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Considerations for people with diabetes during the Coronavirus Disease (COVID-19) pandemic

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ABSTRACT

Introduction: The severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) continues to cause havoc globally, resulting in unprecedented healthcare, societal and economic disruption. People with diabetes have been shown to be at higher risk of complications and death when exposed to pneumonia, influenza and other coronaviruses. Despite pandemic scale infection, there is currently limited understanding on the potential impact of coronavirus disease (COVID-19) on people with diabetes.

Aims: (1) To characterise the outcomes of COVID-19 for people with diabetes and (2) add value to current recommendations for healthcare providers and people with diabetes to encourage optimal management.

Methods: A search of PubMed, Embase and MEDLINE to March 2020 was undertaken, using search terms pertaining to diabetes, coronavirus and acute respiratory distress syndrome (ARDS). We briefly reviewed the epidemiology and pathophysiology of SARS-CoV-2 in the context of diabetes.

Conclusion: People with diabetes are at greater risk of severe infection and death with COVID-19. COVID-19 has significantly impacted the daily lives of individuals living with diabetes through financial implications, food and medication scarcity and its burden on mental health. In Australia, delivery of medical care has been adapted to reduce the risk of transmission, with a particular emphasis on telehealth and remote monitoring.

Abbreviations: ACE2, Angiotensin-converting-enzyme 2; ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; MERS-CoV, Middle East respiratory syndrome coronavirus; SARS-CoV-1, severe acute respiratory syndrome coronavirus 1; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

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1. Introduction

The novel severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) originating in Wuhan, China has spread rapidly around the world. On March 11th 2020, the World Health Organisation (WHO) declared the coronavirus disease (COVID-19) a pandemic [1]. This virus has had devastating consequences on a global scale [2]. People with diabetes are more susceptible to adverse outcomes and death from respiratory tract infections [3], influenza A (H1N1) [4], severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) [5], and the Middle East respiratory syndrome coronavirus (MERS-CoV) infection [6]. Diabetes, particularly in patients aged 70 years or older, has been strongly associated with an increased risk of infection and complications [7,8]. It is unclear if susceptibility to infection in people with diabetes is due to a chronic inflammatory state with associated alterations in glucose metabolism and dysregulation of the immune system or due to the renal, vascular and cardiovascular complications frequently associated with diabetes and increasing age [9].

Our understanding of the health impact of COVID-19 in people with diabetes is evolving. It is clear that community management of diabetes has been directly and indirectly impacted by COVID-19. In order to minimise the transmission risk between healthcare workers and their patients or consumers, public health policies have focussed on early detection, self-isolation of positive cases, infection control precautions and minimising face to face contact through the use of telemedicine [10].

We aimed to review the impact of COVID-19 on people living with diabetes in Australia. We provide practical recommendations for the management of diabetes in the outpatient setting.

2. Methodology

We undertook a search of PubMed, MEDLINE, EMBASE, Google Scholar using the key words “diabetes”, “coronavirus”, “SARS”, “MERS” and “management”. Studies with full text English versions were included. We reviewed the literature on the epidemiology and pathophysiology of COVID-19, which are relevant for people with diabetes. Recommendations were summarised in addition to expert guidance based on the following topic areas: diabetes specific, general prevention and logistical considerations.

3. Epidemiology of COVID-19

The 2019 SARS-CoV-2 outbreak is believed to have originated from a zoonotic source in the Huanan wholesale seafood market, in Wuhan City, China [11]. Highly contagious, SARS-CoV-2 has rapidly spread throughout China and worldwide, with person-to-person spread the main mode of transmission [12]. Since initial detection, there have been over 1 million laboratory confirmed cases globally, with the largest burden of morbidity and mortality arising in European cities and the United States [2].

Whilst all ages are susceptible, children are significantly less affected, with 2–3% of reported cases occurring in individuals under age 19 years [11]. The majority of cases (87%) appear to affect individuals between 30 and 79 years. Disease severity appears to worsen with age and underlying comorbid conditions [13,14]. The incidence of diabetes in COVID-19 cases in China has varied from 5% to 20% however large-scale data suggest incidence may be in the order of 5.3–7.4% (15–21) (refer to Appendix 3). These discrepancies may be attributed to incomplete data due to lack of testing and comorbid analysis of cases of death. In comparison, diabetes was reported in approximately 10.9% of the Chinese population prior to COVID-19 [22,23]. Therefore based on early prevalence studies in China, it appears that people with diabetes are not significantly more likely to be infected with COVID-19.

