



The following information resources have been selected by the National Health Library and Knowledge Service Evidence Virtual Team in response to your question. The resources are listed in our estimated order of relevance to practicing healthcare professionals confronted with this scenario in an Irish context. In respect of the evolving global situation and rapidly changing evidence base, it is advised to use hyperlinked sources in this document to ensure that the information you are disseminating to the public or applying in clinical practice is the most current, valid and accurate. For further information on the methodology used in the compilation of this document—including a complete list of sources consulted—please see our [National Health Library and Knowledge Service Summary of Evidence Protocol](#).

## YOUR QUESTION

What is the effect of blood sugar control in mediating the increased risk of COVID-19 for people with diabetes?

### IN A NUTSHELL

The overall quality of evidence specific to the question was low, consisting mainly of case series, case reports and expert opinion.

However, it has been well established in the literature that COVID-19 can cause more severe symptoms and complications in people living with diabetes<sup>2, 7, 10, 15, 16</sup>. When people with diabetes develop a viral infection, it can be harder to treat due to fluctuations in blood glucose levels and possibly the presence of diabetes complications<sup>15</sup>. Infection with SARS-CoV-2 in people with diabetes may trigger an increased secretion of counter-regulatory hormones such as glucocorticoid and catecholamines which results in elevated blood glucose, abnormal glucose variability and other diabetic complications<sup>11</sup>. A study from the United States found that the median length of stay in patients with diabetes and/or uncontrolled hyperglycemia was greater than those without; the same study found a link between patients with uncontrolled hyperglycemia and a particularly high mortality rate<sup>3</sup>.

Suggestions to help people with diabetes and SARS-CoV-2 infection include:

1. More frequent self-monitoring of blood glucose levels<sup>5</sup>
2. Patient tailored therapeutic strategies, rigorous glucose monitoring and careful consideration of drug interactions to reduce adverse outcomes<sup>6</sup>
3. Intensive monitoring and aggressive supportive care in order to support inadequately controlled patients with diabetes and COVID-19 infection<sup>7</sup>



4. Ensuring sufficient diabetic equipment and supplies at home in order to make regular blood glucose self-tests and awareness to contact a caregiver immediately in case of glycemic imbalance or signs of infection<sup>8</sup>
5. Insulin therapy should be considered to treat any persistent hyperglycemia in patients hospitalized for an acute infection<sup>8</sup>
6. Inpatient glycemic control is particularly important in the comprehensive treatment of COVID-19. Individualized blood glucose goals and treatment strategies should be made according to specific circumstances of COVID-19 inpatients with diabetes<sup>5,9</sup>
7. Blood glucose monitoring, dynamic evaluation and timely adjustment of strategies should be strengthened to ensure patient safety and promote early recovery<sup>9</sup>

One study reported that good blood glucose control may act as an effective auxiliary approach to improve the prognosis of patients with COVID-19 and pre-existing diabetes. Those with better-controlled blood sugar levels and a generally healthier lifestyle are less likely to suffer serious consequences from COVID-19 and are less likely to die from complications<sup>16</sup>.

Management of people with diabetes with COVID-19 generally follows standard sick-day rules<sup>14</sup>, which may include being aware of the signs and symptoms of hypoglycemia and hyperglycemia<sup>2</sup>. Antidiabetic therapy may need adjustments following usual sick day rules<sup>8</sup>.

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## IRISH AND INTERNATIONAL GUIDANCE

### [American Diabetes Association \(2020\) FAQs on Diabetes and COVID-19<sup>1</sup>](#)

'Can patients self-test using blood glucose meters labeled for home use while they are in the hospital during the COVID-19 pandemic?'

Yes. The FDA recognizes that home-use blood glucose meters may be an option to provide relief and support to health care professionals in hospital settings in their attempts to reduce interactions between patients and health care providers, limit exposure to COVID-19 and conserve personal protective equipment. In addition, some home-use blood glucose meters



have built-in wireless data transmission capabilities which can facilitate remote patient monitoring. Therefore, the FDA encourages hospitals to consider policies to allow patients to self-test which may include leveraging patients' own home-use blood glucose meters or dispensing a home-use blood glucose meter upon in-patient admission to the hospital.

