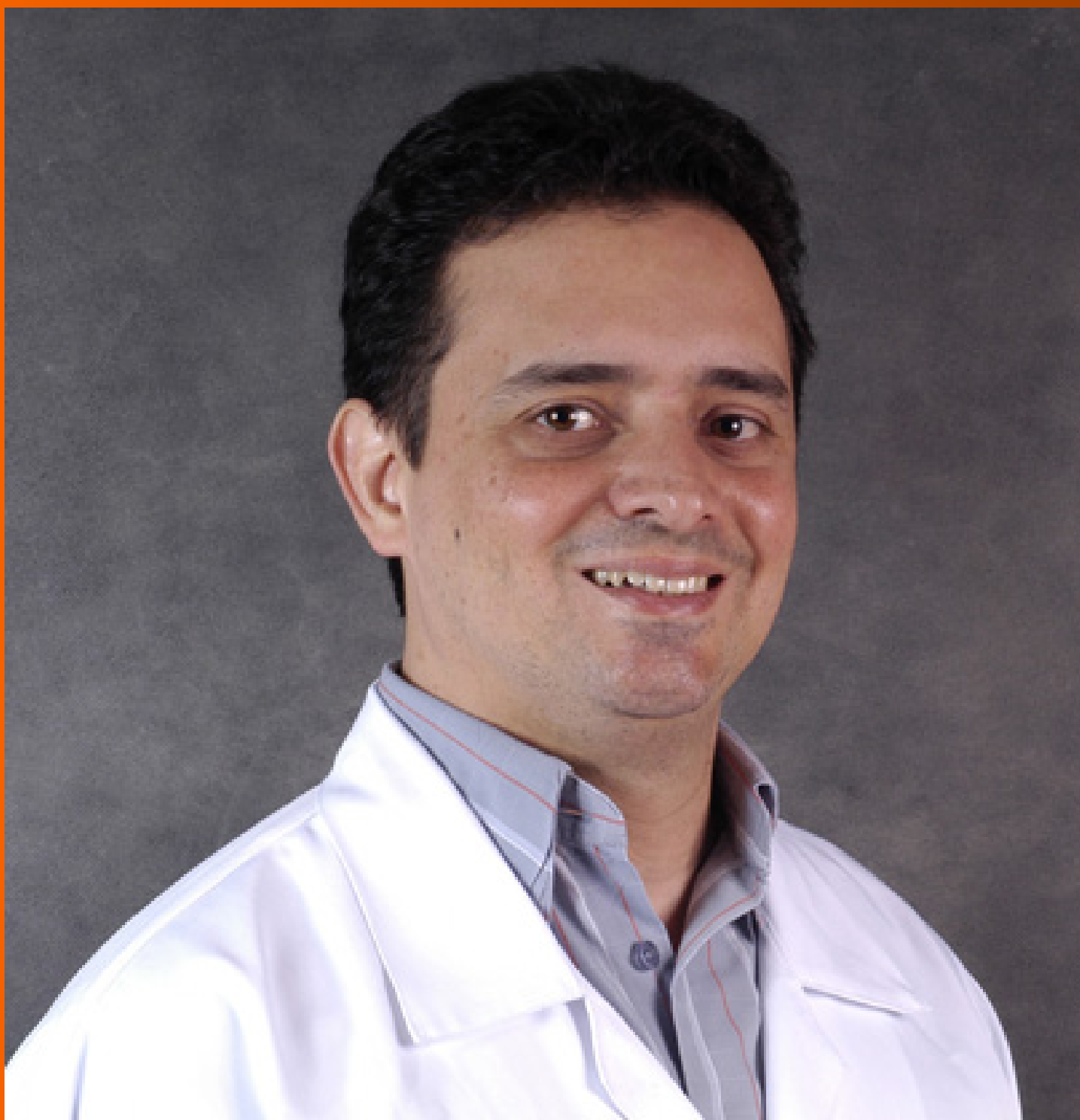


# World Journal of *Diabetes*

*World J Diabetes* 2020 October 15; 11(10): 400-480



**REVIEW**

- 400 Type 1 diabetes mellitus and its oral tolerance therapy  
*Mao RF, Chen YY, Zhang J, Chang X, Wang YF*

**ORIGINAL ARTICLE****Case Control Study**

- 416 Importance of serum phosphate in elderly patients with diabetes mellitus  
*Raikou VD, Kyriaki D, Gavril S*

**Retrospective Cohort Study**

- 425 Association between restrictive pulmonary disease and type 2 diabetes in Koreans: A cross-sectional study  
*Lee DY, Nam SM*
- 435 Comparison of clinical features and outcomes in peritoneal dialysis-associated peritonitis patients with and without diabetes: A multicenter retrospective cohort study  
*Meng LF, Yang LM, Zhu XY, Zhang XX, Li XY, Zhao J, Liu SC, Zhuang XH, Luo P, Cui WP*

**Retrospective Study**

- 447 Risk of anemia in morbidly obese patients after bariatric surgery in Taiwan  
*Wang TY, Huang HH, Hsieh MS, Chen CY*

**SYSTEMATIC REVIEWS**

- 459 Impact of technology use in type 2 diabetes distress: A systematic review  
*Vieira P, Kobayasi R, Pereira F, Zaia IM, Sasaki SU*

**META-ANALYSIS**

- 468 Prevalence and impact of diabetes in patients with COVID-19 in China  
*Du M, Lin YX, Yan WX, Tao LY, Liu M, Liu J*

**ABOUT COVER**

Editorial board member of *World Journal of Diabetes*, Dr. José Carnevalheira is an Associate Professor at the Campinas State University (UNICAMP, Brazil). Having received his Bachelor's degree from Pernambuco University College of Medicine in 1994, Dr. Carnevalheira undertook his postgraduate training at UNICAMP, receiving his PhD in 2004. He became Chief Physician in the Clinical Oncology Division of the Hospital de Clínicas Affiliated to UNICAMP in 2014 and has held the position since. His ongoing research interests involve investigation of how body composition, energy homeostasis, and the underlying mechanisms of whole-body metabolism are linked to cancer survival outcomes. In particular, his studies aim to elucidate the regulatory role of insulin resistance and its attendant pathophysiological features in determination of cancer-mediated disturbances in systemic homeostasis and cancer prognosis. (L-Editor: Filipodia)

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WJD mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, etc..