3.1. *Severity of infection in people with diabetes*

People with diabetes are at increased risk of severe infection [13,24] and poorer prognosis with COVID-19 infection [25]. An early meta-analysis of six studies involving 1527 patients by Li *et al* found that although the incidence of diabetes in patients contracting COVID-19 were similar to that of the general population, there was a two-fold increase of diabetes in those with severe COVID-19 cases, severe infection was defined as patients requiring ICU admission (Risk Ratio 2.21, 95% CI 0.88–5.57, P = 0.09) [13]. The meta-analysis had several limitations including substantial heterogeneity and low to moderate quality studies. Furthermore, a cohort study of 339 patients found a 4-fold rise in severe COVID-19 infection in the presence of diabetes, after adjusting for age, sex, obesity and hypertension (Adjusted- Odds Ratio 2.05, 95% CI 1.01–4.19, P < 0.05) [24]. Moreover, diabetes has been reported in 33–58% of critical COVID-19 cases requiring admission to intensive care unit in the United States, whilst rates in Italy have been modest at 17% [18,26–28].

3.2. *Mortality in people with diabetes*

In a large China cohort study of 1590 individuals, mortality rate of patients with diabetes was significantly higher than people without diabetes (10% vs 2.5% respectively; $p < 0.001^2$) [14]. Mortality is further increased in people with more than one coexisting comorbid condition [14], an important consideration, given that diabetes is commonly associated with multiple organ systems, including renal and cardiovascular complications. From 55,924 laboratory confirmed cases in China in February 2020, mortality was highest in people over 80 years (case fatality rate (CFR) of 21%) and those with comorbidities (CFR for cardiovascular disease 13%, diabetes 9.2%, hypertension 8.4%, chronic respiratory disease 8.0% and cancer 7.6% vs patients with no comorbid condition CFR 1.4%) [11]. Additionally, population based data by the England National Health Service has revealed that diabetes was prevalent in one of four (26%) patients who had died in hospital and tested positive for COVID-19 [29].

3.3. *Australian epidemiology*

As of the 19th of April 2020, 6606 cumulative confirmed cases and a total of 69 deaths have been reported in Australia [30]. Of total cases, 12% were admitted to hospital and a further

17% of those admitted patients required intensive care unit (ICU) admission for ventilatory support. Diabetes was the most prevalent comorbidity among hospitalised cases admitted to an ICU followed by cardiovascular disease in 24% and 22% of patients respectively. Diabetes was also the most commonly reported comorbid condition among SARS-CoV-2 associated death, with 33% of fatalities having diabetes [30]. The median age of SARS-CoV-2 deaths was 79 years (interquartile range: 74–84 years) indicating that frailty was associated with increased severity of infection and mortality [30] which is consistent with international reports [11]. However, stringent social distancing measures and expanded testing criteria by the federal government has led to a sharp decrease in the incidence of new COVID-19 cases in Australia since the beginning of April 2020 (*see* Fig. 1).

4. Pathophysiology of COVID-19

Severe acute respiratory syndrome coronavirus 2 is an enveloped, single stranded, positive-sense RNA virus, which is believed to be in the same subgenus as SARS-CoV-1, and distantly related to MERS-CoV [31]. Coronaviruses have the largest genome out of all RNA viruses with typically 27 to 32 kilobases enclosed within a nucleocapsid [32]. Bound to the coronavirus envelope are spike glycoproteins which give the virus its distinctive "halo" appearance under electron microscope [33,34]. Aside from giving coronavirus its characteristic name, spike glycoprotein receptor binding domains (RBDs) bind to angiotensin-converting-enzyme 2 (ACE2) surface receptors with high affinity, mediating viral entry into the host cell and enhancing the pathogenicity of SARS-CoV-2 [32,34] (Fig. 2). Upon binding to ACE2, SARS-CoV-2 invades the host cell through endocytosis, leading to the subsequent down regulation of surface ACE2 receptor [35].

