# The impact of the COVID-19 pandemic and associated disruptions in health-care provision on clinical outcomes in people with diabetes: a systematic review

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For the **study protocol** see https://osf.io/hevpj/

**The COVID-19 pandemic triggered disruptions to health care and lifestyles that could conceivably impact diabetes management. We set out to identify the impact of disruptions caused by COVID-19 on clinical outcomes in people with diabetes. We performed a systematic review of the available literature in the MEDLINE and OVID databases from Jan 1, 2020, to June 7, 2023, and included 138 studies (n>1 000 000 people). All but five studies were judged to be at some risk of bias. All studies compared prepandemic with pandemic periods. All-cause mortality (six studies) and diabetes-related mortality (13 studies) showed consistent increases, and most studies indicated increases in sight loss (six studies). In adult and mixed samples, data generally suggested no difference in diabetic ketoacidosis frequency or severity, whereas in children and adolescents most studies showed increases with some due to new-onset diabetes (69 studies). Data suggested decreases in hospital admissions in adults but increases in diabetes-related admissions to paediatric intensive care units (35 studies). Data were equivocal on diabetic foot ulcer presentations (nine studies), emergency department admissions (nine studies), and overall amputation rates (20 studies). No studies investigated renal failure. Where reported, the impact was most pronounced for females, younger people, and racial and ethnic minority groups. Further studies are needed to investigate the longer-term impact of the pandemic and the on potential differential impacts, which risk further exacerbating existing inequalities within people with diabetes.**

## Introduction

Diabetes is a well documented risk factor for COVID-19 severity and mortality.[1] However, there is limited research on the indirect impacts of the COVID-19 pandemic and associated prevention measures (lockdowns, social distancing, and closure or limitation of certain industries, including those related to health-care delivery, food access, and exercise) on clinical outcomes in people with diabetes. During the pandemic, routine diabetes care was influenced by various factors including: limited or altered health-care provision due to infection prevention measures; staff shortages due to staff time off for illness and reallocation of resources; patient concerns about visiting health-care sites due to infection risk; and the impacts of the pandemic on disease self-management,[2] nutritional habits, physical activity,[3] and mental health.[4]

Limited health-care access during the pandemic could cause a delayed surge in health-care use post pandemic due to inadequate disease management and prevention, with serious health and economic implications. This phenomenon has been documented during previous natural disasters, which impacted management of diabetes complications including diabetic foot,[5] diabetic retinopathy,[6] and diabetic ketoacidosis.[7]

To our knowledge, there is no comprehensive systematic review of the evidence relating to the impact of COVID-19-related disruptions on clinical outcomes in people with diabetes. Investigating this impact is vital to ensure that any negative consequences are minimised, and to inform responses to future pandemics or natural disasters. We aimed to synthesise and describe the current body of evidence relating to disruptions caused by COVID-19 on clinical outcomes in people with diabetes, both in those with pre-existing diabetes and in those presenting with diabetes for the first time during the pandemic.

## Methods

This systematic review was commissioned by WHO and WHO member states to address key questions and provide high-quality, evidence-informed information regarding COVID-19 and diabetes. A protocol was preregistered on Open Science Framework.

### Search strategy and selection criteria

We searched two electronic databases (MEDLINE and OVID) on June 7, 2023, for articles published between Jan 1, 2020, and June 7, 2023, combining terms related to diabetes (eg, diabetes, diabetic), SARS-CoV-2 (eg, COVID, coronavirus), and clinical outcomes (eg, mortality, hospital admission), published in any language. We also screened reference lists of included studies. Results were screened in duplicate using Covidence with disagreements resolved via discussion or referral to a third reviewer.

Our inclusion criteria were defined using the PICOS (Population, Exposure, Comparator, and Outcomes) framework. For population, we included people diagnosed with any type of diabetes (not including prediabetes), with no limitations by age, disease severity, or duration. Our exposure of interest was COVID-19-associated prevention measures, often described by authors as the pandemic period, excluding studies that only measured the direct impact of COVID-19 infection, compared with prepandemic or postpandemic periods as defined by authors. We were interested in studies

| | NOS | Country | Effect direction | Supporting data |
|---|---|---|---|---|
| Bello-Chavolla and colleagues[19] | 4 | Mexico | ↑ | 148 437 diabetes-related deaths (177 per 100 000 inhabitants) in 2020 compared with an average of 101 496 deaths in 2017–2019 (125 per 100 000 inhabitants), a 41·6% increase. |
| Hernandez-Vasquez and colleagues[20] | 3 | Peru | ↑ | 92% increase in the average number of monthly deaths in people admitted to hospital with type 2 diabetes as cause for admission. |
| Kleibert and colleagues[21] | 4 | Poland | ↑ | Increase in percentage of patients who died during hospitalisation for diabetic foot ulcers (from 3·9% to 4·8%, p=0·03). |
| Laliotis and colleagues[22] | 6 | UK | ↑ | Using national registry data, an excess 4108 deaths due to diabetes are estimated during 2020 compared with before the pandemic. |
| Lee and colleagues[23] | 7 | USA | ↑ | Using US Centers for Disease Control and Prevention data to model mortality, it is reported that deaths from diabetes increased during compared with before the pandemic; an estimated 24 700 excess deaths were attributable to diabetes due to the indirect impacts of the pandemic (95% prediction interval 15 900–33 300). |
| Lozano-Corona and colleagues[24] | 4 | Mexico | ↑ | Increase (not statistically significant) in percentage of patients who died during hospitalisation due to diabetic foot (13% *vs* 12%). |
| Lv 2022[24] | 4 | USA | ↑ | Increase of more than 30% during the pandemic, from 106·8 per 100 000 persons in 2019 to 144·1 in 2020 and 148·3 in 2021, using data from 4 243 254 US adults. |
| McCoy and colleagues[14] | 4 | USA | ↑ | Deaths with diabetes as primary cause increased (incident rate ratio 1·08, 95% CI 1·01–1·15; not statistically significant after adjusting for multiple comparisons), data from 20 054 people in Minnesota with diabetes. |
| Raknes and colleagues[26] | 4 | Norway | ↑ | Using national data, death rates were higher than predicted for diabetes mellitus (4·1%, 95% CI 2·1–3·4). |
| Sekowski and colleagues[27] | 8 | Poland | ↑ | Compared with 2019, the in-hospital mortality rate in 2020 increased by 66·7% among patients hospitalised with type 1 diabetes and by 48·5% among patients hospitalised with type 2 diabetes. |
| Silverio-Murillo and colleagues[28] | 5 | Mexico | ↑ | Using state mortality records, a 36·8% increase in diabetes-related mortality was reported during the pandemic (2020) compared with prepandemic (2019; p<0·001). |
| Todd and colleagues[29] | 6 | USA | ↑ | Using Pennsylvania mortality data, an estimated 41% more deaths than expected due to diabetes were reported during compared with before the pandemic (the authors state that diabetes was one of the top three greatest proportional increases in non-COVID-19 causes of death during the pandemic). |
| Yao and colleagues[30] | 7 | USA | ↑ | Excess mortality was modelled based on national data, giving the estimates that from March, 2020, to March, 2022, deaths that had diabetes as one of multiple causes of death were 47·6% higher than expected and those with diabetes as an underlying cause of death were 18·4% higher than expected. |

NOS=Newcastle-Ottawa Scale.

***Table 1:*** **Diabetes-related mortality during versus before the COVID-19 pandemic**

reporting the following outcomes where they were not solely attributable to COVID-19 infection: mortality; hospital admissions; diabetic ketoacidosis; amputations; sight loss; emergency admissions; foot ulcer presentations; severe hypoglycaemic events; and renal failure.

We excluded letters, editorials, case series, and case reports but otherwise did not restrict studies based on their design, language, or geographical location. We included systematic reviews meeting the above criteria.

## Data extraction and analysis

One reviewer appraised and extracted data on study design, study setting, sample characteristics, time periods of interest, analysis methods, outcome measures, and results; a second (PH or JH-B) checked them. Discrepancies were resolved through discussion. We relied on the outcome measures reported by primary studies, and did not attempt to recategorise outcomes. This means there is overlap between some of the outcomes in our review. For example, where a study reported diabetes-related hospital admissions and did not break this down further (eg, by type, such as diabetic ketoacidosis), it was included in the diabetes-related hospital admissions outcome. If a study reported hospitalisations for diabetic ketoacidosis but not overall diabetes-related hospital admissions, it was included in the diabetic ketoacidosis section. If it reported both, it was included in diabetes-related hospital admissions (admissions including but not limited to diabetic ketoacidosis) and in the diabetic ketoacidosis outcome (including diabetic ketoacidosis admissions only).

## Critical appraisal

Primary studies were appraised using the Newcastle-Ottawa Scale (NOS).[8] Systematic reviews were assessed using the A Measurement Tool to Assess Systematic Reviews (AMSTAR) 2 checklist.[9] Studies were not excluded based on appraisal outcomes.

