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 impact of diabetes mellitus among people infected with COVID-19?

IN A NUTSHELL

Patients with diabetes are considered to be at higher risk for severe illness. They are more likely to need intensive care if they develop COVID-19 compared with patients who do not have diabetes and have a higher case fatality rate. Diabetes may not increase the risk of COVID-19 infection but it can lead to enhanced disease severity. Preliminary findings from the United States suggest that persons with underlying health conditions or other recognized risk factors for severe outcomes from respiratory infections appear to be at a higher risk for severe disease from COVID-19 than are persons without these conditions. The most commonly reported conditions were diabetes mellitus, chronic lung disease and cardiovascular disease. The Centre for Evidence-Based Medicine states that there is little evidence on how people with diabetes can reduce their risk of COVID-19 infection beyond following general infection control guidance. Significant disruptions to routine care may also contribute to poorer outcomes during and following the pandemic. Hyperglycemia should not be overlooked, but adequately treated to improve the outcomes of COVID-19 patients with or without diabetes.

Both the HPSC and WHO highlight evidence suggesting there are two groups of people at a higher risk of acquiring a more severe disease; older people and those with an underlying medical condition such as diabetes. Clinical guidance from the CDC also highlights risk factors for severe illness and reports that fatality is higher for patients with diabetes. Diabetes as a distinctive comorbidity is associated with more severe disease, acute respiratory distress syndrome and increased mortality. In a nationwide
analysis on comorbidity and its impact on patients in China\textsuperscript{23}, Guan et al found that the most prevalent comorbidity was hypertension followed by diabetes. The study concludes that patients with any comorbidity yielded poorer clinical outcomes than those without, and that a greater number of comorbidities also correlated with poorer clinical outcomes. Discussing two earlier CoV infections — SARS and MERS — Bloomgarden et al\textsuperscript{34} report that regardless of the potential for the spread of COVID-19, as with influenza-reported mortality diabetes is an important risk factor for adverse outcome. Diabetes should be considered a risk factor and more intensive attention should be paid to patients with diabetes, in case of rapid deterioration\textsuperscript{20}.

IRISH AND INTERNATIONAL GUIDANCE

What does the Health Service Executive (Ireland) say?

Health Service Executive (2020). HSE Interim Clinical Guidance on Management of Diabetes during the COVID-19 Pandemic, V1 21.04.20\textsuperscript{1} Delivery of high quality diabetes care requires a well-informed patient with good self-management skills to work with a knowledgeable and well-staffed specialist team who can advise the patient on how to manage their condition to avoid the short- and long-term complications of diabetes. The purpose of this document is to highlight for frontline staff involved in delivering care to patients with diabetes some issues that may help with achieving good outcomes during the COVID-19 pandemic. This guidance should be used in conjunction and in line with guidance issued from the Health Protection Surveillance Centre.

What does the Health Protection Surveillance Centre say?

Health Protection Surveillance Centre (2020). Coronavirus (COVID-19) guidance for settings for vulnerable groups\textsuperscript{2} HPSC guidance states that patients are more at risk if they are 60 years of age and older, have a long-term medical condition: eg heart disease, lung disease, high blood pressure, cancer, diabetes or liver disease.
Irish Association of Emergency Medicine. Emergency Department Management of Suspected or Confirmed SARS-CoV-2

Diabetes mellitus is named as a medical co-morbidity risk factor.

**What does the World Health Organization say?**


Evidence suggests that two groups of people are at a higher risk of getting a more severe disease. “These are older people [>60 years]; and those with underlying medical conditions such as cardiovascular disease, diabetes, chronic respiratory disease, and cancer.”

**What do the Centers for Disease Control and Prevention (United States) say?**

*Centers for Disease Control and Prevention (2020). Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19).*

The guidance includes a section describing risk factors for severe illness. Fatality was higher for patients with comorbidities. “10.5% for those with cardiovascular disease, 7.3% for diabetes, and approximately 6% each for chronic respiratory disease, hypertension, and cancer. Heart disease, hypertension, prior stroke, diabetes, chronic lung disease, and chronic kidney disease have all been associated with increased illness severity and adverse outcomes.”

**What does the Centre for Evidence Based Medicine say?**

*Oxford University Centre for Evidence Based Medicine (April 8, 2020). Managing diabetes during the COVID-19 pandemic.*

People with diabetes are at increased risk of serious illness from COVID-19. There is little evidence on how people with diabetes can reduce their risk during the COVID-19 pandemic beyond following general infection control guidance. In this evidence synthesis, the CEBM highlight that with routine care being significantly disrupted during the COVID-19 pandemic, stress levels and disruptions to diet and lifestyle may also contribute to poorer outcomes during and following the pandemic.
Oxford University Centre for Evidence Based Medicine (April 8, 2020). Diabetes and risks from COVID-19, April 8, 2020
People with diabetes appear to be at increased risk of having a more severe COVID-19 infection, though evidence quantifying the increased risk is highly uncertain due to a paucity of data.