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## Prevalence and impact of diabetes in patients with COVID-19 in China

Min Du, Yu-Xin Lin, Wen-Xin Yan, Li-Yuan Tao, Min Liu, Jue Liu

**ORCID number:** Min Du 0000-0002-9958-7686; Yu-Xin Lin 0000-0002-4509-7657; Wen-Xin Yan 0000-0003-2725-9840; Li-Yuan Tao 0000-0003-3497-1326; Min Liu 0000-0002-5059-3743; Jue Liu 0000-0002-1938-9365.

**Author contributions:** Liu J conceived and designed the study; Du M and Yan WX carried out the literature searches; Du M, Yan WX, and Lin YX extracted the data; Du M, Lin YX, and Yan WX assessed the study quality; Du M performed the statistical analysis; Du M and Liu J wrote the manuscript; Liu J, Du M, Liu Min, and Tao LY revised the manuscript.

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**Min Du, Yu-Xin Lin, Wen-Xin Yan, Min Liu, Jue Liu,** Department of Epidemiology and Biostatistics, School of Public Health, Peking University, Beijing 100191, China

**Li-Yuan Tao,** Research Center of Clinical Epidemiology, Peking University Third Hospital, Beijing 100083, China

**Corresponding author:** Jue Liu, PhD, Associate Professor, Department of Epidemiology and Biostatistics, School of Public Health, Peking University, No. 38 Xueyuan Road, Haidian District, Beijing 100191, China. [jueliu@bjmu.edu.cn](mailto:jueliu@bjmu.edu.cn)

### Abstract

#### BACKGROUND

Coronavirus disease 2019 (COVID-19) is an emerging infectious disease that has spread rapidly around the world. Previous studies have indicated that COVID-19 patients with diabetes are prone to having poor clinical outcomes.

#### AIM

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.

#### METHODS

We searched studies published in PubMed, Web of Science, and EMBASE from December 1, 2019 to March 31, 2020 to identify relevant observational study that investigated the prevalence of diabetes among COVID-19 patients or its impact on clinical outcomes. We used a random-effects or fixed-effects model to estimate the pooled prevalence of diabetes and risk ratio (RR) and its 95% confidence interval (CI) of diabetes on outcomes. Funnel plots were used to evaluate the publication bias and the heterogeneity was evaluated by  $I^2$  statistic.

#### RESULTS

Twenty-three eligible articles including 49564 COVID-19 patients (1573 with and 47991 without diabetes) were finally included. The pooled prevalence of diabetes was 10% (95%CI: 7%-15%) in COVID-19 patients. In the subgroup analyses, the pooled prevalence of diabetes was higher in studies with patients aged > 50 years (13%; 95%CI: 11%-16%) than in studies with patients aged ≤ 50 years (7%; 95%CI: 6%-8%), 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%) ( $P < 0.05$  for all). Compared with patients without

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diabetes, the risk of severe cases was higher (RR = 2.13, 95%CI: 1.76-2.56,  $I^2 = 49\%$ ) in COVID-19 patients with diabetes. The risk of death was also higher in COVID-19 patients with diabetes (RR = 3.16, 95%CI: 2.64-3.78,  $I^2 = 34\%$ ). However, diabetes was not found to be significantly associated with admission to ICU (RR = 1.16, 95%CI: 0.15-9.11).

## CONCLUSION

Nearly one in ten COVID-19 patients have diabetes in China. Diabetes is associated with a higher risk of severe illness and death. The present study suggested that targeted early intervention is needed in COVID-19 patients with diabetes.

**Key Words:** Diabetes; COVID-19; Systematic review; Meta-analysis

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**Core Tip:** At present, the prevalence and impact of diabetes in patients with coronavirus disease 2019 (COVID-19) have not been systematically reviewed in China. This meta-analysis for the first time focused on the pooled prevalence of diabetes among COVID-19 patients and its impact on clinical outcomes (ICU admission, severity, and death) in China. The analysis showed that the pooled prevalence of diabetes was 10% [95% confidence interval (CI): 7%-15%] in COVID-19 patients. Besides, the risks of severe cases (risk ratio = 2.13, 95%CI: 1.76-2.56,  $I^2 = 49\%$ ,  $P = 0.007$ ) and deaths (risk ratio = 3.16, 95%CI: 2.64-3.78,  $I^2 = 34\%$ ,  $P = 0.20$ ) were both higher in COVID-19 patients with diabetes compared with those without. Our findings highlight the need for targeted intervention on diabetes among COVID-19 patients.

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## INTRODUCTION

In December 2019, some pneumonia cases of unknown cause were reported in Wuhan, Hubei Province, China, and deep sequencing analysis from lower respiratory tract samples indicated a novel coronavirus that caused coronavirus disease 2019 (COVID-19)<sup>[1]</sup>. As of April 12, 2020, there were 1696588 confirmed cases of COVID-19 in the world, with 105952 deaths, according to the World Health Organization. Previous studies have reported that patients with poor immune function, such as the elderly or patients with chronic diseases, may develop severity or even death, such as diabetes and cardiovascular diseases<sup>[2,3]</sup>. Guo *et al*<sup>[4]</sup> reported that diabetes patients with COVID-19 were prone to have severe pneumonia, releasing tissue damage-related enzymes, excessively uncontrolled inflammation, and hypercoagulable states associated with abnormal glucose metabolism<sup>[4]</sup>. Similarly, COVID-19 is not conducive to blood glucose control in diabetic patients. Zhou and Tan<sup>[5]</sup> monitored the blood glucose of 26 diabetic COVID-19 patients and found that 56.6% showed abnormal blood glucose levels, 69.0% were considered to have a poor blood glucose level, and 10.3% have experienced hypoglycemia at least once<sup>[5]</sup>.