## Data synthesis

Heterogeneity in study design and outcomes precluded meta-analysis. Data were narratively synthesised by clinical outcome, with effect direction plots used where more than six studies contributed data to an outcome, in accordance with Synthesis Without Meta-analysis guidance[10] and the Cochrane Handbook.[11,12] Based on this guidance, we judged effect direction based on point estimates (where available) rather than on statistical significance. Where point estimates were not available but some other indication of direction of effect was given (eg, absolute numbers or narrative description), we used this to inform our categorisation. Where results were described as not statistically significant, and no other

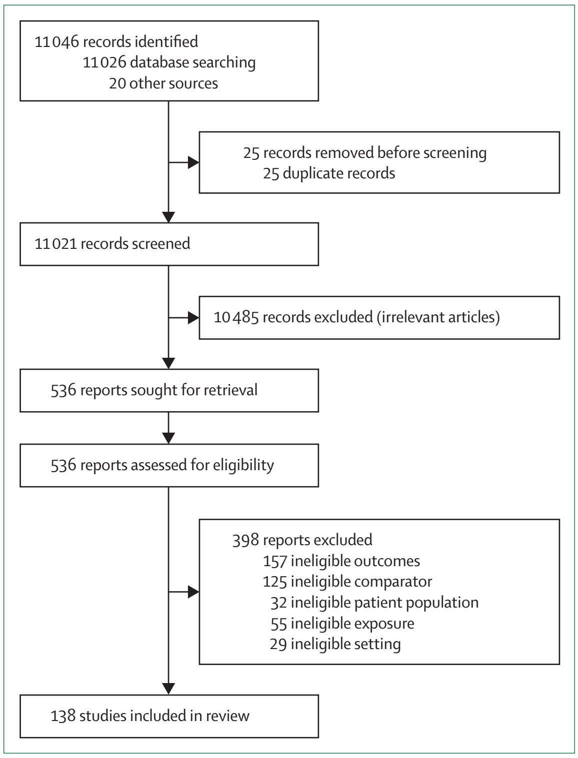


***Figure 1:*** **PRISMA 2020 flow diagram**
Records are of new systematic reviews that included searches of databases and registers only.

information was provided with which to judge an effect direction, we categorised this as no difference and note the absence of further information in table 1. Systematic review findings were narratively synthesised alongside data on each outcome.

### Role of the funding source

WHO approved the review protocol and our decision to submit for publication. NIHR had no role in study design, analysis, interpretation, writing, or the decision to submit for publication.

## Results

### Included studies

We screened 11 021 records, 20 of which were identified through screening reference lists of included studies, and the remainder through database searching. The most common reasons for exclusion at full text stage were that studies did not report on any of our outcomes of interest, or did not compare to prepandemic or postpandemic periods. We included 138 publications (133 primary studies and five systematic reviews; figure 1). The appendix (pp 1–24) contains key characteristics of the primary studies, including NOS scores (range 2–8). Of the 133 primary studies, 58 had NOS scores lower than 5; only five had NOS scores of 8, indicating they were not judged to be at any risk of bias. The appendix (p 25) contains key characteristics of five the included systematic reviews, including AMSTAR 2 scores (range 9–13). All reviews were judged to have two or three critical weaknesses.

See Online for appendix

54 studies were conducted exclusively in people with type 1 diabetes, and four exclusively in people with type 2 diabetes. The remainder were conducted in mixed populations or did not specify diabetes type.

Studies were conducted in North America (39 studies), Western Europe (39 studies), Asia (17 studies), Eastern Europe (14 studies), South America (four studies), Egypt (one study), and Australia (one study). The remainder incorporated multiple regions.

All studies compared prepandemic with pandemic periods. Of the 138 included studies, the following outcomes were covered: all-cause (six studies) and diabetes-related (13 studies) mortality; all-cause (five studies) and diabetes-related (30 studies) hospital admissions; diabetes-related emergency hospital visits (nine studies); diabetic ketoacidosis (69 studies); severe hypoglycaemia (four studies); amputations (20 studies); foot ulcer incidence (nine studies); and sight loss (six studies). No studies reported data on renal failure. Findings are summarised by outcome and effect direction in figure 2.

### All-cause mortality in people with diabetes

Out of the six studies that examined all-cause mortality, all but one found increases during the pandemic. Only one study[13] (NOS 7) excluded COVID-19 deaths from analysis. This study used data from the National Diabetes Audit in England comparing the period July 3–Oct 15, 2021 (n=3 218 570) with the equivalent 15-week period in 2019 (n=2 973 645), and found an increase in non-COVID-related deaths from 2019 to 2021 of 11% (95% CI 9–13). The unadjusted incidence rate ratio (RR) for 2021 compared with 2019 was 1·026 (95% CI 1·009–1·043); this was unchanged after adjustment for age, sex, ethnicity, socioeconomic deprivation, and diabetes type. Both unadjusted and adjusted mortality rates were higher in those who did not receive eight annual care processes during the pandemic (foot surveillance, urine albumin, BMI, blood pressure, smoking, cholesterol, $HbA_{1c}$, and serum creatine) compared with those who received all eight during the pandemic.[13]

The remaining studies did not exclude deaths from COVID-19 from their analysis; four found increases during compared with before the pandemic. McCoy and colleagues[14] (NOS 4, n=20 054) used registry data from people with diabetes in Minnesota, USA to compare all-cause mortality in 2018–19 with that in 2020, and reported an unadjusted incidence RR of 1·30 (95% CI 1·26–1·33). Torre and colleagues[15] (NOS 5, n not reported) used national statistics from Italy comparing 2020 with 2019 and comparing people with and without diabetes. People with diabetes recorded a two times higher rate of excess mortality in 2020 compared with those without diabetes (20·4% *vs* 10·2%). McAlister and colleagues[16] (NOS 8) conducted a population-based retrospective cohort study in Canada and found that within people with diabetes attending a health-care visit, death rates per 1000 visits were higher during the pandemic (1·4 in 30 days and 5·5 in 90 days following the visit) than in the year before (1·2 in 30 days and 4·5 in 90 days following the visit). Khaydarova and colleagues[17] (NOS 3) reviewed medical records in Uzbekistan and found mortality among people with type 2 diabetes increased compared with prepandemic (4·3% in 2020 *vs* 2·8% in 2019). Lastly, Harun and colleagues[18] (NOS 6) examined deaths (any cause) in people with diabetic foot ulcers in one hospital in Saudi Arabia, and found a non-statistically significant decrease.

## Diabetes-related mortality

13 studies compared diabetes-related mortality during (2020–21) versus before (2006 to February, 2020) the pandemic (table 1). We used data on diabetes-related mortality as reported by the study authors. Definitions were rarely provided therefore the underlying definition might have varied between studies. All studies reporting this measure detected increases during compared with before the pandemic.

Three of these studies also analysed data by subgroups. Lv and colleagues[24] (NOS 4), which used US population-wide data, reported that the relative rise in diabetes-related mortality was most pronounced in younger adults (aged 25–44 years). Older adults showed the smallest difference in mortality between before and during the pandemic. The sharpest rise was found in the Hispanic population, followed by non-Hispanic Black, non-Hispanic Asian, and non-Hispanic Native American and Alaskan, whereas the smallest rise was found in the non-Hispanic White population. The mortality increase among the Hispanic population was nearly three times that in the non-Hispanic White population. Excess rates of diabetes-related mortality were 30% for men and 40% for women.

McCoy and colleagues[14] (NOS 4) found no age-related differences, but found that the proportion of diabetes-related deaths in 2020 in people with diabetes belonging to a racial or ethnic minority group was greater than in the prepandemic period (p<0·001). By contrast, Todd and colleagues[29] (NOS 6) reported that although excess mortality due to other causes varied by ethnicity, it did not appear to do so for diabetes, and that excess mortality was higher in older age groups.

## All-cause hospital admissions in people with diabetes

Five studies provided data on all-cause hospital admissions; three noted a decline and two observed no difference. Via a survey in Italy, Bossi and colleagues[31] (NOS 3) interviewed 947 people with diabetes. Compared with November, 2019, most participants (80%) in November, 2020, indicated their number of hospitalisations that year was unchanged, whereas 6% indicated they had decreased and 13% indicated they had increased. Nowak and colleagues[32] (NOS 4) performed a retrospective evaluation of acute hospitalisations in people with type 1 diabetes aged 15–17 years in a hospital in Poland, and found no statistically significant difference in incidence between the prepandemic (23 patients in 2018–19) and pandemic period (16 patients in 2020–21).