Angiotensin-converting-enzyme 2 is a type I membrane bound receptor with a single active site and is abundant in mucosal epithelial cells within lung alveolar tissue, as well as the heart, kidney, intestine and blood vessels [36,37]. Angiotensin-converting-enzyme 2 is also an endogenous inhibitor of the renin-angiotensin system (RAS) through degradation of angiotensin II into angiotensin 1–7 [38] (Fig. 1). Angiotensin 1–7 subsequently binds to the protein-coupled receptor Mas and exerts vasodilatory, antithrombotic, antiproliferative and antioxidative effects [39] (*see* Fig. 2).

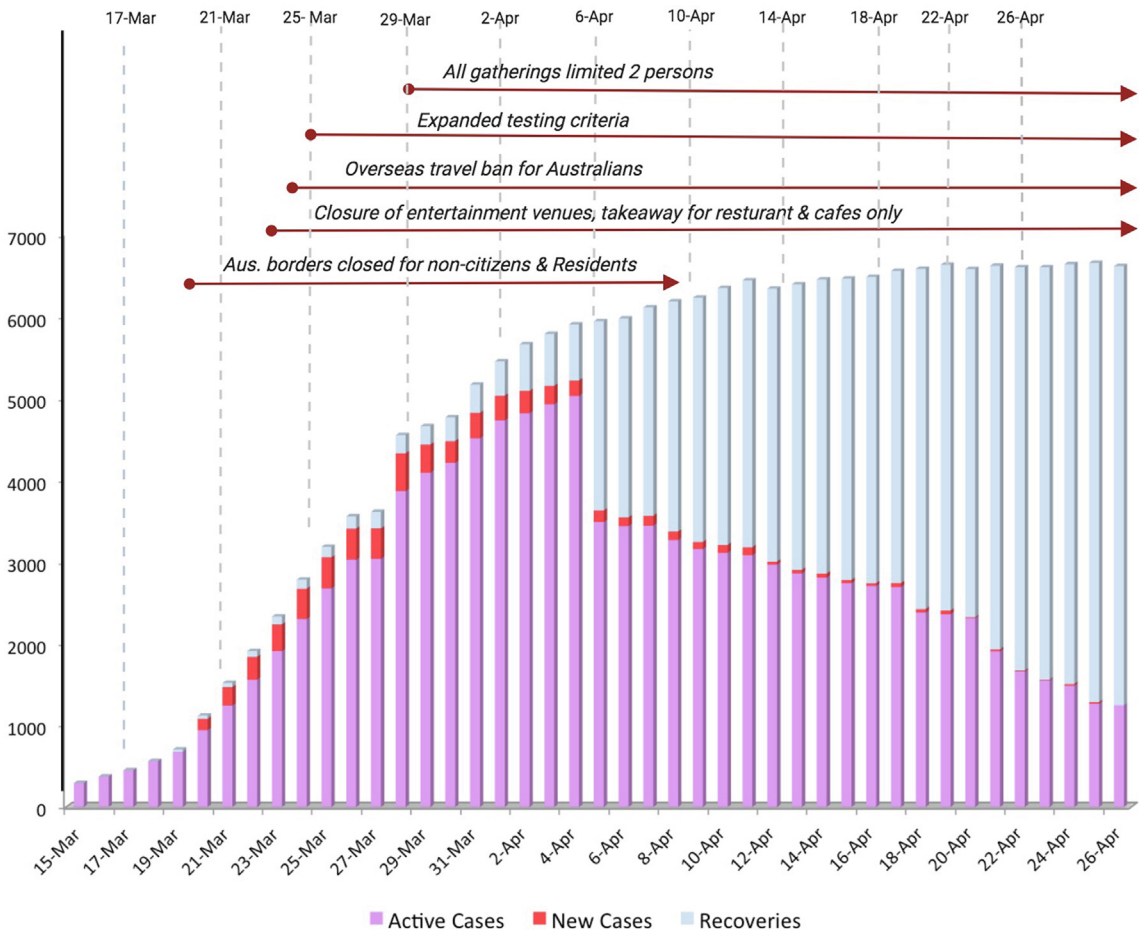

Fig. 1 – Australian timeline for COVID-19 infected cases and recovery in relation to social distancing measures, data adapted from various sources [93,94].