### [Diabetes Canada \(2020\) FAQ about COVID-19 and diabetes<sup>2</sup>](#)

COVID-19 can cause more severe symptoms and complications in some people living with diabetes, older people and those with other chronic health conditions. For those routinely monitoring their blood glucose and subject to the advice of their clinical team monitoring frequency should be increased. If you have diabetes and you become unwell for any reason, it is important that you practice sick day management which may include being aware of the signs and symptoms of hypoglycemia and hyperglycemia. Effective blood glucose management may become a challenge when sick. A plan for those diabetics infected with COVID-19 might include: keeping simple sugars such as glucose tablets on-hand in case you need to treat low blood sugar which may occur more frequently with illness due to changes to eating patterns; and having glucagon available in case of a significant low blood sugar if taking insulin or medications that can cause low blood sugar.

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## INTERNATIONAL LITERATURE

### What does the international literature say?

#### [Bode et al \(2020\) Glycemic Characteristics and Clinical Outcomes of COVID-19 Patients Hospitalized in the United States<sup>3</sup>](#)

Diabetes has emerged as an important risk factor for severe illness and death from COVID-19. There is a paucity of information on glycemic control among hospitalized COVID-19 patients with diabetes and acute hyperglycemia. This retrospective observational study of laboratory-confirmed COVID-19 adults evaluated glycemic and clinical outcomes in patients with and without diabetes and/or acutely uncontrolled hyperglycemia hospitalized March 1 to April 6, 2020. Diabetes was defined as A1C  $\geq 6.5\%$ . Uncontrolled hyperglycemia was defined as  $\geq 2$  blood glucoses (BGs)  $> 180$  mg/dL within any 24-hour period. Data were abstracted from Glytec's data warehouse.



Among 1122 patients in 88 US hospitals, 451 patients with diabetes and/or uncontrolled hyperglycemia spent 37.8% of patient days having a mean BG > 180 mg/dL. Among 570 patients who died or were discharged, the mortality rate was 28.8% in 184 diabetes and/or uncontrolled hyperglycemia patients, compared with 6.2% of 386 patients without diabetes or hyperglycemia ( $P < .001$ ). Among the 184 patients with diabetes and/or hyperglycemia who died or were discharged, 40 of 96 uncontrolled hyperglycemia patients (41.7%) died compared with 13 of 88 patients with diabetes (14.8%,  $P < .001$ ). Among 493 discharged survivors, median length of stay (LOS) was longer in 184 patients with diabetes and/or uncontrolled hyperglycemia compared with 386 patients without diabetes or hyperglycemia (5.7 vs 4.3 days,  $P < .001$ ). Conclusion: Among hospitalized patients with COVID-19, diabetes and/or uncontrolled hyperglycemia occurred frequently. These COVID-19 patients with diabetes and/or uncontrolled hyperglycemia had a longer LOS and markedly higher mortality than patients without diabetes or uncontrolled hyperglycemia. Patients with uncontrolled hyperglycemia had a particularly high mortality rate. We recommend health systems which ensure that inpatient hyperglycemia is safely and effectively treated.

#### [Gentile et al \(2020\) COVID-19 infection in Italian people with diabetes: Lessons learned for our future<sup>4</sup>](#)

Concerning diabetes management, another key issue is: how is glycemia managed during hospitalization for COVID-19? Unfortunately, it is not surprising that patients suffering from COVID-19 with hyperglycemia may have a higher risk and a poorer outcome compared with those with euglycemia. Due to the stress of SARS-CoV-2 infection and the use of glucocorticoids during hospitalization, patients may suffer from a great glycemetic excursion, especially those with DM. We have also to consider that DM management is not so easy to accomplish in ill people. When having to face high glucose levels as anticipated from the impact of infection on unstable metabolic control, patients may be suddenly put on insulin; evidence suggests that insulin treatment might not be safely managed in such situations.

#### [Gupta et al \(2020\) Clinical considerations for patients with diabetes in times of COVID-19 epidemic<sup>5</sup>](#)

Individuals with diabetes are at risk of infection  $\frac{3}{4}$  especially influenza and pneumonia. This risk can be reduced, though not completely eliminated, by



good glycaemic control. All people with diabetes above 2 years of age are recommended pneumococcal and annual influenza vaccinations. Further, patients with diabetes may experience severe disease when infected with respiratory viruses.