Tehrani and colleagues[33] (NOS 4) also examined hospital admissions in children and adolescents with type 1 diabetes in one clinic in Iran, and noted a statistically significant decline during the pandemic (p=0·005). Yoon and colleagues[34] (NOS 6) used data from a cohort of people with diabetes judged to be at high risk within a Veterans Affairs medical centre in the USA, and reported a mean decrease of 0·23 (95% CI –0·28 to –0·19)

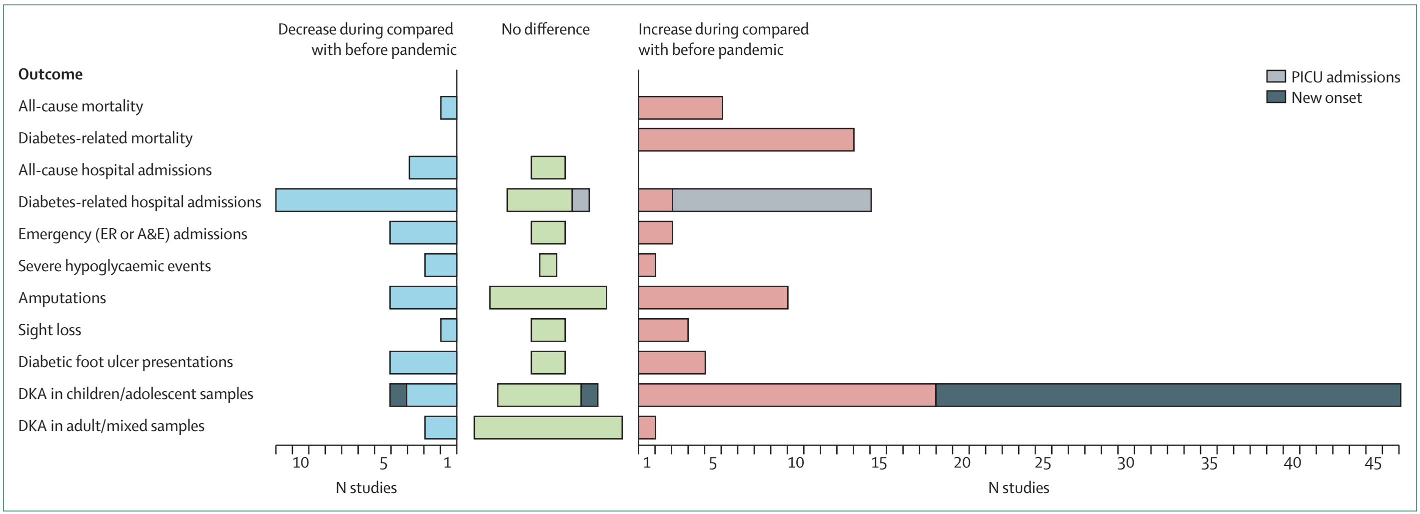


***Figure 2:*** **Number of studies showing increase, decrease, or no difference in outcomes during compared with before the pandemic**
For diabetes-related hospital admissions, cross hatching indicates PICU admissions. For diabetic ketoacidosis in child or adolescent samples, cross hatching indicates new-onset diabetes. A&E=accident and emergency department. ER=emergency room. PICU=paediatric intensive care unit.

in all-cause hospitalisations per patient per quarter in the early-pandemic phase compared with the prepandemic phase. Hammersen and colleagues[35] (NOS 6) used data from a large German registry of people with type 1 diabetes and noted fewer hospitalisations during compared with before the pandemic.

## Diabetes-related hospital admissions

30 studies evaluated diabetes-related hospital admissions (table 2). Findings were mixed, with some showing increases and others showing decreases relative to the prepandemic period. Much of this variation was explained by population and setting, and hence, table 2 is divided into studies in children (where increases were common) and in adults (where most studies showed no difference or an increase).

Three studies analysed trends in diabetes-related hospitalisation by population groups. Loh and colleagues[61] (NOS 6, in children with diabetes) looked at the difference in admissions to hospital due to a new onset or previous diabetes diagnosis between boys and girls aged under 18 years, and reported that in 2020, more girls (62·5%) were admitted to hospital due to diabetes diagnosis (new-onset or already known disease), whereas in 2019, sex was nearly evenly distributed. Moin and colleagues[58] (NOS 6, in mixed samples in hospitals across Ontario) reported no differences in trends based on age, socioeconomic status, sex, or comorbidities. Sekowski and colleagues[27] (NOS 8), using national registry data from adults in Poland, noted an overall decrease in the number of diabetes-related hospitalisations from 2019 to 2020. This decrease was steeper in people with type 2 than type 1 diabetes, in women than in men, in non-insulin-dependent diabetes than in insulin-dependent diabetes, in people with type 1 diabetes aged 20–39 years compared with other age groups, and in people with type 2 diabetes aged 40–49 years or 80 years and older compared with other age groups.

## Emergency admissions in people with diabetes

Findings from the nine studies with data on emergency hospital admissions in people with diabetes during

| | NOS | Country | Effect direction | Supporting data |
|---|---|---|---|---|
| **Children and adolescents** | | | | |
| Breinig and colleagues[36] | 4 | France | ↑ | National database including all children aged 7 days to 18 years admitted in PICU in March–May, 2020, compared with the same period in 2019. Diabetes admissions increased significantly (60%, IRR 2·54 [95% CI 1·30–5·25], p=0·003). |
| Choudhary and colleagues[37] | 4 | USA | ↔ | Children and adolescents with type 1 diabetes seen at least once at the large urban paediatric teaching hospital (or smaller local hospital) during the study period; no change detected from 2019 to 2020. |
| Goldman and colleagues[38] | 5 | Israel | ↑ | Compared data on newly diagnosed young people (aged <18 years) with type 1 diabetes in March–June, 2020 (during lockdown) and the same periods in 2017–2019. ICU admissions were higher in 2020 than in previous years: 34·2% versus 25·7%, 17·6%, and 15·8% (p=0·001). |
| Guemes and colleagues[39] | 6 | Spain | ↑ | During the pandemic, 7 of 10 patients presenting to the emergency department with type 1 diabetes were admitted to the PICU, compared with 0 of 10 in timeframe-matched controls from 2018 and 2019 (p=0·003). |
| Hammersen and colleagues[40] | 4 | Germany | ↓ | Patients with type 1 diabetes younger than 18 years with diabetes duration more than 3 months with visits in 231 centres in 2020; relative risk for hospitalisation was lower compared with the preceding year, most notably in the second lockdown month (risk ratio 0·52 [0·46–0·58], p< 0·001) compared with 2019. |
| Jafari and colleagues[41] | 5 | USA | ↑ | In 175 paediatric patients with type 1 diabetes presenting with diabetic ketoacidosis, the proportion requiring PICU admission increased from 34·2% to 54·6%. |
| Kiral and colleagues[42] | 4 | Türkiye | ↑ | Data from multi-centre PICUs; for 917 children younger than 18 years with type 1 diabetes, PICU stays increased during the pandemic (further data not provided). |
| LahTomulic and colleagues[43] | 4 | Croatia | ↑ | Average number of children with diabetic ketoacidosis admitted to the PICU, 2011–2019 (4·1) and 2020 (11·0). |
| Mameli and colleagues[44] | 6 | Italy | ↑ | In children in Lombardy, Italy with type 1 diabetes, frequency of PICU admission reached its highest value in the first wave (10·0% of new-onset type 1 diabetes) compared with the second wave (8·3%) of 2020, and also compared with the same months of the previous years (7·3% in 2019, 3·7% in 2018, and 6·9% in 2017). |
| McGlacken-Byrne and colleagues[45] | 6 | UK | ↑ | Hospitals from the North Central London Paediatric Diabetes Network: PICU diabetic ketoacidosis admissions were 23·5% during the first COVID- 19 wave compared with 6·7% prepandemic. |
| Miller and colleagues[46] | 7 | USA | ↑ | Retrospective chart review of 132 children with diabetes admitted to two hospitals for diabetes-related causes: 3·08% in 2018, 3·54% in 2019 (p=0·012), 4·73% in 2020 (p=0·077). |
| Pietrzak and colleagues[47] | 4 | Poland | ↑ | Data from regional diabetes centres showed frequency of ICU admissions among type 1 diabetes cases increased between prepandemic and during the pandemic (13·6% *vs* 17·4%, p=0·63), and significantly more children required assisted ventilation (1·3% *vs* 3·4%, p=0·037). |
| Ponmani and colleagues[48] | 5 | UK and Ireland | ↑ | Children aged 6 months to 16 years presenting to 49 emergency departments with diabetic ketoacidosis; observed increases in admissions to intensive care from 38 to 72 (89%) during compared with before the pandemic. |
| Salmi and colleagues[49] | 6 | Finland | ↑ | In one hospital district, incidence of PICU admission due to new-onset type 1 diabetes increased from 2·89 per 100 000 person-years in 2016–2019 to 9·35 per 100 000 person-years in 2020 (IRR 3·24 [1·80–5·83], p<0·001). |
| Zee-Cheng and colleagues[50] | 5 | USA | ↔ | Database from 77 PICUs: prepandemic Q1 1072 (4·6%) cases due to diabetes, during-pandemic Q1 1054 (4·6%); p>0·99. |

(Table 2 continues on next page)