It is anticipated this systematic review will commence in May 2020. The review question will look at how interventions enacted in response to disasters and national emergencies affect diabetes outcomes during and following these events. Results will be published on an ongoing basis and hosted on the CEBM website.

What does NHS England say?
All clinicians have general responsibilities in relation to COVID-19 and should seek and act on national and local guidelines. Topics discussed in this guide include categories of people with diabetes to consider obligatory admissions and inpatients, secondary care services and primary care delivered diabetes services.

POINT-OF-CARE TOOLS

What does BMJ Best Practice say?
This overview topic is continually reviewed and updated, and more conditions will be added to this list. Patients with diabetes are considered to be at higher risk for severe illness. They are more likely to need intensive
care if they develop COVID-19, compared with patients who do not have diabetes, and have a higher case fatality rate.

INTERNATIONAL LITERATURE

What does the international literature say?
*Note: the majority of the literature generated to date on this specific question is from China.


Individuals with diabetes are at risk of infections, 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. Not only this, patients with diabetes have a severe disease when infected with respiratory viruses.

Data about COVID-19 in patients with diabetes is limited at present. Diabetes was present in 42.3% of 26 fatalities due to COVID-19 in Wuhan, China. A report of 72,314 cases of COVID-19 published by the Chinese Centre for Disease Control and Prevention showed increased mortality in people with diabetes: 2.3%, overall and 7.3%, patients with diabetes.


This meta-analysis included 8 studies with a total of 46,248 patients. The results showed that hypertension and diabetes are the two most prevalent comorbidities with diabetes prevalent in 8% of the patients. The review goes on to describe chronic diseases as risk factors. Chronic diseases share several standard features with infectious disorders such as the pro-inflammatory state and the attenuation of the innate immune response. Diabetes occurs in part because the accumulation of activated innate immune cells in metabolic tissues leads to the release of inflammatory mediators, especially, IL-1β and TNFα, which promotes systemic insulin resistance and β-cell damage. Besides, metabolic disorders may lead to low immune function by impairing macrophage and lymphocyte function, which may make individuals more susceptible to disease complications.
Huang et al (2020) Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia: a systematic review, meta-analysis, and meta-regression

Huang et al conducted a systematic review and meta-analysis to investigate the association between diabetes mellitus and poor outcome in patients with COVID-19 pneumonia. They conclude that diabetes mellitus was associated with mortality, severe COVID-19, acute respiratory distress syndrome, and disease progression in patients with COVID-19.


As of March 28, 2020, US states and territories have reported 122,653 COVID-19 cases to CDC, including 7,162 (5.8%) for whom data on underlying health conditions and other known risk factors for severe outcomes from respiratory infections were reported. Among these 7,162 cases, 2,692 (37.6%) patients had one or more underlying health condition or risk factor and 4,470 (62.4%) had none of these conditions reported. The percentage of COVID-19 patients with at least one underlying health condition or risk factor was higher among those requiring ICU admission (358 of 457, 78%) and those requiring hospitalization without ICU admission (732 of 1,037, 71%) than that among those who were not hospitalized (1,388 of 5,143, 27%). The most commonly reported conditions were diabetes mellitus, chronic lung disease, and cardiovascular disease. These preliminary findings suggest that in the United States, persons with underlying health conditions or other recognized risk factors for severe outcomes from respiratory infections appear to be at a higher risk for severe disease from COVID-19 than are persons without these conditions.


Summary of findings from a report of a case series published by the Chinese Centre for Disease Control and Prevention on COVID-19 in China. There were a total of 72,314 cases, updated February 11, 2020. Among the 72,314 case records, 44,762 had a confirmed diagnosis of COVID-19. Most of the patients (87%) were aged 30-89. 81% of cases were classified as mild, with 14% as
severe. The case-fatality rate was raised among those patients with a pre-existing condition: 10.5% with cardiovascular disease, 7.3% with diabetes, 6.3% with chronic respiratory disease, 6.0% with hypertension.


Ten studies including a total of 76,993 patients diagnosed with COVID-19 were included in this meta-analysis. Diabetes Mellitus was included in a list of underlying diseases among hospitalised COVID-19 patients. Using the data of 6 included articles, the prevalence of diabetes among people who were infected with SARS-CoV-2 was estimated to be 7.87% (95%CI: 6.57% – 9.28%).

In summary, the results of the current study have shown that in patients with SARS-CoV-2 infection, hypertension, cardiovascular disease, smoking, and diabetes are the most prevalent co-existing disorders.