It is important that people with diabetes maintain good glycaemic control which may help in reducing the risk  $\frac{3}{4}$  or, subsequently, severity  $\frac{3}{4}$  of infection. More frequent self-monitoring of blood glucose levels is required. Improved glycaemic control may also reduce the risk of superadded bacterial pneumonia.

### [\*\*Hussain et al \(2020\) COVID-19 and diabetes: Knowledge in progress<sup>6</sup>\*\*](#)

We aimed to briefly review the general characteristics of the novel coronavirus SARS-CoV-2 and provide a better understanding of COVID-19 in people with diabetes.

The clinical spectrum of COVID-19 is heterogeneous, ranging from mild flu-like symptoms to acute respiratory distress syndrome, multiple organ failure and death. Older age, diabetes and other comorbidities are reported as significant predictors of morbidity and mortality. Chronic inflammation, increased coagulation activity, immune response impairment and potential direct pancreatic damage by SARS-CoV-2 might be among the underlying mechanisms of the association between diabetes and COVID-19. No conclusive evidence exists to support the discontinuation of angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers or thiazolidinediones because of COVID-19 in people with diabetes. Caution should be taken to potential hypoglycaemic events with the use of chloroquine in these subjects. Patient tailored therapeutic strategies, rigorous glucose monitoring and careful consideration of drug interactions might reduce adverse outcomes.

Suggestions are made on the possible pathophysiological mechanisms of the relationship between diabetes and COVID-19 and its management. No definite conclusions can be made based on current limited evidence. Further research regarding the relationship and its clinical management is warranted.

### [\*\*Kim et al \(2020\) Hyperglycaemic Crises with Coronavirus Disease-19: Case Reports<sup>7</sup>\*\*](#)

Acute hyperglycaemic crises such as diabetic ketoacidosis (DKA) or hyperosmolar hyperglycaemic state (HHS) might be precipitated in poorly



controlled patients with diabetes and COVID-19 infection. Intensive monitoring and aggressive supportive care are needed.

### [\*\*Kosinski et al \(2020\) \[Diabetes and COVID-19 infection\]<sup>8</sup>\*\*](#)

Based on the epidemiological data currently available, diabetes does not seem to be a risk factor for infection with SARS-CoV-2 but may be associated with a more severe course. Diabetes is extremely common in older patients with co-morbidities who are at risk of unfavorable outcomes. As with any other infection, poorly controlled pre-existing diabetes can promote secondary infections and lead to acute complications related to hyperglycemia, worsened itself by the infection. It is important to advise patients to have enough diabetic equipment and supplies at home, to make regular blood glucose self-tests and to contact a caregiver immediately in case of glycemic imbalance or signs of infection. Antidiabetic therapy may need adjustments following usual sick day rules. Insulin therapy should be considered to treat any persistent hyperglycemia in patients hospitalized for an acute infection.

### [\*\*Ma et al \(2020\) The Management of Blood Glucose Should be Emphasized in the Treatment of COVID-19<sup>9</sup>\*\*](#)

Based on the higher mortality and the higher proportion of critically ill adults in coronavirus disease 2019 (COVID-19) patients with diabetes, good inpatient glycemic control is particularly important in the comprehensive treatment of COVID-19. Individualized blood glucose target goals and treatment strategies should be made according to specific circumstances of COVID-19 inpatients with diabetes. For mild patients, a strict glycemic control target [fasting plasma glucose (FPG) 4.4-6.1 mmol/L, 2-hour postprandial plasma glucose (2 h PG) 6.1-7.8 mmol/L] are recommended; a target for the glycemic control of common type patients [FPG 6.1-7.8 mmol/L, 2 h PG 7.8-10.0 mmol/L] and subcutaneous insulin deliver therapy are recommended; a target nonfasting blood glucose range of 10.0 mmol or less per liter for severe-type COVID-19 patients, a relatively less stringent blood glucose control target [FPG 7.8-10.0 mmol/L, 2 h PG 7.8-13.9 mmol/L] for critically ill patients and intravenous insulin infusion therapy are recommended. Due to the rapid changes in the condition of some patients, the risk of diabetic ketoacidosis (DKA) or hyperglycemic hyperosmolar status (HHS) maybe occur during the treatment. Blood glucose monitoring, dynamic evaluation and timely adjustment of strategies should be strengthened to ensure patient safety and promote early recovery of patients.



