

Title	Challenges of Diabetes Management during the COVID-19 Pandemic
--------------	---

Emma S Scott
Royal North Shore Hospital
Department of Endocrinology and Diabetes
St Leonards, New South Wales
Australia

NHMRC Clinical Trials Centre
University of Sydney
Camperdown, New South Wales
Australia

Alicia Jenkins
Professor
University of Sydney
NHMRC Clinical Trials Centre
Camperdown, New South Wales
Australia

Gregory R Fulcher
Royal North Shore Hospital
Department of Endocrinology and Diabetes
University of Sydney
St Leonards, New South Wales
Australia

University of Sydney
Northern Clinical School
St Leonards, New South Wales
Australia

Introline: How to deal with diabetes and COVID-19 - do we just dial in?

Abstract: The COVID-19 pandemic has changed the way that chronic health care is delivered. The need for social distancing to minimise viral spread has necessitated the rapid uptake of telehealth modalities to deliver health care. Individuals with diabetes may be more susceptible to COVID-19 or its more serious consequences. Glycaemic control and smoking status will likely modulate such risk. It is imperative that these individuals maintain regular contact with their health providers to facilitate tight glycaemic control and to enable education regarding sick day management in the event of illness.

Text	
Text word count	1499 words

The emergence of the corona virus SARS-CoV-2, and the subsequent announcement by the World Health Organisation of a global pandemic has altered health care across the public and private sectors. Clearly, COVID-19 is having a huge impact on general practitioners, emergency physicians, respiratory physicians, intensivists and related staff, and is also impacting the day-to-day delivery of chronic health care.

Conditions such as Type 1 and Type 2 Diabetes require regular usually face-to-face contact with general practitioners, endocrinologists, diabetes educators, dieticians and podiatrists to optimise glycaemic control. However, with recommendations regarding social isolation to minimise spread of corona virus (1), the delivery of such health care is increasingly being delivered using telehealth. This has been greatly facilitated in Australia with the announcement of temporary MBS telehealth (videoconference and telephone) item numbers during the COVID-19 pandemic (2). The eligibility criteria for bulk-billing includes individuals who are immunosuppressed or with chronic health conditions, which of course includes diabetes mellitus. Significantly, the eligibility criteria also include pregnancy. At a time when individuals are being asked to socially isolate to minimise exposure to SARS-COV-2, many of the people who greatly need ongoing health care are avoiding these appointments out of fear of infection from those also attending the clinic and perhaps from clinicians, who are recognised to be at high risk of infection. It is therefore crucial that telehealth care services are offered (and if

not available fast-tracked). This may be via videoconference, or a phone call for those who are less able to use newer technologies, or if videoconferencing services are not available. Services traditionally offered in a group setting, such as group education for those with gestational diabetes or Type 2 diabetes may also be able to be delivered via this technology.

The use of diabetes technology can benefit healthcare and the telehealth consultation. Continuous glucose monitoring (CGM) or flash glucose monitoring (FGM) can be used with both Type 1 and 2 diabetes with therapeutic benefit. Many of these devices can upload automatically to cloud-based software such as Dexcom Clarity™ or Freestyle LibreView™. Other devices such as insulin pumps and blood glucose meters can be uploaded by the user prior to the consultation, which of course places a greater burden on the individual. Involvement of parents, carers and diabetes educators prior to the appointment may be of benefit. This may lead to improvements in the individual diabetes self-management.

The electronic medical record is vital in updating changes to medications, results and scheduled appointments. Many pathology providers facilitate electronic access to test results, but anecdotally some patients may avoid having pathology tests taken in order to minimise travel and exposure to others.

