.35–1.96 ; I ² =77.4%). Possible presence of publication bias	↑↑	NR	
Parohan 2020	NR		OR 2.41, 95% CIs 1.05–5.51 , I ² 93.6%,	↑↑	NR	
Parveen 2020	2 studies, 179 patients, 49 ICU admissions OR: 0.78; 95% CI: 0.06–9.34; p = 0.842; I²: 75.9% with substantial heterogeneity	↓	Odds of survival: 2 studies, 465 patients, 167 deaths. The pooled estimate (OR: 0.56; 95% CI: 0.35–0.90 ; p = 0.017; I ² :0.0%) suggested that diabetes was significantly lower in the survivors	↑↑	3 studies, 1374 patients, 271 severe (defined as having respiratory distress, RR>30 beats/minute in a resting state, a mean oxygen saturation of <93%, and an arterial blood oxygen partial pressure (PaO ₂)/oxygen concentration (FiO ₂) <300 mmHg) The pooled estimate of two cohort studies and one case-series suggested significant association between diabetes and severity (OR: 1.66; 95% CI: 1.20–2.30 ; p = 0.002; I ² : 0.0%)	↑↑
Patel 2020 (2)	NR		Meta-regression model: Mortality odds ratio 1.02 (0.94–1.11) -age adjusted for diabetes	↑	Diabetes was not found to be associated with need for invasive mechanical ventilation (IMV)	
Pinedo-Torres 2020**	ICU admission, 1 study, N=138, prevalence 57.97% (95% CI 25.36 -111.03)		Death, 2 studies, N=716, prevalence 96.33% (95% CI 61.36 -137.66), I ² 0%		NR	

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
Plasencia-Urizarri 2020**	NR		NR		Severe clinical presentations: OR: 3.53; 95 % CI: 2.79-4.47. 13 studies, n not reported. I2=59%	↑↑
Poly 2021 (2)	NR		RR 1.19 (95% CI 1.07–1.32)	↑↑	NR	
Qui 2020	NR		The pooled prevalence of diabetes in COVID-19 death patients was estimated to be 22.2% (95% CI 19.30 ~ 25.10%). The heterogeneity of the study was low (I2 = 28.4%, P = 0.1519)		NR	
Radwan 2020	NR		NR		“Severity” (intensive care unit (ICU) admission, mechanical ventilation and death): OR=2.46, 95%CI=1.53-3.96 , 7 studies, n=1885, I2=31%	↑↑
Rahman 2021 (2)	NR		NR		“Diabetes is significantly associated with an increased severity of COVID-19 (RR = 1.57, 95% CI 1.25 to 1.98).”	↑↑
Rico-Martin 2021	NR		OR 1.57 (95% CI 1.08-2.29)	↑↑	NR	
Rod 2020	NR		NR		No synthesis, but diabetes identified as one of main predictors of COVID-19 severity	
Roncon 2020	PWD had a significant increased risk of ICU admission (OR: 2.79, 95 % CI 1.85–4.22 , p < 0.0001, I2= 46 %), 4 studies, 240/1380	↑↑	PWD had higher mortality risk (OR 3.21, 95 % CI 1.82–5.64 , p < 0.0001, I2= 16 %), 4 studies 214/354	↑↑	NR	
Sacks 2020	Narrative only, cites mixed evidence of increased risk		Narrative only, cites consistent evidence of increased risk		NR	
Saha 2021	NR		“The weighted prevalence of mortality was 1.82-time higher in DM (20.0 %, 95 % CI: 15.0–26.0; I2, 96.8 %) than non-DM (11.0 %, 95 % CI: 6.0–16.0; I2, 99.32 %) hospitalized COVID-19	↑↑	NR	