### [Singh et al \(2020\) Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations<sup>10</sup>](#)

We sought to review and analyze the data regarding the association between diabetes and COVID-19, pathophysiology of the disease in diabetes and management of patients with diabetes who develop COVID-19 infection. There is evidence of increased incidence and severity of COVID-19 in patients with diabetes; COVID-19 may also impact the pathophysiology of diabetes. Blood glucose control is important not only for patients who are infected with COVID-19, but also for those without the infection.

### [Wang et al \(2020\) Timely blood glucose management for the outbreak of 2019 novel coronavirus disease \(COVID-19\) is urgently needed<sup>11</sup>](#)

At this stage, the largest epidemiological investigation in China indicated that the mortality of COVID-19 with diabetes is up to 7.3% [80/1102], which is dramatically higher than that of the patients without any comorbidities [0.9%, 133/15,536]. Infection of SARS-CoV-2 with diabetes might trigger stress condition and increased secretion of hyperglycemic hormones such as glucocorticoid and catecholamines which results in elevated blood glucose, abnormal glucose variability and diabetic complications. For the COVID-19 patients with diabetes, tailored therapeutic strategy and optimal goal of glucose control should be formulated based on clinical classification, coexisting comorbidities, age and other risk factors. Blood glucose should be controlled for all patients during hospitalization to monitor the progress of illness and avoid aggravation. For critical cases, early identification and timely reduction adverse drug reaction—for instance, glucocorticoid-induced hyperglycemia—could prevent more severe symptoms. During the 4-week follow-up period after discharge, blood glucose homeostasis should be maintained continuously and patients need to avoid infectious diseases due to a lower immune response. Long-term follow-up is still essential for diabetic patients to reduce diabetes-related complications and mortality.

### [Zhou and Tan \(2020\) Diabetes patients with COVID-19 need better blood glucose management in Wuhan, China<sup>12</sup>](#)

In order to investigate current blood glucose management of patients with both diabetes and COVID-19, we retrospectively analyzed 29 inpatients diagnosed with type-2 diabetes and laboratory confirmed COVID-19 and admitted to a designated isolation medical center in Wuhan from February 13



to March 1. These patients had a median age of 69 (54–81) years and diagnosis of diabetes for 6 (1.5–14) years. All patients had at least one BG test. The clinical management varied according to their BG levels and physicians' advice. We utilized the BG targets suggested for inpatients by the American Association of Clinical Endocrinologists and American Diabetes Association— 7.8 mmol/L for preprandial BG and 10.0 mmol/L for postprandial BG—as the cutoff values. A total of 881 capillary BG tests were performed for these patients. Among them, 56.6% (499/881) of the tests showed abnormal BG levels, including 29.4% (58/197) of the preprandial BG tests and 64.5% (441/684) of the postprandial tests. 69.0% (20/29) patients were considered with non-ideal BG levels. And 10.3% (3/29) of the patients suffered at least one episode of hypoglycemia ( $<3.9$  mmol/L). These results suggested a failure of current BG management strategies for patients suffering both diabetes and COVID-19, especially that of postprandial BG. As diabetes and hyperglycemia may lead to higher secondary infection risk and mortality, we suggest that the BG management of these patients should be better valued and optimized.

### [Zhu and She \(2020\) Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes<sup>13</sup>](#)

Type 2 diabetes (T2D) is a major comorbidity of COVID-19. However, the impact of blood glucose control on the degree of required medical interventions and on mortality in patients with COVID-19 and T2D remains uncertain. We performed a retrospective, multi-centered study of 7,337 cases of COVID-19 in Hubei Province, China, among which 952 had pre-existing T2D. We found that subjects with T2D required more medical interventions and had a significantly higher mortality [7.8% versus 2.7%; adjusted hazard ratio, 1.49] and multiple organ injury than the non-diabetic individuals. Further, we found that well-controlled blood glucose [glycemic variability within 3.9 to 10.0 mmol/L] was associated with markedly lower mortality compared to individuals with poorly controlled blood glucose [upper limit of glycemic variability exceeding 10.0 mmol/L] during hospitalization. These findings provide clinical evidence correlating improved glycemic control with better outcomes in patients with COVID-19 and pre-existing T2D.