The individuals who are at greatest risk of complications from COVID-19 are still being determined. It seems clear that individuals with diabetes and other chronic comorbidities are at increased risk of morbidity. A number of small observational

studies have analysed comorbidities in individuals with severe SARS-CoV-2 infection from China. Rates of diabetes (type unspecified, but most likely to be Type 2 diabetes given the low incidence of Type 1 diabetes in China) are reported between 7.4% in confirmed cases infection (3), and up to 17% in cases with severe pneumonia (4). A recent meta-analysis of six studies (including 1527 people) analysed the prevalence of comorbidities amongst individuals with severe and non-severe COVID-19 (5). Diabetes complicated 11.7% of severe cases compared to 4% of cases of non-severe COVID-19. This did not reach statistical significance; however this is clearly limited by a lack of statistical power and further analyses are required. Retrospective analysis of survivors and non-survivors of the previous coronavirus (SARS-CoV) suggested that diabetes was a predictor for mortality (6). This association seemed to be driven by glycaemic control, with an independent association with elevated fasting plasma glucose. This further highlights the need to maintain ongoing medical care to optimise glucose control throughout the current COVID-19 pandemic.

Whilst there is not an evidence-base as yet, it seems prudent for people with diabetes who currently smoke to cease smoking. In addition, having the recently available influenza vaccine, which is usually recommended for people with diabetes, would be advisable, although patients should be aware that this will not protect against COVID-19.

Individuals with both Type 1 and Type 2 diabetes need to have clear action and sick day plans in the eventuality that they become unwell and should be encouraged to seek face-to-face care for complications such as myocardial infarction or high risk foot ulcer.

This should be emphasized even for individuals with long-standing diabetes, who's initial diabetes education may have been years ago. Individuals with Type 1 diabetes should have ketone monitoring strips available, preferably blood ketone test-strips, know when to test for ketones and should be aware of the need to give additional insulin doses (via injection or continuous subcutaneous insulin infusion (CSII)) during an intercurrent illness. Excellent sick day management resources are available on the Australian Diabetes Educators Association (ADEA) and NDSS websites.

Individuals using hybrid closed loop (insulin) pumps (Medtronic 670G) should be educated that during illness the wearer may need to exit auto mode to enable more rapid correction of hyperglycaemia with manual correction boluses of insulin and a temporary increased basal rate (7). The algorithm within the hybrid closed pump may otherwise not adapt quickly enough to manage hyperglycaemia during acute illness.

With the increased use of SGLT2 inhibitors in Australia and internationally, all individuals treated with SGLT2 inhibitors should be educated of the need to withhold these drugs during illness to minimize the risk of ketoacidosis (8). This should be reiterated to general practitioners and emergency physicians to screen for SGLT2 use in those presenting with COVID-19 or any illness.

There have been mixed anecdotal reports as to whether non-steroidal anti-inflammatory drugs (NSAIDs) may predispose to COVID-19. There has been suggestion that NSAIDs may upregulate ACE2 (9), and therefore potentially predispose by a similar

mechanism suggested for ARBs. Currently there are no guidelines to avoid the use of NSAIDs.

In relation to COVID-19, there is also increasing interest in the use of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) in individuals with Type 1 or Type 2 diabetes and other chronic care conditions, such as diabetes. SARS-CoV-2 binds to the human angiotensin-converting enzyme2 (ACE2) allowing entrance into the host cells (10). ACE inhibitors and ARBs can result in upregulation of ACE2 in some tissues in both human and animal models (9, 11, 12). However, not all groups have found a link between these antihypertensives and upregulation of ACE2 (13). It has been proposed that ACE inhibitors and ARBs may theoretically increase the susceptibility to COVID-19 via increased ACE2. However, there is currently no evidence to link the use of these agents to increased risk or severity of COVID-19. Indeed, other research groups have hypothesized that the use of ARBs may be a potential therapeutic modality (14). Following SARS-CoV-2 binding to ACE2, there is downregulation of ACE2 with subsequent increased angiotensin and exacerbation of COVID-19 related lung injury. Gurwitz *et al* propose that the downregulation of ACE2 by ARBs might protect against such injury (14). Other groups have suggested that ARBs may stabilise the binding of ACE2 to the type 1 angiotensin receptor, and therefore may reduce available binding sites for SARS-Cov-2 (15). Currently, there is little evidence to suggest changing antihypertensive therapy and multiple national and international bodies including the Australian Diabetes Society, American College of Cardiology and European Society of Hypertension have recommended that ACE inhibitors and ARBs should not be ceased. Trials are currently

underway to assess the impact of these agents during COVID-19 infection. Patients should be encouraged to continue their ACE/ ARB drugs, and if not prepared to do so be offered alternate drugs for blood pressure control.