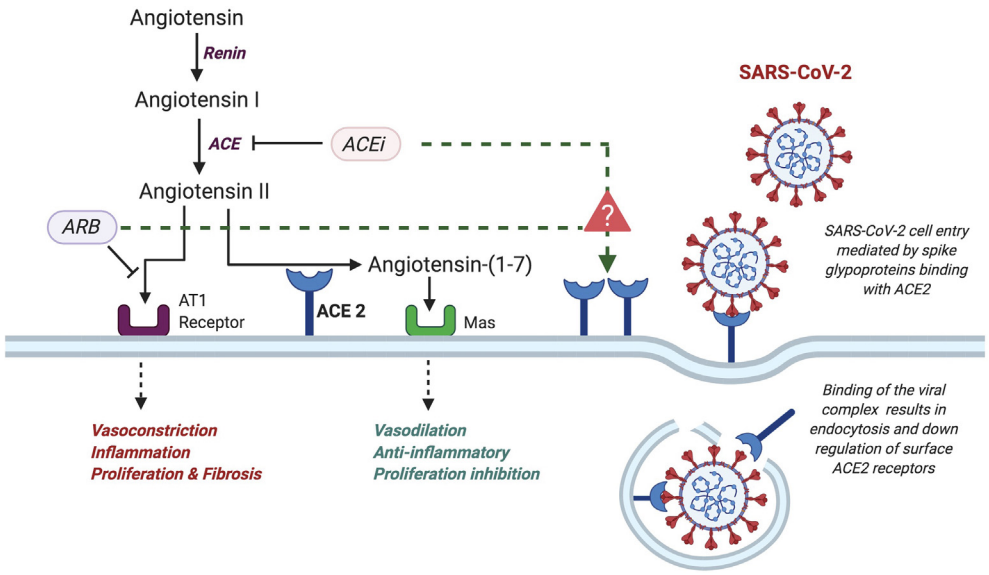

Fig. 2 – The Role of ACE2 in Renin Angiotensin System and SARS-CoV2 infection. (a) ACE2 cleaves angiotensin II into angiotensin 1–7 which exerts anti-inflammatory vasoprotective effects; (b) Conflicting studies have suggested that ACEi and ARBs may interfere with ACE2 activity and expression leading to significant interest in the role of ACEi and ARBs in modulating COVID-19 disease; (c) ACE2 is located on cell membrane and mediates entry of SARS-CoV-2 by binding to spike glycoprotein resulting in endocytosis of viral complex and down regulation of ACE2.

5. Possible link between diabetes and COVID-19

5.1. *ACE2 and inhibition of the renin-angiotensin system*

In healthy individuals, circulating ACE2 is low [40]. However, circulating ACE2 is increased in individuals with diabetes, hypertension and nephropathy [38,41]. This has been ascribed to a compensatory mechanism to account for overactivity of angiotensin II and the RAS in people with diabetes [43]. Importantly there is currently no clinical data in humans to indicate that a change in ACE2 activity alters susceptibility to SARS-CoV-2 infection.

Many people with cardiovascular complications and nephropathy due to diabetes are prescribed ACE inhibitors (ACEi) or angiotensin II receptor blockers (ARBs) for cardiovascular [42] and renoprotective effects [43,44]. There has been speculation that the use of ACEi and ARBs may upregulate ACE2 [45]. An animal study showed that binding of angiotensin II to angiotensin type I (AT_1) receptor activated MAP kinase-phosphotase signalling pathways, which reduced ACE2 mRNA gene expression and activity [46]. Therefore it is suggested that ACEi may increase ACE2 by inhibiting the formation of angiotensin II and subsequently its' negative regulation of ACE2 (*see* Fig. 2). Others suggest that angiotensin II binds to the AT_1 receptor, which mediates internalisation of ACE2 and degradation by lysosomes. This process was inhibited by the ARB, Losartan [47].