The purpose of this meta-analysis was to analyse the correlation between hypertension, diabetes, coronary heart disease and COVID-19 disease severity. From their findings, Chen et al conclude that hypertension, diabetes, and coronary heart disease can affect the severity of COVID-19. It may be related to the imbalance of angiotensin-converting enzyme 2 (ACE2) and the cytokine storm induced by glucolipid metabolic disorders (GLMD).

Bhatraju et al (2020) COVID-19 in Critically Ill Patients in the Seattle Region: Case Series

Report of 24 patients with confirmed diagnosis of COVID-19 from the Seattle area who were admitted to ICU in February–March 2020. The mean age was 64. 14 patients (58%) had diabetes mellitus. 5 (21%) patients had chronic kidney disease.


Although the overall mortality rate of COVID-19 is low (1.4–2.3%), patients with comorbidities are more likely to have severe disease and subsequent mortality. Most of the available studies have shown that diabetes mellitus (DM) as a distinctive comorbidity is associated with more severe disease, acute respiratory distress syndrome and increased mortality. Further, in the
largest series reported by the Chinese Center for Disease Control and Prevention comprising of 72,314 cases of COVID-19, patients with DM had higher mortality (7.3% in DM vs. 2.3% overall”).

**Guo et al (2020) Diabetes is a risk factor for the progression and prognosis of COVID-19**

174 patients included in the study were admitted to hospital in Wuhan from February 10th 2020 to February 29th 2020. All patients had a positive diagnosis of COVID-19. The most common of underlying comorbidities were chronic diseases, such as hypertension (24.7%) and diabetes (21.2%). The authors examined the effects of COVID-19 on diabetes. They concluded that whether interference from other comorbidities is present or not, SARS-CoV-2 pneumonia patients with diabetes are more severe than those without diabetes. Therefore, diabetes should be considered as a risk factor for the outcome of SARS-CoV-2 pneumonia, and more intensive attention should be paid to patients with diabetes, in case of rapid deterioration.

**Roncon et al (2020) Diabetic Patients with COVID-19 infection are at higher risk of ICU admission and poor short-term outcome**

Diabetic patients with COVID-19 are at higher risk of ICU admission and show a higher mortality risk.


This study found that the most prevalent co-morbidities were hypertension (30%) and diabetes (19%).


A total of 1,590 confirmed cases in hospitalised patients in China from December 2019-January 2020 with mean age of 48.9 years. The most prevalent comorbidity was hypertension (16.9%), followed by diabetes (8.2%). Among laboratory-confirmed cases of COVID-19, patients with any comorbidity yielded poorer clinical outcomes than those without. A greater number of comorbidities also correlated with poorer clinical outcomes.

Patients with diabetes have an increased risk of severe complications including Adult Respiratory Distress Syndrome and multi-organ failure. Depending on the global region, 20–50% of patients in the coronavirus disease 2019 (COVID-19) pandemic had diabetes. Given the importance of the link between COVID-19 and diabetes, we have formed an international panel of experts in the field of diabetes and endocrinology to provide some guidance and practical recommendations for the management of diabetes during the pandemic. We aim to briefly provide insight into potential mechanistic links between the novel coronavirus infection and diabetes, present practical management recommendations, and elaborate on the differential needs of several patient groups.


There is evidence of increased incidence and severity of COVID-19 in patients with diabetes. COVID-19 could have effect on 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 disease. Innovations like telemedicine are useful to treat patients with diabetes in these times.

**Ceriello et al (2020) COVID-19 and diabetes management: What should be considered?**

Management of diabetes today has been addressed as an exciting confusion. Ceriello addresses several of the important topics related to the most appropriate way to manage people with diabetes during this pandemic. Topics discussed include the susceptibility to this new infection, the severity of the complications, as well as the role of the drugs to use for the glycemic control.


This year, Ramadan will occur during the global COVID-19 pandemic. Reports show that diabetes appears to be a risk factor for more severe disease with COVID-19. In addition, the UK experience has shown diabetes and COVID-19 is associated with dehydration, starvation ketosis, diabetic ketoacidosis and hyperglycaemic hyperosmolar state. This makes fasting in Ramadan
particularly challenging for those Muslims with diabetes. Hanif et al discuss the implications of fasting in Ramadan during the COVID-19 pandemic and make recommendations for those with diabetes who wish to fast.


This article reports on the COVID-19 outbreak in China focusing on epidemiology, clinical features, treatment prevention and control. A total of 26 cases with fatalities were used to disclose the dangerous comorbidities, showing that the major comorbidities are hypertension (53.8%), diabetes (42.3%), coronary heart disease (19.2%), cerebral infarction (15.4%) and chronic bronchitis (19.2%) … Though the symptom compositions reported for the confirmed cases are similar to that of the fatality cases we collected, the percentages of hypertension, diabetes, and coronary heart diseases are much higher among the fatality cases than among the confirmed cases. This may indicate that the comorbidities are risk factors for COVID-19 patients.