| | NOS | Country | Effect direction | Supporting data |
|---|---|---|---|---|
| (Continued from previous page) | | | | |
| **Adults or mixed samples** | | | | |
| Cassell and colleagues[51] | 4 | USA | Mixed | National health-care billing database. Estimated IRR (ratio of observed and predicted cases per diagnosis per month, with monthly predictions made by using trends in previous years): 0·6–0·9 March–May, 2020; 0·9–1·1 June–Dec, 2020; 0·6–0·9 Jan, 2021; 0·9–1·1 Feb, 2021; 1·1–1·4 March–April, 2021; 0·9–1·1 May–June, 2021. |
| Dayal and colleagues[52] | 5 | India | ↑ | Hospital admissions of new cases of type 1 diabetes during lockdown compared with before: 19 in April, 2019–March, 2020: 4 in April, 2020 (p value not reported). |
| Grudziaz-Sekowska and colleagues[53] | 3 | Poland | ↓ | National registry data on people with type 1 diabetes; compared with the prepandemic period, there was a significant decrease (–27% compared with 2019; p value not reported) in the number of diabetes-related hospitalisations. |
| Guimaraes and colleagues[54] | 4 | Brazil | ↓ | National data in adults aged 20 years or older; there was a statistically significant decrease (p<0·001) in hospitalisations due to diabetes (–24·0% [–25·0% to –22·0%]) when comparing Jan–Feb, 2020 (prepandemic) with March, 2020–May, 2021. |
| Harun and colleagues[18] | 6 | Saudi Arabia | ↓ | Hospital admissions in 358 people with diabetic foot disease in one hospital non-significantly decreased during (2·07 [0·60–3·54]) compared with before the pandemic (2·29 [0·50–4·08], p=0·289). |
| Hernandez-Vasquez and colleagues[22] | 3 | Peru | ↓ | In adults aged 18 years or older from a multihospital database, there was a positive linear slope from 2017 to March, 2020. The difference in the slope after March 2020 was –2·4 admissions per month (–32·56 to 27·70; p<0·872) in the number of cases. |
| Kim and colleagues[55] | 6 | USA | ↓ | In data from more than 3 million people with chronic illnesses, admissions for diabetes decreased 31% during spring, 2020, and 36% during summer, 2020, compared with the same periods in 2017–19. |
| Kleibert and colleagues[23] | 4 | Poland | ↔ | The number of diabetic foot ulcer-related hospitalisations extracted from national health fund data did not change significantly in 2020 in comparison with 2017–19 (averaged; 13 375 *vs* 14 383, p=0·17). |
| Lui and colleagues[56] | 5 | Hong Kong | ↓ | Total hospitalisation rate for all diabetes: IRR study period versus inter-year control 0·73 (0·09–0·78; p<0·001); IRR study period versus intra-year control 0·77 (0·02–0·83; p<0·001). |
| Michalowsky and colleagues[57] | 5 | Germany | ↓ | In adults older than 65 years, diabetes hospital admissions were 0·6 in March, 2019, versus 0·3 in March, 2020 (–49%); 0·6 in April, 2019, versus 0·4 in April, 2020 (–39%); and 0·6 in May, 2019, versus 0·3 in May, 2020 (–50%; p values not reported). |
| Moin and colleagues[58] | 6 | Canada | ↓ | Ontario, Canada hospitals showed a 16% decrease in hospital admissions for diabetes complications (majority type 2 diabetes). |
| Reschen and colleagues[59] | 4 | UK | ↔ | For one UK National Health Service trust, number of diabetes (non-COVID) admissions were 917 (22%) prepandemic and 558 (22%) in the first pandemic wave (p=0·8). |
| Santana and colleagues[60] | 3 | Brazil | ↓ | In one paediatric hospital, 143 patients with type 1 diabetes were evaluated, of whom 12 (8·4%) needed hospitalisation because of diabetes during the pandemic. In the same period prepandemic, the rate was 10·0%. |
| Sekowski and colleagues[28] | 8 | Poland | ↓ | Using national registry data, among patients with type 1 diabetes, hospitalisation rate per 100 000 decreased from 74·6 in 2019 to 53·0 in 2020 (–28·9%). An even greater drop was observed among patients with type 2 diabetes, from 99·4 in 2019 to 61·6 in 2020 (–38·0%). |
| Yoon and colleagues[34] | 6 | USA | ↓ | Using data from a cohort of people with diabetes judged to be at high risk within a US Veterans Affairs medical centre, a mean decrease was reported of 0·002 (–0·002 to –0·001) in diabetes-related hospitalisations per patient per quarter in the early pandemic phase compared with the prepandemic phase. |

ICU=intensive care unit. IRR=incident rate ratio. NOS=Newcastle-Ottawa Scale. PICU=paediatric intensive care unit.

*Table 2:* **Diabetes-related hospital admissions during versus before the COVID-19 pandemic**

compared with before the pandemic were mixed (table 3). Two studies did not detect any difference, four studies detected decreases, and three detected increases.

## Diabetic ketoacidosis

Four systematic reviews evaluated associations between the pandemic and diabetic ketoacidosis. Three found increases in diabetic ketoacidosis and severe diabetic ketoacidosis in children or new-onset type 1 diabetes during compared with before the pandemic (appendix p 25).

AlFayez and colleagues[66] (AMSTAR 2 10/16; critical domains 5/7) combined data from 20 studies, and found the risks of diabetic ketoacidosis and severe diabetic ketoacidosis increased during compared with before the pandemic (diabetic ketoacidosis RR 1·35 [95% CI 1·20–1·53], $I^2$=71%; severe diabetic ketoacidosis RR 1·76 [1·33–2·33], $I^2$=44%). In those with new-onset diabetes, the risk of diabetic ketoacidosis was 44% higher (RR 1·44 [1·26–1·65], $I^2$=64%).

Elgenidy and colleagues[67] (AMSTAR 2 9/16; critical domains 4/7) analysed data across 24 studies in children with newly diagnosed type 1 diabetes and found a statistically significant increase in the risk of diabetic ketoacidosis (RR 1·41 [1·19–1·67]) and severe diabetic ketoacidosis (RR 1·66 [1·30–2·11], p<0·01, $I^2$=86%) during the pandemic compared with before. No significant differences were detected among people with pre-existing type 1 diabetes (RR 1·07 [0·79–1·46]) or mixed patients (RR 1·04 [0·84–1·29]).

Rahmati and colleagues[68] (AMSTAR 2 9/16; critical domains 4/7) analysed data from 21 studies on new-onset type 1 diabetes in children. Meta-analyses showed increased incidence of diabetic ketoacidosis (RR 0·064 [0·043–0·084], $I^2$=3%) and severe diabetic ketoacidosis (RR 0·049 [0·029–0·066], $I^2$=14%) during compared with before the pandemic.

O'Mahoney and colleagues[69] (AMSTAR 2 9/16; critical domains 5/7) did not statistically synthesise data on diabetic ketoacidosis, but found no clear

| | NOS | Country | Effect direction | Supporting data |
|---|---|---|---|---|
| Aubert and colleagues[62] | 4 | USA | ↔ | In veterans aged 65 years and older with type 2 diabetes, there was no evidence of a difference in hypoglycaemia-related or hyperglycaemia-related emergency room visits or hospitalisations during the pandemic compared with July, 2018–February, 2020. Hypoglycaemia: March, 2020 RR 1·01 (95% CI 0·54–1·09); April–November, 2020 RR 0·86 (0·68–1·09). Hyperglycaemia: March, 2020 RR 1·02 (0·66–1·58); April–November, 2020 RR 0·95 (0·80–1·11). |
| Bossi and colleagues[31] | 3 | Italy | ↔ | Self-reported emergency department access during compared with before the pandemic in people with diabetes: unchanged 78%, decreased 9%, increased 13%. |
| Caruso and colleagues[5] | 5 | Italy | ↑ | Patients admitted for diabetic foot ulcer emergency: 19 (76%) in 2020, ten (26%) in 2019 (p<0·001). |
| Celona and colleagues[63] | 6 | USA | ↑ | Analysis of medical record data from a large hospital, for young adults (aged 20–26 years) with chronic health conditions presenting at the emergency department, reports that the proportion of emergency department encounters requiring emergency hospital admissions increased from 41·8% to 61·1% during the pandemic among people with diabetes. |
| Giannouchos and colleagues[64] | 3 | USA | ↓ | Emergency department visits for diabetes: January–March: 131 in 2019 versus 109 in 2020 April: 31 in 2019 versus 19 in 2020 May–August: 138 in 2019 versus 81 in 2020 |
| McCalister and colleagues[16] | 8 | Canada | ↓ | Emergency department visits for any cause, per 1000 healthcare visits: in 30 days after visit, 108·0 before pandemic, 83·6 during pandemic (p<0·001); in 90 days after visit, 299·5 before pandemic, 242·2 during pandemic (p<0·01). |
| Moin and colleagues[58] | 6 | Canada | ↓ | 18% decrease in emergency department admissions for acute diabetes complications in the first 6 months of the pandemic compared with the two previous 6-month periods. |
| Sarikaya and colleagues[65] | 5 | Türkiye | ↑ | In 89 children with type 1 diabetes, an increase in frequency of admissions to emergency services was noted during the pandemic compared with previously. |
| Yoon and colleagues[34] | 6 | USA | ↓ | Using data from a cohort of people with diabetes judged to be at high risk within a US Veterans Affairs medical centre, a mean decrease was reported of 0·22 (95% CI –0·24 to –0·21) in emergency department visits per patient per quarter in the early pandemic phase compared with the prepandemic phase. |

NOS=Newcastle-Ottawa Scale. RR=rate ratio.

***Table 3:*** **Emergency hospital admissions in people with diabetes during versus before the COVID-19 pandemic**

evidence of a difference during compared with before the pandemic.

A further 69 primary studies[32,35,37,38,40–49,52,53,56,59,61,70–120] included diabetic ketoacidosis data (table 4). Of these, 13 were in adult or mixed cohorts; three of these found a decrease in occurrence or severity of diabetic ketoacidosis during compared with prepandemic, two found an increase, and the remainder found no clear evidence of a difference in either outcome. However, most studies restricted to children and adolescent samples (47 of 56) found that diabetic ketoacidosis occurrence or severity increased during the pandemic compared with before, whereas four found a reduction and six found no clear difference. Of the 30 studies in people with new-onset diabetes, 28 found increased occurrence or severity of diabetic ketoacidosis during compared with before the pandemic.