As a chronic illness, diabetes is characterized by elevated levels of blood glucose, and accompanied by disturbed metabolism of fats and proteins<sup>[6]</sup>. Several studies reported the prevalence of diabetes among COVID-19 patients. In China, Shi *et al*<sup>[7]</sup> discovered that the comorbidity rate of diabetes was 5.95% in Zhengzhou, while it was 7.23% in the study by Lian *et al*<sup>[8]</sup>. Huang *et al*<sup>[9]</sup> found that the prevalence of diabetes in Wuhan was 11.8%, while Chen *et al*<sup>[10]</sup> reported the rate at 14%. Bhatraju *et al*<sup>[11]</sup> found that prevalence of diabetes among COVID-19 patients was 58% in the United States. It was reported that the prevalence of diabetes was about three-fold higher in intensive care unit (ICU) cases than in non-ICU cases<sup>[12]</sup>. The results on the prevalence of diabetes varied across different studies.

Although epidemiological data on COVID-19 infection are growing, the prevalence

and impact of diabetes in COVID-19 patients have not been systematically reviewed at the country level. Thus, we conducted a systematic review and meta-analysis to assess the prevalence of diabetes among COVID-19 patients in China and identify its impact on clinical outcomes.

## MATERIALS AND METHODS

According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement, we performed this systematic review and meta-analysis<sup>[13]</sup>.

### Data sources and search strategy

The literature was searched independently by two investigators (Du M and Yan WX), which was published online from December 1, 2019 to March 31, 2020, from three databases including PubMed, Web of Science, and EMBASE using the following search term: ("novel coronavirus", "2019-nCoV", "coronavirus disease 2019", "COVID-19", or "SARS-CoV-2") and "diabetes". There was no limitation to language or region. Moreover, we also searched highly relevant reference articles by reviewing the list of references. To exclude duplicates, EndNote X 9.0 software was used to manage the records.

### Inclusion and exclusion criteria

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. The exclusion criteria were as follows: (1) The subjects of the study were irrelevant (animal experiments, pathological researches, or molecular researches); (2) Reviews, editorials, or case reports; (3) Overlapped studies. The latest one was selected if studies overlapped; (4) Studies that were not conducted in China; (5) Duplicated studies; and (6) Key information could not be extracted, for example the prevalence of diabetes.

Two investigators (Lin YX and Yan WX) independently identified the studies, based on the inclusion and exclusion criteria. When discrepancies occurred, they were solved by consensus or decided by a third investigators (DM).

### Data extraction and study quality assessment

The primary outcomes were prevalence of diabetes among COVID-19 patients and its impact on clinical outcomes (admission to ICU, severe cases, and death). In view of the piloted forms, the information which was extracted independently by two investigators (Du M and Yan WX) from the selected studies included three main parts: (1) Basic information of the studies comprising first author, publication year, survey time, study design, and journal; (2) Characteristics of the study population including sample size, location, median/mean age, gender ratio; and (3) Primary outcomes including the numbers of patients with diabetes and non-diabetes in the total COVID-19 patients and in different subgroups (ICU patients *vs* non-ICU patients, severe *vs* non-severe patients, and dead patients *vs* survivors). The methodological quality of the included studies was evaluated by using the tool developed by Hoy and colleagues<sup>[14]</sup>, which had been used in other meta-analyses for pooled prevalence<sup>[15]</sup>. To generate an overall quality score that ranged from 0 to 10, we assigned each item a score of 1 (yes) or 0 (no), and summed scores across items. Then, according to the overall scores, the methodological quality of studies was classified into three levels: Low ( $> 8$ ), moderate (6–8), or high ( $\leq 5$ ) risk of bias<sup>[14]</sup>. The study quality was independently assessed by two investigators (Du M and Lin YX), and disagreements were resolved by consensus.

### Data synthesis and statistical analysis

In order to get an overall summary estimate of diabetes prevalence across studies, a meta-analysis was used to summarize prevalence data and a random-effects or fixed-effects model was used to pool the study-specific estimates. We used the  $I^2$  statistic to assess the magnitude of heterogeneity, with 25%, 50%, and 75% heterogeneity representing low, moderate, and high degrees of heterogeneity, respectively<sup>[16]</sup>. According to the analysis results, the proper effect model was selected: If  $I^2 \leq 50\%$ , the fixed-effects model was used, otherwise the random-effects model was used.

If substantial heterogeneity was detected, to investigate the possible sources of heterogeneity, subgroup analysis was performed by using the following grouping variables: Sample size, location, age, admission to ICU or not, severe cases or not, and death or not. Subgroup comparisons were made using the  $Q$  test. A  $P$  value less than



0.05 was considered to indicate a significant difference between subgroups. We performed sensitivity analysis by deleting the lowest quality score of study and by using a different model (fixed-effect or random-effect model). The risk ratio (RR) and the corresponding 95% confidence interval (CI) were calculated to quantify the impact of diabetes on clinical outcomes (ICU *vs* non-ICU patients, severe *vs* non-severe patients, and dead patients *vs* survivors), and a *P* value < 0.05 was deemed significant. We used forest plots to describe the pooled rate of diabetes and the risk ratio of diabetes to related outcomes. To assess publication bias, we used funnel plots and Egger's publication bias test. We analyzed data using R version 3.5.3 and Stata version 16.0.