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
			patients: ES 0.20 (0.15, 0.26). An adjusted meta-regression model including sample size and COVID-19 severity as predictors depicted a 452% (p = 0.014) increased risk of mortality in DM patients with severe COVID-19 infection compared to the reference group"			
Sahni 2021	NR		NR		The risk of critical or fatal COVID-19 infection was significantly increased with diabetes: OR: 2.27, 95% CI: 1.87–2.74	↑↑
Sahu 2021					Diabetes was associated with significantly increased risk of severe disease (OR: 2.29, 95% CI: 1.56–3.39)	↑↑
Saleh 2021	NR		"The SRR for death in patients with COVID-19 was 1.54 (95% CI 1.44 to 1.64, I2=92%, n=145, low certainty) for diabetes compared with patients without"	↑↑	NR	
Sayed 2020	NR		China observational report (1023 deaths/4462 confirmed cases) overall CFR 2.3%, CRF in people with diabetes 7.3%; USA 1122 patients in 88 hospitals, 38.5% had either DM or uncontrolled hyperglycaemia had "a more than 4 times higher mortality rate compared to no diabetes/hyperglycaemia"		NR	
Sepandi 2020	NR		Type 2 OR: 2.42(1.06-5.52) , 9 studies, I2=90%. Number of participants NS.	↑↑	NR	
Shang 2020			28 studies. COVID-19 patients with DM had higher mortality rate compared with those non-diabetic patients (28.5 vs. 13.3%, p<0.01).	↑↑	COVID-19 patients with DM had higher severe infection rate compared with those non-diabetic patients (21.4 vs.10.6%, p<0.01). DM was found to be associated with a	↑↑

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
			COVID-19 patients with DM had a higher risk of death (pooled OR 2.21, 95% CI: 1.83-2.66 , $p<0.001$; $I^2=50\%$, $p<0.01$). No evidence of publication bias.		significantly greater risk of severe COVID-19 infection (pooled OR 2.38, 95% CI: 2.05-2.78 , $p<0.001$; $I^2=39\%$, $p<0.01$), 54 studies. No evidence of publication bias.	
Shoar 2020	NR		(OR = 1.7, p = 0.03 95% CI 1.04, 2.78), $I^2=47\%$. N studies/participants not reported for this analysis, 12 studies (n=3257) included overall	↑	NR	
Shresthra 2021	NR		Mortality rate "16.03% among known DM patients (CI: 10.95-22.88, $I^2=54.35$)"		"The occurrence of adverse events among COVID-19 cases was 15.29% occurrence among non-diabetic patients (CI: 9.06-24.65, $I^2=84.47$); 20.69% among known DM patients (CI: 8.12-43.50, $I^2=90.14$), and 45.85% among those with new-onset DM (CI: 22.23-71.50, $I^2=94.21$)"	
Silviero 2021	NR		Diabetes associated with in hospital mortality; coefficient: 1.02; 95% CI 1.01–1.05 ; $p = 0.043$	↑↑	NR	
Singh 2020 (1)	NR		No new analyses; cites existing studies finding increased risk		NR	
Singh 2020 (2)**	NR		Estimated pooled RR of mortality from COVID-19 if you have a comorbidity compared to if you do not. RR 1.83 95%CI 0.89,3.73 p -value 0.100, 2 studies, total n not stated, $I^2=0\%$	↑	RR 2.11 [1.40, 3.19] , 7 studies (total n not stated), $I^2=84.6\%$, possible publication bias detected	↑↑
Singh 2020 (3)	NR		Increased risk of mortality in patients with comorbidities however this is a literature review with no pooled effect data		NR	
Ssentongo 2020**	NR		Risk of mortality in PWD compared to people without diabetes: RR 1.48 [1.02 to 2.15] , 16 studies, $I^2=84\%$, n not reported	↑↑	NR	

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
Tadic 2020	Narrative only, cites studies finding increased risk of admission to ICU		In most of the studies exists the trend toward higher prevalence of diabetes among non-survivors, but in majority of studies, it did not reach statistical significance due to the small sample size		NR	
Tan 2020**	Prevalence of Diabetes within COVID patients admitted to ICU/HDU: 26.6% (22.7-30.8), I2= 84, P < 0.01		NR		NR	
Taylor 2021	NR		Diabetes associated with significantly increased risk of ICU mortality: OR 1.41 (95%CI 1.22–1.63)	↑↑	NR	
Tian 2020	NR		Of 1103 that died from COVID-19, 31.2% had diabetes. Of 3212 that survived COVID-19, 21.2% had diabetes. OR (95% CI) = 1.97 (1.67-2.31) , p<0.00001. 12 studies. I2 0%	↑↑	NR	
Tisminetsky 2022	NR		“Diabetes was associated with high case fatality rates”	↑	NR	
Treskova-Schwarzbach 2021	NR		Diabetes was associated with a statistically significant increased risk of death (HR 2.0 (95% CI 1.15–3.5))	↑↑	NR	
Vardavas 2022	OR 1.138 (0.816–1.585) ; no further information provided	↑	Diabetes was associated with significantly increased risk of mortality in the hospital setting: OR 1.395 (95% CI 1.204–1.617) ; high certainty evidence. There was no significant effect in ICU settings: OR 0.989 (95% CI 0.704–1.39) low certainty evidence; or in community settings: OR 1.363 (95% CI 0.871–2.131)	↑↑	(Composite outcome) “Diabetes was estimated to significantly increase the risk for ICU admission or death in the community setting (OR 1.374 (95%CI 1.235-1.528)); moderate certainty evidence.”	↑↑