Three studies analysed trends based on socio-demographic characteristics; Misra and colleagues[70] (NOS 7, national dataset from England) also analysed by diabetes type, and found that diabetic ketoacidosis emergency hospital admissions were lower in people with pre-existing type 1 diabetes during compared with before the pandemic, but higher in people with type 2 diabetes and in people with newly diagnosed diabetes. Increases were particularly pronounced in those of non-White ethnicities. Alassaf and colleagues[71] (NOS 3, 137 with type 1 diabetes) found no significant difference in age at diagnosis (p=0·914) or monthly income (p=0·254) when comparing patients presenting with diabetic ketoacidosis in new-onset type 1 diabetes during the pandemic with the preceding year,. Female patients had higher risk of presenting with diabetic ketoacidosis during the prepandemic year (p=0·047). Monkemoller and colleagues[72] (NOS 6, data from 216 diabetes centres in Germany) found that the largest increase from prepandemic to during the pandemic was seen in children aged 6 years and younger (141·6% increase), followed by those aged 12–18 years (91·8% increase) and 6–11 years (52·3% increase). Children aged 6 years and younger also saw the largest increase in severe diabetic ketoacidosis incidence (97%), followed by those aged 6–11 years (33·1%) and 12–18 years (19·1%). The percentage increase during compared with before the pandemic was similar between men (88·2%) and women (81·3%) for diabetic ketoacidosis, but severe diabetic ketoacidosis saw a steeper rise in women (52·6%) than in men (40·4%). Children with a migration background (definition not provided) saw steeper percentage increases in diabetic ketoacidosis (92·4% *vs* 80·8%) and severe diabetic ketoacidosis (62·0% *vs* 36·5%) during compared with before the pandemic in comparison with those without a migration background.

## Severe hypoglycaemic events

Four studies provided data on occurrence of severe hypoglycaemic events during compared with before the pandemic; findings were mixed. Alsalman and colleagues[73] (NOS 2) conducted interviews in a sample of 164 paediatric patients with type 1 diabetes from a Saudi university hospital; they reported that the need to visit the emergency department for hypoglycaemia reduced significantly during lockdown (p=0·001). Rabbone and colleagues[74] (NOS 6) also reported a decrease (statistical significance not tested) in incidence of severe

| | NOS | Country | Effect direction | Supporting data |
|---|---|---|---|---|
| **Children and adolescents** | | | | |
| Abdou and colleagues[76] | 4 | Egypt | ↑ | 324 children with type 1 diabetes, hypokalaemia, as complication of diabetic ketoacidosis management: 18% of patients admitted during the pandemic developed hypokalaemia as a complication, in comparison with 6·7% of patients before the pandemic, which was statistically significant (p=0·001). |
| Al Agha and colleagues[77] | 2 | Saudi Arabia | ↓ | 150 children with type 1 diabetes; percentage of patients who experienced diabetic ketoacidosis decreased from 35% before the lockdown to 11% during the lockdown. |
| Alaqeel and colleagues[78] | 4 | Saudi Arabia | ↑ | In 260 children with type 1 diabetes, diabetic ketoacidosis was higher in 2020 than in 2019 (83% *vs* 73%; RR 1·15 [95% CI 1·04–1·26], p=0·05), after adjusting for age and sex. Diabetic ketoacidosis frequency among children with new-onset type 1 diabetes was higher in 2020 than in 2019 (26% *vs* 13%, p≤0·001). |
| Alassaf and colleagues[71] | 3 | Jordan | ↑ | 137 children and adolescents with type 1 diabetes, from March 2, 2020, to March 1, 2021, compared with those diagnosed with type 1 diabetes in the year preceding the pandemic. The percentage of patients diagnosed with diabetic ketoacidosis as first presentation of type 1 diabetes during the pre-pandemic year was 35% compared with 52% during the pandemic year (p=0·049). |
| Alsalman and colleagues[73] | 2 | Saudi Arabia | ↓ | 164 paediatric patients with type 1 diabetes self-reported a decrease in need for ICU admission due to diabetic ketoacidosis during compared with before the pandemic. |
| Ansar and colleagues[79] | 2 | USA | ↑ | Children with type 1 diabetes and type 2 diabetes (n not reported); mean monthly rates of severe diabetic ketoacidosis (pH≤7·1) increased from 0·85 prepandemic to 2·14 during the pandemic (p<0·0001). |
| Baechle and colleagues[80] | 8 | Germany | ↑ | National registry data of 30 840 children and adolescents with new-onset type 1 diabetes; incidence of diabetic ketoacidosis during the pandemic was higher than predicted (2020 IRR 1.34 [1·23–1·46]; 2021 IRR 1·37 [1·26–1·49]). |
| Basamatur and colleagues[81] | 4 | UK | ↑ | In children with type 1 diabetes, median diabetic ketoacidosis referrals in March–July in the 5 preceding years was 12 (range 11–20), and in Mar–July 2020 it was 31 (p value not reported). |
| Birkebaek and colleagues[82] | 4 | New Zealand, Australia, USA, Europe | ↑ | 104 290 children with type 1 diabetes; adjusted observed prevalence of diabetic ketoacidosis at diagnosis of type 1 diabetes was 39·4% (95% CI 34·0–45·6) in 2020 and 38·9% (33·6–45·0) in 2021, significantly higher than the predicted prevalence of 32·5% (27·8–37·9) for 2020 and 33·0% (28·3–38·5) for 2021 (p<0·0001 for both years). |
| Boboc and colleagues[83] | 4 | Romania | ↑ | 459 patients at a children's hospital; proportion of diabetic ketoacidosis type 1 diabetes onset increased during the pandemic with 67%, from 39% in the pre-pandemic group to 66% in the pandemic group (OR 2·98 [1·97–4·49], p<0·0001). In the pandemic group, a higher percentage of people with diabetic ketoacidosis developed the severe form compared with the prepandemic group (42% *vs* 27%; OR 1·99 [1·13–3·51], p=0·016). |
| Bogale and colleagues[84] | 3 | USA | ↔ | 412 children and adolescents with new type 1 diabetes in a tertiary referral centre; percentages of diabetic ketoacidosis diagnoses at admission were very similar between the prepandemic and postpandemic groups (47% *vs* 48%), as were the severity percentages (13% *vs* 14% mild diabetic ketoacidosis, 33% *vs* 31% moderate or severe diabetic ketoacidosis; p=0·89). |
| Botelho and colleagues[85] | 3 | Portugal | ↑ | Newly diagnosed type 1 diabetes from a single paediatric hospital; 54 cases **(**73%) of non-diabetic ketoacidosis prepandemic, 14 (48%) during the pandemic. |
| Chambers and colleagues[86] | 5 | USA | ↔ | 412 admitted for new-onset type 1 or type 2 diabetes; "percentage of diabetic ketoacidosis diagnoses at admission were very similar" (no data provided). |
| Cherubini and colleagues[87] | 6 | Italy | ↑ | Newly diagnosed type 1 diabetes at 47 diabetes centres in Italy; during all periods of extreme and partial restrictions, the frequency of severe diabetic ketoacidosis was significantly higher in 2020 than in 2017–2019. March–May, 2020 versus 2017–19: OR 2·31 (1·34–4·01); June–September, 2020 versus 2017–19: OR 1·68 (1·00–2·84); October–December 2020 versus 2017–19: OR 1·54 (0·93–2·57). |
| Choudhary and colleagues[37] | 4 | USA | ↔ | More than 1600 patients with type 1 diabetes at a large teaching hospital; no change observed in diabetic ketoacidosis hospitalisation frequency (271 admissions in 2019, 270 in 2020). |
| Danne and colleagues[88] | 5 | Multiple | ↑ | 28 892 people aged 21 years and younger with type 1 diabetes; diabetic ketoacidosis rates were reported to have increased significantly in May–June (p=0·034) and August–September (p=0·007), 2020, compared with 2019. |
| d'Annunzio and colleagues[89] | 6 | Italy | ↑ | Paediatric hospitals in one region of Italy (99 people with newly diagnosed type 1 diabetes); frequency of diabetic ketoacidosis at admission was statistically significantly higher during the pandemic compared with the period immediately beforehand (61% *vs* 38%, p=0·03). |
| Dayal and colleagues[52] | 5 | India | ↑ | Children with type 1 diabetes and severe diabetic ketoacidosis admissions. April 2019–March 2020: 2 of 12 admissions severe; April 2020: 3 of 3 admissions severe (p value not reported). |
| Dovc and colleagues[90] | 6 | Slovenia | ↔ | 326 children, adolescents, and young adults with type 1 diabetes; no diabetic ketoacidosis severe events or hospitalisations reported prepandemic or during the pandemic. |
| Dzygalo and colleagues[91] | 5 | Poland | ↑ | 86 children with type 1 diabetes. Diabetic ketoacidosis at the time of type 1 diabetes diagnosis: 2019 cohort 40%; 2020 cohort 53% (p=0·276). Diabetic ketoacidosis severity at the time of type 1 diabetes diagnosis: 2019 cohort six severe cases (12%) of 52; 2020 cohort 11 severe cases (32%) of 34 (p=0·0262). |
| Fathi and colleagues[92] | 5 | USA | ↑ | 93 patients with new type 1 diabetes at PICU; more severe acidosis during than before the pandemic (pH 7·10 *vs* 7·17, p=0·044). |
| Goldman and colleagues[38] | 5 | Israel | ↑ | Individuals younger than 18 years who were newly diagnosed with type 1 diabetes between March 15 (coinciding with the commencement of the first nationwide lockdown period) and June 30, 2020; and during the same periods in 2019, 2018, and 2017. Diabetic ketoacidosis incidence was 58·2%, significantly higher than in 2019 (aOR 2·18 [1·31–3·60], p=0·003), 2018 (aOR 2·05 [1·26–3·34], p=0.004), and 2017 (aOR 1·79 [1·09–2·93], p=0·022). |