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## OTHER

### [Centre for Evidence-Based Medicine \(2020\) \[Evidence Summary\] Managing diabetes during the COVID-19 pandemic<sup>14</sup>](#)

There is little evidence on how people with diabetes can reduce their risk during the COVID-19 pandemic beyond following general infection control guidance. More frequent blood glucose monitoring in people who self-monitor and taking influenza and pneumonia vaccinations have been suggested, although it is unclear what evidence was used to make these recommendations.

Interventions to improve self-management of or self-education for diabetes may be limited in their generalisability to the COVID-19 pandemic. Text-message interventions and self-monitoring of blood glucose are the most promising strategies based on the literature at hand.

Management of people with diabetes with COVID-19 generally follows standard sick-day rules. There may be specific considerations around ACE inhibitors, glucose control if hospitalised and access to medical care and supplies.

### [International Diabetes Federation \(2020\) \[Webpage\] COVID-19 and diabetes<sup>15</sup>](#)

Older people and people with pre-existing medical conditions such as diabetes, heart disease and asthma appear to be more vulnerable to becoming severely ill with the COVID-19 virus. When people with diabetes develop a viral infection, it can be harder to treat due to fluctuations in blood glucose levels and possibly the presence of diabetes complications.

Firstly, the immune system is compromised, which makes it harder to fight the virus and may lead to a longer recovery period. Secondly, the virus may thrive in an environment of elevated blood glucose.

If you have diabetes:

- Pay extra attention to your glucose control. Regular monitoring can help avoid complications caused by high or low blood glucose.
- Any infection is going to raise your glucose levels and increase your need for fluids so make sure you can access a sufficient supply of water.



— Make sure you will be able to correct the situation if your blood glucose drops suddenly.

### [Wilké \(2020\) \[Webpage\] Blood sugar control for diabetics more vital than ever during coronavirus pandemic<sup>16</sup>](#)

As we know by now, those with underlying conditions and chronic health issues are more likely to suffer serious consequences should they become infected with the new coronavirus. According to a study reported in the journal *Cell Metabolism*, there is evidence that those with type 2 diabetes are more prone to suffering serious complications should they be infected with the new coronavirus. If blood sugar is well-controlled, this might not be the case, according to expert opinion.

"We were surprised to see such favourable outcomes in well-controlled blood glucose groups among patients with COVID-19 and pre-existing type 2 diabetes," says senior author Hongliang Li of Renmin Hospital of Wuhan University. "Considering that people with diabetes had a much higher risk for death and various complications and that there are no specific drugs for COVID-19, our findings indicate that controlling blood glucose well may act as an effective auxiliary approach to improve the prognosis of patients with COVID-19 and pre-existing diabetes."

Li also mentioned that those with better-controlled blood sugar levels and a generally healthier lifestyle are less likely to suffer serious consequences from COVID-19 and are less likely to die from complications. Li pointed to three new findings:

1. People with diabetes have a higher chance to die of COVID-19 and should take extra precautions such as self-isolation and physical distancing.
2. People with diabetes should keep monitoring their blood sugar level to keep it under control.
3. If a diabetic does become infected, a medical expert should constantly monitor their blood sugar level.



Produced by the members of the National Health Library and Knowledge Service Evidence Team<sup>†</sup>. Current as at 18 May 2020. This evidence summary collates the best available evidence at the time of writing and **does not replace clinical judgement or guidance**. Emerging literature or subsequent developments in respect of COVID-19 may require amendment to the information or sources listed in the document. Although all reasonable care has been taken in the compilation of content, the National Health Library and Knowledge Service Evidence Team makes no representations or warranties expressed or implied as to the accuracy or suitability of the information or sources listed in the document. This evidence summary is the property of the National Health Library and Knowledge Service and subsequent re-use or distribution in whole or in part should include acknowledgement of the service.

The following PICO(T) was used as a basis for the evidence summary:

	DIABETICS WITH COVID-19
	BLOOD SUGAR CONTROL MEASURES

The following search strategy was used:

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'glucose blood level'/exp  
((glucose OR sugar) ADJ3 (blood OR serum)):ab,ti  
(glucosaemia: ab,ti OR glucosemia: ab,ti OR glycaemia:ab,ti OR glycemia:ab,ti OR normoglycaemia:ab,ti OR  
normoglycemia:ab,ti)  
AND  
[COVID-19 query string]
```

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