## RESULTS

### Study selection and study characteristics

One hundred and ninety articles were searched totally, of which 64 reported duplicate results. After skimming the title and abstracts, we excluded 101 reviews, guidelines, or irrelevant studies. After reading the full articles, six articles that provided insufficient information were excluded. Four articles from other sources were included. As a result, 23 eligible articles were included in the meta-analysis<sup>[1,3,4,7-9,17-34]</sup>. Figure 1 shows the flow chart of study selection.

The total sample size of the included studies was 49564, with the number of subjects in each study varying from 18 to 44672. Baseline characteristics are shown in Table 1.

### Pooled prevalence of diabetes and subgroup analysis

Among the 23 studies included, the rate of diabetes varied widely from 2.47% to 22.22%. The pooled prevalence of diabetes was 10% (7%-15%) among 49564 COVID-19 patients from 23 studies (Figure 2). For the subgroup analyses, the pooled prevalence of diabetes was higher in studies on patients with a median age > 50 years (13%; 95%CI: 11%-16%) than in those on patients with a median age ≤ 50 years (7%; 95%CI: 6%-8%), 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%, Table 2).

### Impact of diabetes on clinical outcomes

Compared with patients without diabetes, the risks of severe cases (RR = 2.13, 95%CI: 1.76-2.56; *I*<sup>2</sup> = 49%) and deaths (RR = 3.16, 95%CI: 2.64-3.78, *I*<sup>2</sup> = 34%) were both higher in COVID-19 patients with diabetes (Figure 3B and C). However, there was no relationship between diabetes and admission to ICU (RR = 1.16, 95%CI: 0.15-9.11; Figure 3A).

In the sensitivity analysis, we found the pooled results of meta-analysis had no difference between the fixed-effects model and random-effects model or when deleting the study with the lowest quality score, which showed that the results of pooled diabetes prevalence and RRs were stable. Both funnel plots (Figure 4B and C) and Egger's tests showed publication bias on the pooled prevalence of diabetes (*P* < 0.001; Figure 5) and the association of diabetes and ICU admission (*P* < 0.05; Figure 4A), while showed no evidence of publication bias on the association of diabetes and severe cases (*t* = -1.36, *P* = 0.23) or death (*t* = 0.03, *P* = 0.98).

## DISCUSSION

Diabetes is an important public health problem. Uncontrolled diabetes could lead to complications in many organs, resulting in loss of vision and kidney function, heart attacks, strokes, and lower limb amputations which cause disability and death<sup>[6]</sup>. Previous studies reported that the presence of comorbidities in severe acute respiratory syndrome patients increased the risk of death by nearly two-fold<sup>[31]</sup>. Yuan *et al*<sup>[31]</sup> found that the incidence of comorbidities in the death group was significantly higher than that of the survival group (80% *vs* 29%, *P* = 0.018), especially for comorbid diabetes, hypertension, and heart disease<sup>[31]</sup>. Some studies suggested that chronic diseases such as hypertension and diabetes might be important risk factors for poor prognosis in patients with COVID-19<sup>[36]</sup>. In this systematic review and meta-analysis, we included 23 studies related to COVID-19 cases and diabetes. Our results showed that the prevalence of diabetes in COVID-19 cases was 10%. The pooled prevalence of

**Table 1** Baseline characteristics of the 23 included studies

Ref.	Survey period	Sample size	Location	Age (mean or median)	Sex (male, %)	Prevalence of diabetes (%)	Quality score
Chen <i>et al</i> <sup>[17]</sup>	2020.1.1-2020.1.20	99	Wuhan China	55.5	67.68	12.12	7
Huang <i>et al</i> <sup>[1]</sup>	2019.12.16-2020.1.2	41	Wuhan China	49.0	73.17	19.51	7
Liu <i>et al</i> <sup>[18]</sup>	2019.12.30-2020.1.24	137	Wuhan China	57	44.53	10.22	7
Wang <i>et al</i> <sup>[19]</sup>	2020.1-2020.1.31	138	Wuhan China	56	54.35	10.14	7
Zhang <i>et al</i> <sup>[20]</sup>	2020.1.06-2020.2.3	140	Wuhan China	57	50.71	12.14	7
Chen <i>et al</i> <sup>[21]</sup>	2019.1-2020.2	150	Wuhan China	59	56.00	13.33	5
Guan <i>et al</i> <sup>[22]</sup>	2020.12.11-1.31	1590	China	48.9	56.86	8.18	9
Guo <i>et al</i> <sup>[23]</sup>	2020.1.23-2020.2.23	187	Wuhan China	58.5	48.66	14.97	7
Guo <i>et al</i> <sup>[4]</sup>	2020.2.10-2020.2.29	174	Wuhan China	59	43.68	21.26	6
Huang <i>et al</i> <sup>[9]</sup>	2019.12.21-2020.1.28	34	Wuhan China	56.24	41.18	11.76	4
China CDC <sup>[24]</sup>	As of 2020.2.11	44672	China	-	51.44	2.47	6
Lian <i>et al</i> <sup>[8]</sup>	2020.1.17-2020.2.12	788	Zhejiang China	45.8	51.65	7.23	7
Shi <i>et al</i> <sup>[7]</sup>	As of 2020.2.17	487	Zhejiang China	46	53.18	5.95	3
Li <i>et al</i> <sup>[25]</sup>	2020.1.18-2020.2.7	78	Zhuhai China	44.6	48.72	5.13	5
Liu <i>et al</i> <sup>[3]</sup>	2020.1.15-2020.2.18	56	Hainan China	53.75	55.36	7.14	6
Wan <i>et al</i> <sup>[26]</sup>	2020.1.23-2020.2.28	135	Chongqing China	47	53.33	8.89	5
Wang <i>et al</i> <sup>[27]</sup>	2020.1.21-2020.2.5	18	Zhengzhou China	39	55.56	16.67	5
Wu <i>et al</i> <sup>[28]</sup>	2019.12.25-2020.1.26	201	Wuhan China	51	63.68	10.95	7
Xu <i>et al</i> <sup>[29]</sup>	2020.1.23-2020.2.4	90	Guangzhou China	50	43.33	5.56	6
Yuan <i>et al</i> <sup>[30]</sup>	2020.1.11-2020.2.4	94	Shenzhen China	40	44.68	5.32	6
Yuan <i>et al</i> <sup>[31]</sup>	2020.1.1-2020.1.25	27	Wuhan China	60	44.44	22.22	5
Zhao <i>et al</i> <sup>[32]</sup>	2020.1.23-2020.1.31	37	Wuhan China	41	37.84	10.81	6
Zhou <i>et al</i> <sup>[33]</sup>	2019.12.29-2020.1.31	191	Wuhan China	56	62.30	18.85	7