(Table 4 continues on next page)

| | NOS | Country | Effect direction | Supporting data |
|---|---|---|---|---|
| (Continued from previous page) | | | | |
| Grudziaz-Sekowska and colleagues[53] | 3 | Poland | ↑ | Children and adolescents with type 1 diabetes; compared to the prepandemic period there was a reported substantial increase (22% compared with 2019) in the number of diabetic ketoacidosis cases. |
| Hammersen and colleagues[40] | 4 | Germany | ↔ | People with type 1 diabetes younger than 18 years and with a diabetes duration longer than 3 months with visits in 231 German centers; diabetic ketoacidosis rates in 2020 were not significantly different from those in 2019. |
| Han and colleagues[93] | 3 | Korea | ↑ | Rate of paediatric patients with diabetic ketoacidosis admitted to the emergency room in 2020 (0·459%) was more than twice the mean rate of 0·206% for the first 6 months of each of 2017–20. |
| Hawkes and colleagues[94] | 6 | USA | ↑ | In 73 children with type 1 diabetes, diabetic ketoacidosis presentations in newly diagnosed type 1 diabetes in March–July, 2017, 2018, and 2019 was 38%, and in March–July, 2020 was 45% (p=0·3). Severe diabetic ketoacidosis presentations in newly diagnosed type 1 diabetes in March–July, 2017, 2018, and 2019 was 12%, and in March–July, 2020 was 15% (p=0·4). |
| Ho and colleagues[95] | 4 | Canada | ↑ | From two children's hospitals, the frequency of diabetic ketoacidosis at type 1 diabetes onset was significantly higher in the pandemic period (68·2% in 2020 *vs* 45·6% in 2019, p<0·001) and incidence of severe diabetic ketoacidosis was also higher (27·1% in 2020 *vs* 13·2% in 2019, p=0·01). |
| Jafari and colleagues[41] | 5 | USA | ↓ | Using pH as a severity measure, data from one hospital found special cause variation with a downward shift in the mean pH on diabetic ketoacidosis presentation from 7·2 in 2019 to 7·1 in 2020 for all patients. |
| Jalilova and colleagues[96] | 6 | Türkiye | ↑ | In 199 children with new-onset type 1 diabetes, it was reported that although the rate of diabetic ketoacidosis was similar, the rate of severe diabetic ketoacidosis during the pandemic was higher than in previous years (30% in 2020 *vs* 46% in 2019, 24% in 2018, 19% in 2017, and 17% in 2016; p=0·027), and that durations of symptoms were longer in the pandemic period than in the previous years (p>0·05) |
| Kaya and colleagues[97] | 4 | Türkiye | ↑ | Increased frequency of diabetic ketoacidosis in new-onset type 1 diabetes during (n=44, 68%)compared with before the pandemic (n=79, 41%); no statistically significant difference in frequency of severe diabetic ketoacidosis. |
| Kiral and colleagues[42] | 4 | Türkiye | ↑ | The percentage of children with new-onset type 1 diabetes presenting with diabetic ketoacidosis was higher during the pandemic (p<0·0001) than before the pandemic. The incidence of severe diabetic ketoacidosis was also higher during the pandemic (p<0·0001) and was higher among children with new-onset type 1 diabetes (p<0·0001). |
| Knip and colleagues[98] | 6 | Finland | ↑ | Data from the Finnish Pediatric Diabetes Register; children and adolescents with type 1 diabetes, pandemic cohort 228 of 741 (30·8% [27·6–34·2]), control cohort 448 of 1982 (22·6% [20·8–24·5], p<0·001). Severe ketoacidosis p=0·009. |
| LahTomulic and colleagues[43] | 4 | Croatia | ↑ | A statistically significant increase was reported in the proportion of children with new-onset type 1 diabetes presenting with diabetic ketoacidosis at the PICU during the pandemic. |
| Lawrence and colleagues[99] | 4 | Australia | ↑ | A statistically significant increase was reported in the frequency of children and adolescents presenting with severe diabetic ketoacidosis at onset of type 1 diabetes during the pandemic. OR of during compared with before the pandemic 16·7 (95% CI 2·0–194·7; n=11 during pandemic period, 6-10 per year prepandemic). |
| Lee and colleagues[100] | 4 | South Korea | ↑ | Newly diagnosed people with type 1 or type 2 diabetes, aged younger than 18 years: proportion of diabetic ketoacidosis was higher in 2020 than in 2018–2019 (60.8% *vs* 39·0%; p=0·038), with more severe initial presentation in 2020 than in 2018–2019 (p=0·040). Newly diagnosed people with type 1 diabetes in 2020 had 2·286 times higher odds (1·190–4·390; p=0·013) of diabetic ketoacidosis compared with those in 2018–2019; this was not the case for type 2 diabetes. |
| Leiva-Gea and colleagues[101] | 5 | Spain | ↑ | New onset in paediatric type 1 diabetes. During 2020–2021, the number of patients with diabetic ketoacidosis increased significantly by 12% (95% CI 7·2–20·4). In this period, 48% of patients with new-onset cases presented diabetic ketoacidosis (26% mild, 38% moderate, and 36% severe), whereas during the 2015–2019 period, a lower percentage of diabetic ketoacidosis was reported, 36% (33% mild, 32% moderate, and 34% severe). A higher percentage of patients with moderate and severe diabetic ketoacidosis was seen in this period, although this increase was not significant. |
| Loh and colleagues[61] | 6 | Germany | ↑ | Children and adolescents who were admitted to hospital during the first lockdown of the COVID-19-pandemic from March 15 to October, 2020, with new-onset or known diabetes and poor metabolic control, compared with the same period in 2019. The incidence of diabetic ketoacidosis was 50% (pre-lockdown) versus 66·7% (lockdown). Binary logistic regression calculated a 1·65 times higher odds ratio (95% CI 0·58–4·74) for being admitted with diabetic ketoacidosis in 2020 compared with 2019, adjusted for age, gender, and BMI. |
| Mameli and colleagues[44] | 6 | Italy | ↑ | New paediatric patients (aged 0–17 years) with type 1 diabetes onset in the Lombardy region. Frequency of diabetic ketoacidosis was higher in 2020 compared with 2017–19 but did not reach statistical significance: 45·3% *vs* 34·4% in 2017, 42% in 2018, and 34·4% in 2019 (p=0·07). |
| Mangus and colleagues[102] | 7 | USA | ↑ | Data from 14 emergency departments; adjusted odds of diabetic ketoacidosis were higher during the pandemic (0·52%) than prepandemic (0·16%; OR 2·40 [2.07–2·78]). |
| McCluskey and colleagues[103] | 4 | USA | ↑ | There were 1936 PICU admissions for children with diabetic ketoacidosis in 2020 and 1795 admissions per year to those same PICUs in 2018–19. The difference between 2020 admissions and 2018–19 admissions was not different from zero before school closure, and significantly higher than zero after school closure, but was significantly increased in 2020 at more than 30 days after school closure (p=0·039). |
| McGlacken-Byrne and colleagues[45] | 6 | UK | ↑ | Newly diagnosed type 1 diabetes in London hospitals. Children presented more frequently with diabetic ketoacidosis during the first COVID-19 wave compared with prepandemic (prepandemic: mild 13%, moderate 6·7%, severe 10%; first COVID-19 wave: mild 5·9%, moderate 24%, severe 47%; p=0·002). |
| Miller and colleagues[46] | 7 | USA | ↑ | Retrospective chart review of 132 children with diabetes admitted to two hospitals for diabetes-related causes; rates of new-onset diabetes presenting with diabetic ketoacidosis increased from 0·24% in 2018 to 0·96% in 2020 (p=0·0014). |

(Table 4 continues on next page)