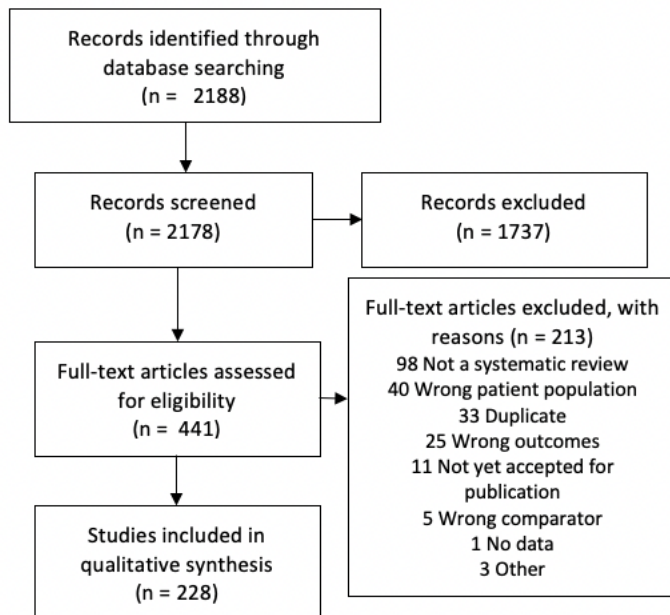
First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
Varikasuvu 2020**	NR		Diabetic proportions were 259/879 and 429/3292 in mortal and survival groups of COVID-19...diabetes related significantly with COVID-19 disease mortality (OR = 2.52, 95% CI = 1.93–3.30 , Z = 6.79, p < 0.00001, I2 = 31%, p = 0.08) 22 studies	↑↑	The diabetic proportions were 750/2894 and 931/6203 in severe and non-severe groups of COVID-19 cases... diabetes related significantly with COVID-19 disease severity (OR=2.20, 95% CI=1.69–2.86 , Z = 5.82, p < 0.00001, I2 = 58%, p < 0.0001) Severe not defined. 35 studies	↑↑
Wang 2020 (2)**	NR		NR		1558 patients with COVID-19 in 6 studies Risk of exacerbation: OR 2.47, 95% CI 1.67 to 3.66 , I2=39	↑↑
Wingert 2021	Reported only that it was 'uncertain' if diabetes increased risk of ICU admission		Reported "moderate association" between diabetes and COVID-19 mortality, with RR/OR ranging from 1.71 to 1.99	↑	Assert "low certainty" of association between diabetes and "severe disease or mechanical ventilation"	
Wu 2020	NR		OR 1.75 (95% CI 1.31–2.36 ; P = 0.0002). 6 studies, n=1471, I2=5%	↑↑	NR	
Wu 2021	NR		Diabetes was associated with significantly increased risk of mortality: OR 2.14 (95% CI 1.76-2.60 , I2=37%, p<0.00001)	↑↑	NR	
Xiang 2021	NR		Diabetes was associated with significantly increased risk of mortality: OR 1.63 (95% CI 1.44-1.84 , I2=29.1%)	↑↑	NR	
Xie 2021	NR		NR		"Diabetes was significantly associated with increased severity of COVID-19 outcomes: OR 2.46 [95% CI 1.77, 3.40] <0.00001"	↑↑
Xu 2020	NR		NR		Narrative only, states PWD more likely to develop severe COVID-19	
Yanai 2020	NR		NR		Metabolic syndrome and its components are significantly as-sociated with the susceptibility to SARS-CoV-2 infection and severity of COVID-19.	