One study<sup>[34]</sup> only reporting information on severe patients is not shown in the table. CDC: Centers for disease control.

diabetes in COVID-19 cases in our study (10%) was slightly higher than the estimation in the general population (8.5%)<sup>[6]</sup>. Li *et al*<sup>[12]</sup> found that the prevalence of diabetes is about 9.7% in COVID-19 cases by meta-analysis including five studies<sup>[12]</sup>, which was similar to our findings. Yang *et al*<sup>[37]</sup> found that the prevalence of diabetes is about 9% by a meta-analysis that include eight studies. The differences between these studies might be related to the number of studies included, sample size, and characteristics of the included patients.

We found that diabetes was associated with severe illness (RR = 2.13, 95%CI: 1.76, 2.56) and death (RR = 3.16, 95%CI: 2.64-3.78). A meta-analysis by Li *et al*<sup>[12]</sup> reported that the prevalence of diabetes in ICU patients was not significantly higher than that in non-ICU patients (RR = 2.21, 95%CI: 0.88, 5.57)<sup>[12]</sup>. Yang *et al*<sup>[37]</sup> found that the



Table 2 Pooled prevalence of diabetes among coronavirus disease 2019 patients in China

Item	Number of studies	Sample size	Diabetes	Prevalence(95%CI, %)	P	P values	
						Heterogeneity	Subgroup difference
Overall	23	49564	1573	10 (7-15)	97%	< 0.01	-
Subgroup analysis							
Sample size							0.002
≤ 100	10	574	55	9 (6-11)	28%	0.14	
100-200	8	1252	178	14 (11-16)	60%	0.02	
> 200	5	49588	1340	7 (4-9)	94%	< 0.0001	
Location							< 0.0001
Wuhan, China	13	1556	222	14 (12-16)	35%	0.12	
Outside of Wuhan, China	8	1746	119	7 (6-8)	0%	0.79	
China (all cities)	2	46262	1432	5 (0-11)	99%	< 0.0001	
Age group							< 0.0001
≤ 50 yr	10	3358	257	7 (6-8)	10%	0.27	
> 50 yr	12	1534	214	13 (11-16)	45%	0.05	
ICU admission							0.94
ICU	2	112	20	15 (4-26)	47%	0.17	
Non-ICU	2	1519	118	14 (3-35)	78%	0.03	
Severity							< 0.0001
Severe	8	553	99	17 (14-20)	0%	0.92	
Non-severe	7	2190	143	6 (5-8)	41%	0.05	
Death							0.02
Death	5	1146	120	30 (13-46)	89%	< 0.0001	
Survival	5	45508	1191	8 (2-15)	99%	< 0.0001	

ICU: Intensive care unit.

proportion of diabetic patients between severe and non-severe patients had no significant difference by meta-analysis<sup>[37]</sup>. These two meta-analyses described the prevalence of diabetes among COVID-19 patients with limited studies (less than 10 studies) included in the analysis. Huang *et al*<sup>[38]</sup> reported that diabetes was associated with severe illness (RR = 2.45, 95%CI: 1.79-3.35) in a meta-analysis of 30 studies, which was similar to our findings<sup>[38]</sup>. It should be noted that, the pooled prevalence of diabetes was 30% (95%CI: 12%-51%) in the dead patients, which was much higher than 8% (95%CI: 3%-14%) in the survivors in our study. Pooled RR for the association between diabetes and death was 3.16 (95%CI: 2.64-3.78), which was similar to the study of Kumar *et al*<sup>[39]</sup>, who did a meta-analysis of 33 case-control studies to examine the association between diabetes and mortality in COVID-19 patients. They found that diabetes was significantly associated with mortality of COVID-19 (RR = 1.90, 95%CI: 1.37-2.64)<sup>[39]</sup>. The findings indicated that the risk of death among COVID-19 patients with diabetes should be paid more attention.

Diabetes and susceptibility of the body have certain physiological mechanisms. Because of the accumulation of activated innate immune cells in metabolic tissues, the inflammatory mediators such as IL-1 $\beta$  and TNF- $\alpha$  are released, which accelerates  $\beta$ -cell damage and systemic insulin resistance. Conversely, metabolic problems may further impair the immunologic function of macrophages and lymphocytes, which makes the individual easy to develop other complications<sup>[40]</sup>. Recently, it was found that the proportion of CD3<sup>+</sup> or CD4<sup>+</sup> T cells and the absolute count of CD3<sup>+</sup>, CD4<sup>+</sup>, or CD8<sup>+</sup> T cells in the death group were significantly higher than those in the survival group by analyzing the clinical data of viral pneumonia patients retrospectively, and the death group had higher levels of different inflammatory factors compared to the survival