| | NOS | Country | Effect direction | Supporting data |
|---|---|---|---|---|
| (Continued from previous page) | | | | |
| Monkemoller and colleagues[72] | 6 | Germany | ↑ | Data of 532 patients with new-onset type 1 diabetes from 216 diabetes centres showed that the risk for diabetic ketoacidosis increased by 84·7% and the risk for severe diabetic ketoacidosis increased by 45·3% compared with the years 2018 and 2019. |
| Nagl and colleagues[104] | 4 | Austria | ↑ | National dataset of all newly diagnosed children with type 1 diabetes aged under 15 years. During the lockdown period caused by the COVID-19 pandemic in 2020, a significant increase of 17·2% was observed in onset-diabetic ketoacidosis prevalence (p=0·022) from 42·1% during non-lockdown time periods from the five previous years to 59·3%. 20% of children had severe diabetic ketoacidosis at type 1 diabetes diagnosis during the lockdown period, compared with 14% during the comparison period. |
| Ordooei and colleagues[105] | 5 | Iran | ↑ | Dataset from one hospital of children with diabetic ketoacidosis, with significantly more severe diabetic ketoacidosis cases reported during the pandemic than before (35·7% *vs* 21·2%), whereas the frequency of moderate diabetic ketoacidosis cases was not noticeably different in the two periods (37·1% *vs* 36·4%). |
| Pelletier and colleagues[106] | 4 | USA | ↑ | Paediatric admissions in 39 US hospitals for diabetic ketoacidosis between January and June 2020 were above the model 95% CI for previous years. |
| Pietrzak and colleagues[47] | 4 | Poland | ↑ | In regional paediatric diabetes centres there were 521 diabetic ketoacidosis cases noted in 2019–2020 (37·5%), and 826 in 2020–2021 (49·4%). The increase was significant both at the patient level (p<0·0001) and at the observation region level (mean increase across the regions 11·1% [SD 7·2%], p=0·0001). At the national level (considering all new-onset type 1 diabetes cases diagnosed during each month), the major increase was noted in February, 2020, denoting a shift in diabetic ketoacidosis incidence (p=0·00008, significant even after considering Bonferroni-adjusted threshold of 0·0022). A month later, a nationwide lockdown was introduced, during which the observed diabetic ketoacidosis incidence reached its peak (60%). Diabetic ketoacidosis severity overall, n=1332 (p=0·0089) (difference between prepandemic and during pandemic); mild 2019–2020: 288 (55·4%), 2020–2021: 392 (47·8%), difference –7·8%; moderate 2019–2020: 125 (24·5%), 2020–2021: 246 (29·9%), difference +5·4%. |
| Pillai and colleagues[107] | 5 | USA | ↑ | From one children's hospital, diabetic ketoacidosis at diagnosis in 2018: eight (24%); 2019: nine (35%); 2020: nine (60%; p=0·048). |
| Ponmani and colleagues[48] | 5 | UK and Ireland | ↑ | Children aged 6 months to 16 years presenting to 49 emergency departments with diabetic ketoacidosis; increases were observed in children presenting with new-onset diabetes in diabetic ketoacidosis (395 in March 1, 2020–Feb 28, 2021, to 566 in March 1, 2019–Feb 28, 2020; 43% increase) and severe diabetic ketoacidosis (141 to 252, 79% increase). |
| Rabbone and colleagues[74] | 6 | Italy | ↓ | Children with type 1 diabetes across 53 centres: 86 (41% of those presenting with type 1 diabetes) had diabetic ketoacidosis at onset of type 1 diabetes in February–April, 2019, and 61 (38%) in February–April, 2020 (p=0·08). There were 22 diabetic ketoacidosis episodes in patients with established diabetes in February–April, 2019, and 13 in February–April, 2020 (p value not reported) Proportion of diabetic ketoacidosis patients with severe diabetic ketoacidosis at onset February–April, 2019, was 31 (36%); that at onset February–April, 2020 was 27 (44%; p=0·03). |
| Rivero-Martin and colleagues[108] | 6 | Spain | ↑ | New-onset type 1 diabetes data from seven hospitals showed differences with respect to previous years, with ketoacidosis present in 39·5% of patients in 2018 and 26·5% in 2019 compared with 52·5% in 2020 (p<0·01). |
| Rusak and colleagues[109] | 6 | Poland | ↑ | Patients with type 1 diabetes in one paediatric centre, comparing the same period in 2020 with 2019: number with diabetic ketoacidosis was 35·2% in 2019 and 47·5% in 2020 (p=0·005); number with severe diabetic ketoacidosis was 14·1% in 2019 and 18·4% in 2020 (p=0·118). |
| Salmi and colleagues[49] | 6 | Finland | ↑ | Children on national diabetes registry with type 1 diabetes. Number of children with severe diabetic ketoacidosis (blood pH<7·10) was 20 (9%) in 2016–19 and 13 (16%) in 2020 (p=0·10). |
| Sellers and colleagues[110] | 5 | Canada | ↑ | Eight paediatric centres, new-onset type 1 diabetes. The percentage of children presenting with diabetic ketoacidosis was significantly higher in 2020 compared with the same period in 2019 (55·0% [143/260] versus 36·4% [86/236]; p<0·0001). In addition, there was also an increase in the percentage of children presenting with severe diabetic ketoacidosis in the 2020 period compared with the same period in 2019 (69 [48%] of 143 *vs* 29 [33%] of 860, p=0·044). |
| Vorgucin and colleagues[111] | 7 | Serbia | ↑ | Data on type 1 diabetes from four regional centres. Diabetic ketoacidosis frequency during the pre-COVID-19 period 2017–19 (45 [34%] of 132) is statistically different from diabetic ketoacidosis frequency during the period 2020–21 (42 [42%] of 99; z=–6·28, p<0·001). Mild diabetic ketoacidosis: 2017–19 19 (14%), 2020–21 14 (14%). Moderate diabetic ketoacidosis: prepandemic 10 (8%), during pandemic 13 (13%). Severe diabetic ketoacidosis: 2017–19 16 (12%), 2020–21 15 (15%). |
| Zubkiewicz-Kucharska and colleagues[112] | 5 | Poland | ↔ | Type 1 diabetes registry. In the first 4 months of 2020, diabetic ketoacidosis was associated with the diagnosis of diabetes in 36·67% of patients, similarly to previous years (p=0·69), including 2019 (p=0·94). Diabetic ketoacidosis was present in 50% of patients diagnosed with type 1 diabetes in March and April, 2020; nevertheless, its incidence was similar to previous years (p=0·36), including 2019 (p=0·75). |
| **Adults and mixed samples** | | | | |
| Ayoub and colleagues[113] | 6 | Saudi Arabia | ↔ | Using 285 medical records from one emergency department, not statistically significant relationship between the number of patients with diabetic ketoacidosis and the period of visitation to the emergency department. |
| Elbarbary and colleagues[114] | 3 | 75 countries | ↔ | Health-care professionals reported increases in new-onset diabetes with diabetic ketoacidosis during compared with before the pandemic: 44 (15%) of 297 reported higher incidence, 253 (85%) did not. |
| Godsey and colleagues[115] | 3 | USA | ↔ | Overall, the authors report no statistically significant difference in ICU admissions with diabetic ketoacidosis during the pandemic compared to prepandemic years. They also projected the number of admissions during the pandemic period had the pandemic not happened, and compared this with observed rates during the pandemic. They report a possible reduction of 22% (p=0·014). |

(Table 4 continues on next page)

| | NOS | Country | Effect direction | Supporting data |
|---|---|---|---|---|
| (Continued from previous page) | | | | |
| Hammersen and colleagues[35] | 6 | Germany | ↓ | Data from a large German registry of people with type 1 diabetes; event rates for diabetic ketoacidosis before and during the pandemic did not differ significantly (p=0·91). |
| Lavik and colleagues[116] | 4 | USA | ↑ | From seven hospitals, mixed children and adults; the percentage of total patients with type 1 diabetes (established or newly diagnosed) presenting in diabetic ketoacidosis month over month in 2019 versus 2020 saw a statistically significant (p=0·001) increase during the pandemic. |
| Lockhart and colleagues[117] | 2 | Ireland | ↔ | Young Adult clinic, patients aged 16–24 years with type 1 diabetes; no clear evidence of difference in one hospital (four reported patients with diabetic ketoacidosis in the pre-lockdown period and three in the lockdown period; p=0·70). |
| Lui and colleagues[56] | 5 | Hong Kong | ↔ | In adults with any type of diabetes, diabetic ketoacidosis hospitalisation rate in January–April, 2019 was 95, in October, 2019–January, 2020 was 118, and in January–April, 2020 was 96 (p value not reported). |
| Misra and colleagues[118] | 8 | UK | ↓ | In 108 adults with type 1 diabetes, diabetic ketoacidosis cases in February–May, 2017–19 on average were 44 (32–59), and in February–May, 2020 were 43 (31–58). |
| Misra and colleagues[70] | 7 | UK | ↑ | National dataset of types 1 and 2 diabetes; compared with preceding years, diabetic ketoacidosis rates were 6% (95% CI 4–9; p<0·0001) higher in the first wave of the pandemic (n=8048), 6% (3–8; p<0·0001) higher in the post-first wave (n=8260), and 7% (4–9; p<0·0001) higher in the second wave (n=9610). |
| Nowak and colleagues[32] | 4 | Poland | ↔ | In one hospital, the incidence of diabetic ketoacidosis episodes did not statistically differ between prepandemic (39%, n=9) and during the pandemic (31%, n=5). |
| Raucci and colleagues[119] | 4 | Italy | ↔ | There were 11 cases of ketoacidosis in the prepandemic period: four cases in patients with known type 1 diabetes and seven cases in patients with new-onset diabetes. In the pandemic there were three cases of ketoacidosis, all new-onset diabetes. |
| Reschen and colleagues[59] | 4 | UK | ↔ | Emergency department admissions in one hospital for diabetic ketoacidosis in adults: 23 prepandemic, 27 in the first pandemic wave (p=0·58). |
| Wallett and colleagues[120] | 4 | England, UK | ↔ | All patients treated for diabetic ketoacidosis at hospital system: "No significant difference in the severity of diabetic ketoacidosis at presentation (median for COVID-positive, COVID-negative, and pre-COVID groups): pH (7·15 *vs* 7·2 *vs* 7·2), bicarbonate (11·4 mmol/L *vs* 11 mmol/L *vs* 13·3 mmol/L), glucose (25·85 mmol/L *vs* 30·9 mmol/L *vs* 29·1 mmol/L), lactate (2·7 mmol/L *vs* 3·2 mmol/L *vs* 2·8 mmol/L), serum osmolality (314·6 mmol/L *vs* 323·1 mmol/L *vs* 316·2 mmol/L). There was also no significant difference between the groups for the duration of diabetic ketoacidosis (from the time of admission to resolution of diabetic ketoacidosis: 12·5 h *vs* 14·9 h *vs* 17·9 h for COVID-positive, COVID-negative, and pre-COVID groups, respectively." p values not reported. |

aOR=adjusted odds ratio. ICU=intensive care unit. IRR=incident risk ratio. NOS=Newcastle-Ottawa score. OR=odds ratio. PICU=paediatric intensive care unit. RR=rate ratio.