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
Yang 2020	NR		NR		Diabetes in “severe” versus “non-severe” group: OR 2.07, 95% CI 0.89 to 4.82 . 4 studies, total n not reported, I2 = 62%	↑
Yin 2021 (1)	NR		NR		Note “the poor prognosis of COVID-19 in patients with diabetes is associated with severe illness, ICU treatment, death, and other adverse outcomes”	
Yin 2021 (2)	NR		NR		Diabetes was found to significantly increase the ‘risk of disease exacerbation’: (OR = 2.49, 95% CI 2.10– 2.96)	↑↑
Zaki 2020	NR		NR		Diabetes, hypertension, and cholesterol levels possess an apparent relation to COVID-19 severity	
Zhao 2020 (1)	NR		NR		NR	
Zhao 2020 (2)	(RR=1.26; 95% CI=0.11 to 14.42 ; P=0.85 I2=80%) 2 studies, n=179	↑	NR		NR	
Zheng 2020	NR		NR		Diabetes incidence significantly higher in “critical/mortal” patients compared to “non-critical” OR 3.68, 95% CI 2.68 to 5.03 . 11 studies, I2=45%, total n 2579	↑↑
Zheng-Hong 2021	NR		Results showed a close relationship between diabetes and mortality of COVID-19, with a pooled OR of 1.75 (95% CI 1.31–2.36; P=0.0002)	↑↑	NR	
Zhou 2020 (1)	NR		The death group had significantly higher proportions of patients with diabetes (OR=2.51, 95% CI: 1.86-3.35, P<0.001 I2=87.32%).	↑↑	NR	
Zhou 2020 (2)**	4 studies recorded ICU admission (a sample of 6652 patients, 1138 (17.1%) of whom were	↑↑	5 studies compared the rates of comorbidities in survivors versus non-survivors, with a sample of 3436 patients, 1624 (47.3%) of whom died.	↑↑	NR	

First author/Year	ICU admission and direction of effect		Mortality and direction of effect		Other measures of severity ⁵ and direction of effect	
	classified as admitted to the ICU). Regarding diabetes, OR (95% CI), 2.98 (1.49, 5.98) , p=0.002 I ² =48.		In subgroup analysis based on severe clinical outcomes associated with COVID-19, 4 studies used for diabetes (n not reported). OR (95% CI), 2.08 (1.38, 3.15) , P=0.001 I ² =0.0%, Ph=0.728			

Figures

Figure 1. PRISMA diagram of study flow



Appendix 1. Search strategies

MEDLINE	
1	exp Coronavirus/
2	exp Coronavirus Infections/
3	(coronavirus* or corona virus* or OC43 or NL63 or 229E or HKU1 or HCoV* or ncov* or covid* or sars-cov* or sarscov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus*).mp.
4	((pneumonia or covid* or coronavirus* or corona virus* or ncov* or 2019-ncov or sars*).mp. or exp pneumonia/) and Wuhan.mp.
5	(2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV on nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19) and pandemic*2) or (coronavirus* and pneumonia)).mp.
6	COVID-19.rx,px,ox. or severe acute respiratory syndrome coronavirus 2.os.
7	1 or 2 or 3 or 4 or 5 or 6
8	exp Diabetes Mellitus/ or Metabolic Diseases/
9	(diabet* or t2d or t1d or niddm or iddm or metabolic disease).ti,ab,kw.
10	8 or 9
11	7 and 10
12	limit 11 to yr="2019 -Current"
13	limit 11 to ("systematic review" or "reviews (maximizes specificity)")
14	((systematic or evidence) adj3 review) or rapid review or overview).ti.
15	12 and 14
16	13 or 15

EMBASE	
1	exp Coronavirus/
2	exp Coronavirus Infections/
3	(coronavirus* or corona virus* or OC43 or NL63 or 229E or HKU1 or HCoV* or ncov* or covid* or sars-cov* or sarscov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus*).mp.
4	((pneumonia or covid* or coronavirus* or corona virus* or ncov* or 2019-ncov or sars*).mp. or exp pneumonia/) and Wuhan.mp.
5	(2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV on nCoV or covid or coronavirus* or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19) and pandemic*2) or (coronavirus* and pneumonia)).mp.
6	1 or 2 or 3 or 4 or 5
7	exp *Diabetes Mellitus/ or Metabolic Disease/
8	(diabet* or t2d or t1d or niddm or iddm or metabolic disease*).ti,ab,kw.
9	7 or 8

10	6 and 9
11	limit 10 to yr="2019 -Current"
12	limit 11 to (meta analysis or "systematic review" or "reviews (maximizes specificity)")

OTHER DATABASES	
Terms	Database
Diabetes AND "systematic Review"	LitCOVID
diabetes AND "rapid review"	LitCOVID
diabetes AND "literature review"	LitCOVID
diabetes AND meta-analysis	LitCOVID
(coronavirus OR COVID-19) AND diabetes - limited to Systematic Reviews and Evidence-based Synopses	TRIP
(covid-19 OR coronavirus) AND diabetes AND ("systematic review" OR "rapid review" OR "literature review" OR meta-analysis)	Google Scholar
48 of 1st 100 results included	

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