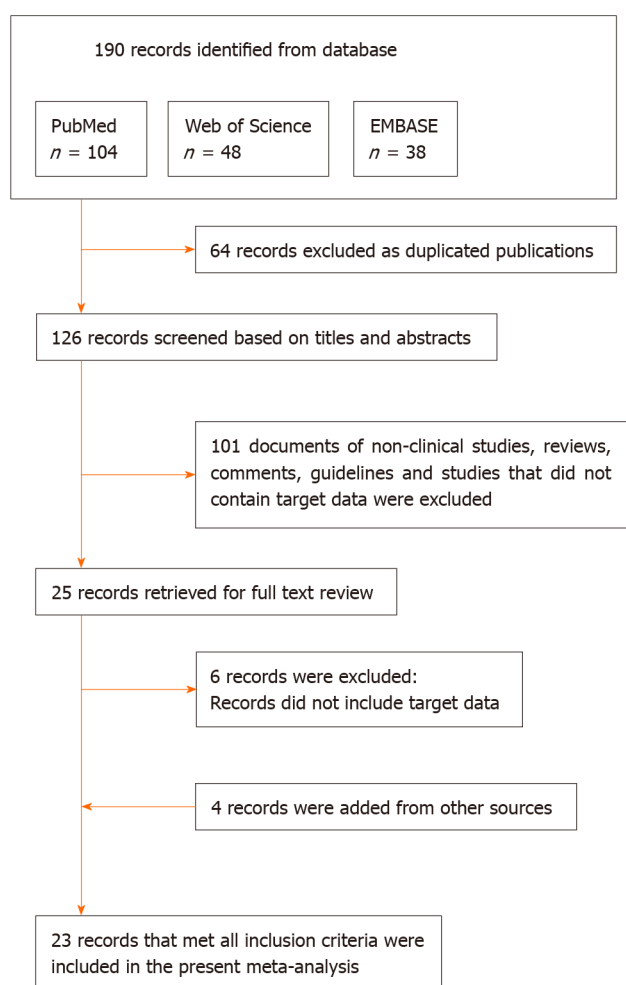


Figure 1 Flow diagram of the study selection process.

group<sup>[17]</sup>. Huang *et al*<sup>[1]</sup> also found that the plasma concentrations of inflammatory factors (such as IL-2, IL-7, and IL-10) in ICU patients with COVID-19 were higher than those of the non-ICU COVID-19 patients<sup>[1]</sup>. Studies have found that coronaviruses (including SARS-CoV and SARS-CoV-2) can bind to target cells because of angiotensin-converting enzyme 2 (ACE2), which may promote the proliferation of SARS-CoV-2 and enhance its ability to infect<sup>[41]</sup>. ACE inhibitors and type I angiotensin II receptor blockers (ARBs) that are used in patients with type 1 or type 2 diabetes can result in a significant increase in ACE2<sup>[41,42]</sup>. Besides ACE2, dipeptidyl peptidase-4 (DPP4) was also found to be a coronavirus receptor protein<sup>[43]</sup>. DPP4 inhibitors, one of the glucose-lowering agents, are widely used in treatment of diabetes and known to modify the biological activities of multiple immunomodulatory substrates<sup>[44]</sup>. The potential role of DPP4 inhibition in preventing SARS-CoV-2 infection and progression needs to be clarified in the future<sup>[44]</sup>. Previous studies found that ACE2 and DPP4 were established transducers of metabolic signals and pathways regulating inflammation and glucose homeostasis<sup>[43]</sup>. Guo *et al*<sup>[45]</sup> analyzed the biochemical indicators of diabetic and non-diabetic patients in new coronavirus cases and found that compared with non-diabetic patients, the levels of serum inflammation-related biomarkers, including IL-6, C-reactive protein, serum ferritin, and D-dimer increased significantly in diabetic patients ( $P < 0.01$ ), suggesting that patients with diabetes might have a worse prognosis<sup>[45]</sup>. Diabetes may not be related to the risk of COVID-19 infection, but it could deteriorate clinical outcome of COVID-19 patients<sup>[46]</sup>.

This study has some limitations. First, publication bias might exist in this meta-analysis. Second, due to the limitation of sample size and short study periods, limited studies had completed follow-up of the COVID-19 patients and reported the results of its impact on clinical outcomes.