Finally, this is a time of great concerns to all individuals, and perhaps more so to those who have been informed they are at greater risk of COVID-19 and its complications. This may necessitate a greater state of preparedness. The current advice is that there will be no shortage of insulin supplies or consumables needed for insulin pump therapy or blood glucose monitoring equipment, yet anecdotally, local pharmacy shortages of insulins, ketone strips and oral hypoglycaemic drugs have been reported and are being addressed by government prescription limits . Should patients be unable to obtain their usual prescriptions suitable alternatives can be recommended to them by their diabetes care clinicians. It is critical that individuals with diabetes and other chronic conditions do not hoard these medical supplies and inadvertently create a critical supply shortage.

Continuation of health care to at risk individuals is crucial throughout the pandemic. Telehealth is the key for the delivery of such care. It is important that people with diabetes are educated regarding the management of their condition during acute illness, including medication changes. It is also critical that there is not a deterioration in the medical management of glycaemia and other complications of diabetes, which if neglected, may result in increased morbidity and mortality independent of COVID-19.

References

References should be in [Vancouver style](#) and should **not** appear as endnotes.

References to material on the Internet should include the organisation, the page title, the article title and the author (if there is one) as well as the URL and the month the page was visited ([see examples here](#)).

1. Ebrahim SH, Ahmed QA, Gozzer E, et al. Covid-19 and community mitigation strategies in a pandemic. *BMJ*. 2020;368:m1066.
2. Australian Government Department of Health. MBS changes factsheet. 2020. [http://www.mbsonline.gov.au/internet/mbsonline/publishing.nsf/Content/0C514FB8C9FBBEC7CA25852E00223AFE/\\$File/COVID-19bbspecialists.pdf](http://www.mbsonline.gov.au/internet/mbsonline/publishing.nsf/Content/0C514FB8C9FBBEC7CA25852E00223AFE/$File/COVID-19bbspecialists.pdf) (accessed March 2020).
3. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020.
4. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020.
5. Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol*. 2020.
6. Yang JK, Feng Y, Yuan MY, et al. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. *Diabet Med*. 2006;23(6):623-8.
7. Aleppo G, Webb KM. Integrated Insulin Pump and Continuous Glucose Monitoring Technology in Diabetes Care Today: A Perspective of Real-Life Experience with the Minimed() 670g Hybrid Closed-Loop System. *Endocr Pract*. 2018;24(7):684-92.

8. Goldenberg RM, Berard LD, Cheng AYY, et al. SGLT2 Inhibitor-associated Diabetic Ketoacidosis: Clinical Review and Recommendations for Prevention and Diagnosis. *Clin Ther.* 2016;38(12):2654-64 e1.
9. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *Lancet Respir Med.* 2020.
10. Wan Y, Shang J, Graham R, et al. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. *J Virol.* 2020;94(7).
11. Esler ME, D. Can angiotensin receptor-blocking drugs perhaps be harmful in the COVID-19 pandemic? *Journal of Hypertension.* 2020;38:000-.
12. Ocaranza MP, Godoy I, Jalil JE, et al. Enalapril attenuates downregulation of Angiotensin-converting enzyme 2 in the late phase of ventricular dysfunction in myocardial infarcted rat. *Hypertension.* 2006;48(4):572-8.
13. Ramchand J, Patel SK, Srivastava PM, et al. Elevated plasma angiotensin converting enzyme 2 activity is an independent predictor of major adverse cardiac events in patients with obstructive coronary artery disease. *PLoS One.* 2018;13(6):e0198144.
14. Gurwitz D. Angiotensin receptor blockers as tentative SARS-CoV-2 therapeutics. *Drug Dev Res.* 2020.
15. Sparks MH, S. The coronavirus conundrum: ACE2 and hypertension edition nephjc.com 2020 <http://www.nephjc.com/news/covidace2> (Accessed March 2020).