***Table 4:*** **Diabetic ketoacidosis incidence and severity during versus before the COVID-19 pandemic**

hypoglycaemia at 53 type 1 diabetes centres in Italy, from 10 cases during lockdown in 2020 compared with 13 in the same period in 2019. Ruan and colleagues[75] (NOS 6), using data from one hospital trust in England, reported that the incidence of severe hypoglycaemia was significantly higher during waves 1 (February–June, 2020) and 2 (September, 2020–April, 2021) of the pandemic compared with the prepandemic period (11·7% and 11·5% *vs* 10·3%). Hammersen and colleagues[35] (NOS 6), using data from a large German registry of people with type 1 diabetes, reported that rates were similar during compared with before the pandemic.[35]

## Amputations

20 studies provided data on amputations (appendix p 26).[5,23,26,120–135] Of the nine that did not differentiate by amputation type, three showed an increase, two showed a decrease, and four indicated no difference. Within major amputations, nine of 12 studies showed an increase, two showed a decrease, and one showed no difference. The pattern was reversed for minor amputations, with three of the four studies showing a decrease and the remainder showing an increase. Valhabjji and colleagues[121] (NOS 8, national dataset from England) noted that the decline in amputations observed during the pandemic was primarily in those older than 65 years. The authors stated that COVID-19 may have been a competing endpoint in the study because this decline was mainly observed in older patients.

## Presentations with foot ulcers

Nine studies presented data on patients presenting with diabetic foot ulcer disease.[23,122,129,130,133,136–139] Of the four studies judged to be at lowest risk of bias, three showed an increase and one showed no clear difference; the four judged to be at higher risk of bias showed a decrease (appendix p 27).

## Sight loss

One systematic review by Im and colleagues[140] (AMSTAR 2 8/16; critical domains 4/7; appendix p 25) analysed the impact of delayed antivascular endothelial growth factor injections on visual acuity in various retinal diseases, including diabetic macular oedema. They found a statistically significant decrease in visual acuity across all diseases, including when restricting just to studies in people with diabetic macular oedema.

Six primary studies also reported mixed findings (appendix p 28);[141–146] three reported an increase in sight loss, two did not detect a difference, and one found a decrease. There were no clear patterns across the six studies.

## Discussion

This systematic review found generally worse clinical outcomes in people with diabetes during the pandemic compared with prepandemic rates. All-cause and diabetes-related mortality showed consistent increases during compared with before the pandemic, and most studies indicated increases in major amputations and sight loss. In adult and mixed samples, data generally suggested no difference in overall amputations or in diabetic ketoacidosis frequency or severity during compared with before the pandemic, whereas in children and adolescents most studies showed increases in diabetic ketoacidosis. This increase was more pronounced in people with new-onset diabetes compared with those with a previous history of diabetes, but data suggest overall increases observed were not solely driven by new-onset diabetes in this population. Within people with new-onset type 1 diabetes, the proportion with diabetic ketoacidosis was increased compared with previous years (ie, the increase does not seem to have been solely driven by observed increases in type 1 diabetes diagnoses during this period). Hospital admissions data suggested decreases in the adult population with diabetes, but increases in diabetes-related admissions to paediatric intensive care units. Data were equivocal on diabetic foot ulcer presentations and emergency department admissions.

Few (nine of 138) studies analysed trends based on sociodemographic characteristics. Where reported, data suggested the impact of the pandemic on diabetes outcomes was worse for females (four studies) and racial and ethnic minority groups (four studies). Data were mixed on age trends, but single studies suggested outcomes might be worse for younger adults and for younger children.[147]

Strengths of our study include the comprehensive search strategy and large number of included studies. The limitations are that all but five studies were judged to be at risk of bias, reporting was often poor—including no differentiation between diabetes types—and we were unable to rule out publication bias. Some studies were very small, meaning they were underpowered but also that they could result in extreme point estimates. There might be some overlap between studies (eg, a study using a national dataset might overlap with a study using a regional dataset in the same country), and some of the primary studies are included in systematic reviews. Due to heterogeneity in reported outcome data, it was not possible to complete meta-analyses. Additionally, the included study timepoints varied between comparing either immediately prepandemic or the same time point in the preceding year(s), making interpretation challenging. Similarly, due to the challenging nature of defining a postpandemic period (considering that incidence is ongoing), no studies have compared during the pandemic with postpandemic and, therefore, some downstream consequences of changes in health-care use are likely to be underestimated. Different countries incorporated different lengths and degrees of lockdowns, resulting in varying impacts on health-care provision and access. We found no eligible randomised controlled trials for inclusion in the review, and so cannot comment on any preventative efforts. Finally, most studies were in high-income countries, and their findings might not be generalisable to low-income or middle-income countries.

Interpreting some health-care use outcomes is challenging. For instance, some studies observed reductions in the number of severe hypoglycaemic events, which could be due to either lower occurrence or avoidance of treatment due to the pandemic. Given the negative impact of the pandemic on factors such as medication adherence,[148] lifestyle behaviours,[149] mental health,[150] and disease self-management,[151] it is likely that these events were occurring at the same (or a greater) rate, but that they were less likely to result in admission or hospitalisation due to COVID-19 pressures on the health-care system. This would be consistent with observed increases in diabetic ketoacidosis severity in some studies; patients might not have accessed health care (whether by choice or not) until their condition deteriorated, resulting in greater long-term health-care use. However, it is also possible that recent acceleration in the use of digital diabetes management might have improved diabetic control; a recent systematic review found improved glycaemic control in people with type 1 diabetes during lockdown attributed to increased use of continuous glucose monitors,[152] which would be expected to reduce hypoglycaemia-related events or admissions. Other studies have reported changes to underlying risk factors during the pandemic, including increased bodyweight and increases in blood pressure and lipids, which might also contribute to meaningful increases in diabetes-related complications.[153,154]

These findings have important implications for health-care service provision during future pandemics, and for prioritising patient care during the recovery phase.[155] People considered at higher risk should be prioritised, but health care should be provided to all people with diabetes as required. Primary data is limited, but suggestions include: using telemedicine and digital health platforms to provide patient care and facilitate self-monitoring and peer support; providing patients with emergency medication kits, including extended diabetes supplies and medicines; webinars about diabetes management during emergencies; home-based exercise and structured education programmes; mental health support through virtual counselling and helplines for people with diabetes feeling overwhelmed; nutritional support through easy, diabetes-friendly recipes using non-perishable items; community volunteers to support tasks like medication pickups; flexible medication delivery options from pharmacies; and emergency preparedness workshops teaching people with diabetes how to prepare for emergencies in collaboration with local health departments.[156] Without such efforts, risks include downstream worsening of health outcomes and a delayed surge in health-care use. The full impact of the observed reduction in health-care use will become even more apparent in the coming years. Future research must investigate the impact of the pandemic on long-term condition incidence, management, and outcomes in order to support future preventative strategies, particularly in underserved communities.[157]

In summary, this systematic review found that the COVID-19 pandemic and associated disruptions in health-care provision were associated with mixed trends in hospitalisation and generally increased diabetes-related morbidity and mortality. Future research should focus on investigating the longer-term impact of the pandemic. Further studies are also needed to understand potential differential impacts of these disruptions, which risk further exacerbating existing inequalities within people with diabetes.

**Contributors**

JHB and KK conceived the review. JHB, PH, KR, JS, FC, LOM, EM, LK, SS, and KK designed and approved the protocol. PH, KR, IO, JS, FC, LOM, LK, JM, RL, SM, EM, and JHB contributed to screening. PH, KR, IO, JS, FC, LOM, LK, JM, RL, SM, EM, and JHB contributed to data extraction and appraisal. JHB and PH led the write-up of the review and verified the data in the review. All authors edited and approved the final manuscript, had full access to all the data in the review, and were responsible for the decision to submit for publication.

**Declaration of interests**

SS reports receiving grants from Sanofi, AstraZeneca, Novo Nordisk, Boehringer Ingelheim, and Servier; speaker honoraria from Boehringer Ingelheim, Lilly, MSD, Novartis, Novo Nordisk, Janssen, Amgen, Sanofi, AstraZeneca, Abbott, and Menarini; advisory board honoraria from Boehringer Ingelheim, Lilly, Novo Nordisk, AstraZeneca, and Abbott; and support for attending meetings or travel from AstraZeneca, Abbott, and Menarini. KK reports acting as a consultant or speaker for or receiving grants for investigator-initiated studies from AstraZeneca, Abbott, Amgen, Bayer, Novartis, Novo Nordisk, Roche, Servier, Sanofi-Aventis, Lilly, MSD, Boehringer Ingelheim, Oramed Pharmaceuticals, and Applied Therapeutics; and being chair of the Scientific Advisory Group for Emergencies Ethnicity Subgroup. All other authors declare no competing interests.

**Data sharing**

Completed data extraction sheets are available upon reasonable request to the corresponding author (note all data have been published so are also in the public domain).

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