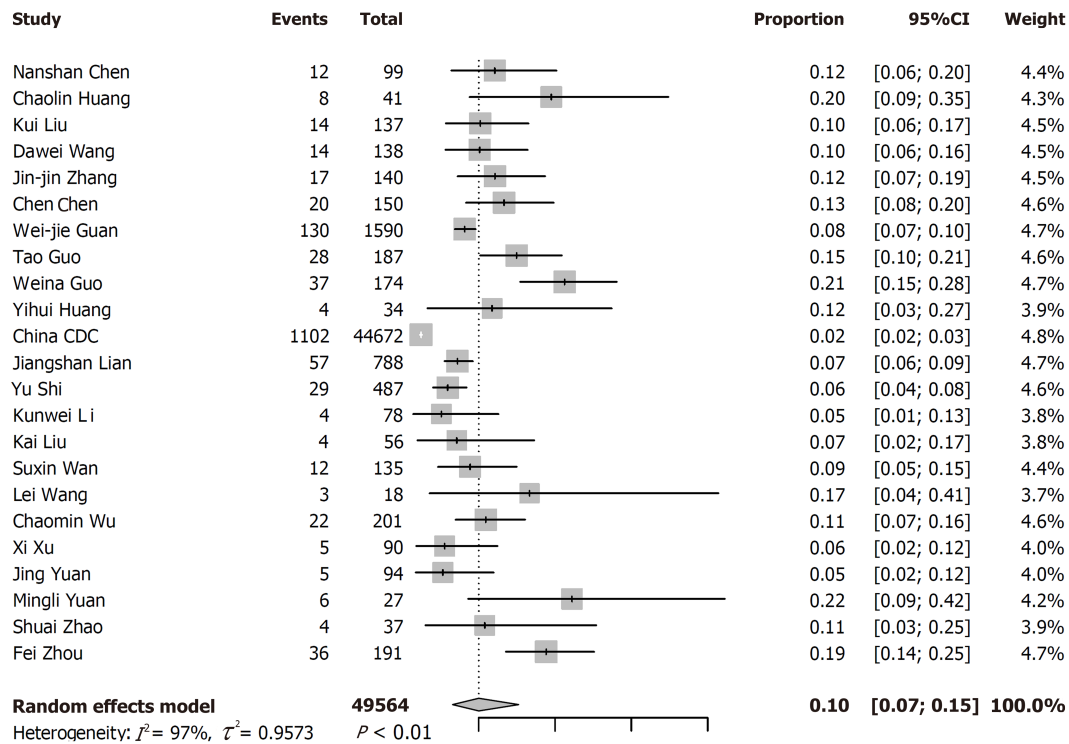
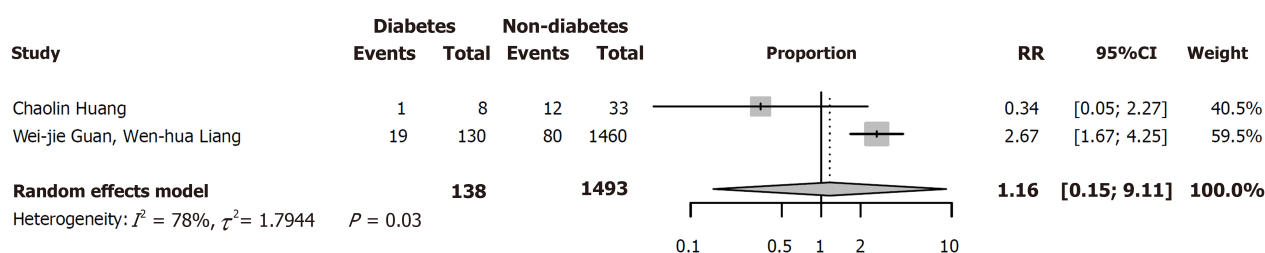
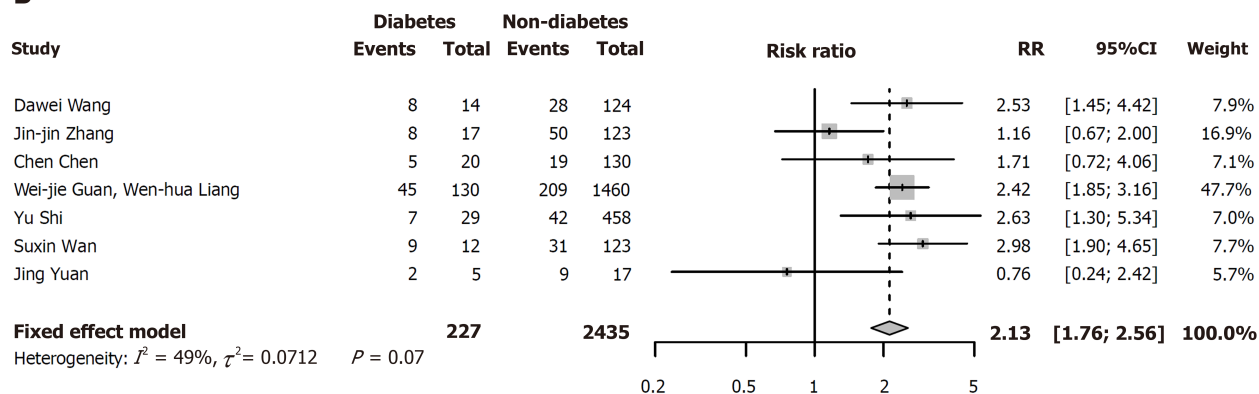
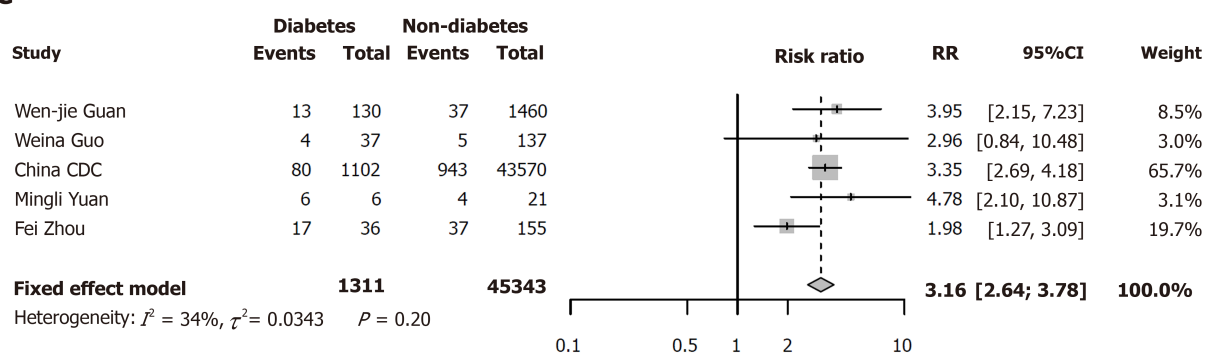