Leung (2020) Clinical features of deaths in the novel coronavirus epidemic in China

46 fatal cases of COVID-19 were included in this study based on clinical data published by the Chinese government. The average age was 70 years. Hypertension (40.5%) and diabetes (26.2%) were the two most prevalent co-morbidities.

Zhang et al (2020) Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China

The data on 140 hospitalised patients with confirmed diagnosis of SARS–Cov2 viral infection was extracted by the authors. Median age was 57 years. The most common co-morbidities found were hypertension (30%), Diabetes Mellitus (12.1%) and COPD (1.4%).


In this editorial, Angelidi et al review the clinical observations related to diabetes and COVID-19 in China, Italy, and the United States. They review the pathogenesis of, and immune response to SARS-CoV-2 infection. They also outline proposed mechanisms that may predispose individuals with diabetes both to infection and severe disease. Finally, they highlight areas that
warrant further investigation and discuss management considerations for clinicians.


It is unknown if people with diabetes are more susceptible to COVID-19, but they appear at higher risk of infection and severe disease. The first 3 deaths in Hong Kong from COVID-19 were patients with diabetes. Citing Guan: It is currently unknown why people with diabetes, hypertension or other chronic diseases are more severely affected by COVID-19, but one possible explanation involves angiotensin-converting enzyme 2 (ACE2). Furthermore, people with diabetes and hypertension are often treated with ACE inhibitors and angiotensin receptor blockers (ARBs), which can lead to increased expression of ACE2, thereby facilitating viral uptake and increasing the risk of severe infection for people with diabetes.


The authors highlight results of a meta-analysis of studies reporting the prevalence of diabetes among people infected with the SARS-CoV-2. 12 Chinese studies were included with a total of 2108 patients with a confirmed diagnosis of SARS-Cov-2. The mean age was 49.6 years, with the prevalence of diabetes comorbidity at 10.3%. The authors also included the figures of a nationwide prevalence of diabetes in China from 2013 which was 10.9%. Based on these data, the authors conclude that diabetes may not increase the risk of SARS-CoV-2 infection but can worsen the outcome of this new coronavirus disease. This finding is consistent with the association between diabetes and excess mortality from any acute and chronic condition, including infections.

**Bloomgarden (2020) [Commentary] Diabetes and COVID-19**

Regardless of the potential for the spread of COVID-19, as with influenza-related mortality, diabetes is an important risk factor for adverse outcome. Evidence of risk among persons with diabetes has been reported for the two earlier CoV infections, severe acute respiratory syndrome (SARS) beginning in 2002 and affecting more than 8000 persons, mainly in Asia and the Middle East respiratory syndrome (MERS) in 2012 affecting more than 2000 persons.
OTHER

Associations

- International Diabetes Federation: COVID-19 and Diabetes
- Diabetes UK: Updates: Coronavirus and Diabetes
- Diabetes Ireland: COVID-19 and Diabetes
- American Diabetes Association: Diabetes and Coronavirus

Social Media
A group of specialist clinicians in Britain have set up a social media account to provide information: Diabetes 101 @ diabetes101.
Produced by the members of the National Health Library and Knowledge Service Evidence Team1. Current as at 28.04.2020. 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:

**PEOPLE WITH DIABETES INFECTED WITH COVID-19**

**PROGNOSIS, PROGRESSION, CLINICAL OUTCOMES**

The following search strategy was used:

**MEDLINE**
1. (mh "coronavirus+")
2. Covid-19 or coronavirus or "corona virus" or (wuhan n2 virus) or ("2019-ncov" or "2019 ncov") or "severe acute respiratory syndrome coronavirus 2" or ("2019" and (new or novel) and coronavirus)
3. 1 or 2
4. (mh "diabetes mellitus+") or (mh "diabetes mellitus, type 2+") or (mh "diabetes mellitus, type 1+") or (mh "diabetes complications+")
5. Diabet*.ab,ti.
6. 4 or 5
7. 3 and 6
8. Limit 7 to yr="2019 – 2020"

**EMBASE**
1. Coronavirusae/ 2. Covid-19.abt. 3. Coronavirus.abt. 4. "corona virus".abt. 5. (wuhan adj3 virus).abt. 6. ("2019-ncov" or "2019 ncov").abt. 7. "severe acute respiratory syndrome coronavirus 2".abt. 8. ("2019" and (new or novel) and coronavirus).abt. 9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8

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31 Angelidi AM, Belanger MJ, Mantzoros CS. COVID-19 and diabetes mellitus: What we know, how our patients should be treated now, and what should happen next [published online ahead of print, 2020 Apr 19]. Metabolism. 2020;154245. doi:10.1016/j.metabol.2020.154245