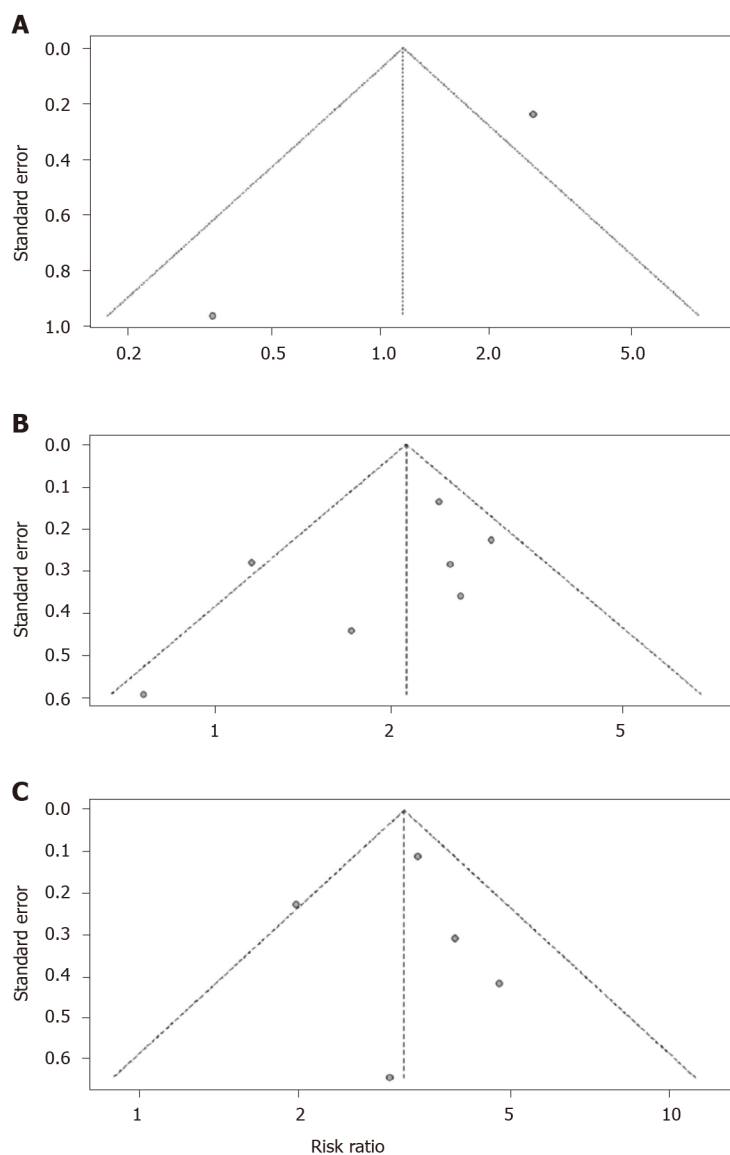
Figure 2 Meta-analysis for the prevalence of diabetes in coronavirus disease 2019 cases in China.

## CONCLUSION

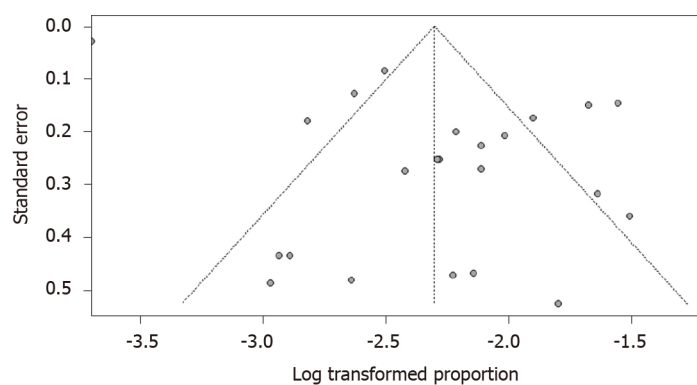
This study indicated that nearly one in ten COVID-19 patients have diabetes and diabetes increases the risk of severe illness and death. Targeted public health measures should be carried out timely to make the protection of patients with diabetes from COVID-19 and other respiratory infections even better. More adequate and vigorous research should be conducted to prove the associations found in this study.

**A****B****C**

**Figure 3 Forest plots for impact of diabetes on clinical outcomes.** A: Intensive care unit vs non-intensive care unit; B: Severe vs non-severe; C: Death vs survival. RR: Risk ratio; CI: Confidence interval.



**Figure 4** Funnel plots for impact of diabetes on clinical outcomes. A: Intensive care unit vs non-intensive care unit; B: Severe vs non-severe; and C: Death vs survival.



**Figure 5** Funnel plot for the prevalence of diabetes in coronavirus disease 2019 cases.

## ARTICLE HIGHLIGHTS

**Research background**

Coronavirus disease 2019 (COVID-19) has spread around the world rapidly. The prevalence of diabetes varies across different studies. Previous studies showed that COVID-19 patients with diabetes were prone to having poor clinical outcomes. However, a systematical review of the prevalence of diabetes in COVID-19 patients and the impact of diabetes on clinical outcomes has not been done in China.

**Research motivation**

We hypothesized that the presence of diabetes is associated with a poor prognosis. To our knowledge, this is the first meta-analysis which focused on evaluating the prevalence of diabetes among patients with COVID-19 infection in China and its impact on clinical outcomes.

**Research objectives**

The aim of this study was 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.

**Research methods**

A systematic review and meta-analysis of observational studies were performed.

**Research results**

Twenty-three eligible articles including 49564 COVID-19 patients (1573 with and 47991 without diabetes) were included. The pooled prevalence of diabetes was 10% [95% confidence interval (CI): 7%-15%] in COVID-19 patients. In the subgroup analyses, the pooled prevalence of diabetes was higher in studies on patients with a median age > 50 years (13%; 95%CI: 11%-16%) than studies on patients with a median age ≤ 50 years (7%; 95%CI: 6%-8%), 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%, all  $P < 0.05$ ). Compared with patients without diabetes, the risks of severe cases [risk ratio (RR) = 2.13, 95%CI: 1.76-2.56,  $I^2 = 49\%$ ] and death (RR = 3.16, 95%CI: 2.64-3.78,  $I^2 = 34\%$ ) were both higher in COVID-19 patients with diabetes. However, diabetes was not found to be significantly associated with admission to ICU (RR = 1.16, 95%CI: 0.15-9.11).

**Research conclusions**

Nearly one in ten COVID-19 patients have diabetes in China. Diabetes is associated with a higher risk of severe illness and death. The present study suggested that targeted early intervention is needed in COVID-19 patients with diabetes.

**Research perspectives**

A systematic review and meta-analysis of observational studies which summarizes the evidence on this topic is meaningful. More adequate and vigorous research should be conducted to prove the associations found in this study.

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