Whilst some animal studies have demonstrated upregulation of ACE2 gene expression in response to ACE inhibition [48,49], normotensive models were used and these studies failed to investigate whether increased ACE2 gene expression correlated with increased ACE2 activity. Other animal studies have contradictorily shown no increase in ACE2 gene expression or activity levels with ACEi or ARBs [50,51]. To date, human studies have shown no evidence of upregulation of ACE2 activity in patients on ACEi or ARBs [38,52]. Thus the ongoing use of usual ACEi and ARBs for blood pressure management in patients with diabetes continues to be supported by the Australian Diabetes Society (ADS) as well as other international bodies [53].

5.2. *Alterations of the immune system in people with diabetes*

Diabetes mellitus is characterised by a chronic low-grade inflammatory state induced by excess adipose tissue [54]. Elevated levels of tumour necrosis factor (TNF)-a, interleukin (IL)-6, C-reactive protein, plasminogen activator inhibitor and reactive oxygen species (ROS) have been demonstrated in adipose tissue of obese mice [55,56]. These inflammatory cytokines are believed to inhibit insulin signalling by serine phosphorylation of insulin receptor substrate via activation of Iκβα kinase β (IKKβ) and c-Jun N-terminal kinase I (JNK1) mediators [57]. Activated IKKβ also results in transcription of various other inflammatory genes [57]. In addition to the pathogenesis of insulin resistance and type 2 diabetes, increased proinflammatory macrophages, cytokines, chemokines and proteases contribute to the development of diabetes related retinopathy, nephropathy, neuropathy and cardiovascular disease [58].

Individuals with diabetes are at increased risk of infection due to dysregulation of the innate and humoral immune system. Previous studies demonstrated that hyperglycaemia upregulates adhesion molecules (intracellular cell adhesion molecule-1, vascular cell adhesion molecule-1 and E-selectin and CD11b) on endothelial cells and neutrophils

[59,60], which is believed to diminish neutrophil chemotaxis at sites of infection [1]. Acute hyperglycaemia also impairs neutrophil phagocytosis and bactericidal activity [59,61,62], respiratory burst capacity [63,64] and formation of granular elastase and myeloperoxidase extracellular traps leading to susceptibility to infection [65]. Acute hyperglycaemia has also been associated with reduced complement fixation and opsonization of microorganisms [66]. Suppression of cytokine production by peripheral blood mononuclear cells and monocytes isolated from individuals with diabetes has been reported [57]. These inflammatory mediators are important for inducing the adaptive immune response, and therefore may explain the increased susceptibility to invading pathogens in people with diabetes [67]. Further evidence suggests that insulin treatment may restore immune function by improving chemotaxis, phagocytosis and bactericidal capacities of neutrophils [9,68] and thereby supporting the importance of adequate blood glucose management during COVID-19.

6. Effect of diabetes control on COVID-19 disease outcome

Zhu et al. utilized a retrospective longitudinal multi-centered cohort study to investigate the relationship between plasma glucose levels and COVID-19 outcome in 952 patients with diabetes [69]. They found inpatient plasma glucose levels more than 10 mmol/L were associated with adverse outcomes and death from COVID-19. The hazard ratio (HR), adjusted for age, gender, comorbidities, and site effect, of the all-cause mortality in the well managed type 2 diabetes mellitus (T2DM) group (blood glucose < 10 mmol/L) compared to the suboptimally managed T2DM group (blood glucose > 10 mmol/L) was 0.13 (95%CI, 0.04–0.44; p < 0.001) [69]. The prevalence of acute respiratory distress syndrome and acute heart injury were also lower in the well managed T2DM group, HR 0.41 [95% CI, 0.25–0.66, p < 0.001) and 0.21 (95% CI, 0.07–0.59, p = 0.003) respectively [69]. However, authors did not have access to pre-hospital data and therefore were unable to determine the associations between pre-hospital glycemic status on the natural history of COVID-19, nor investigate if active inpatient management of hyperglycaemia improved COVID-19 adverse outcomes.

Patients with stress hyperglycaemia, without a previous history of diabetes, is associated with an increase in COVID-19 disease severity and mortality as seen in those with established diabetes [70]. Additionally, in these individuals, increased levels of raised inflammatory biomarkers, hypercoagulopathy as well as leukocytosis and neutrophilia were also comparable to those seen in patients with established diabetes [70,71], suggesting that perhaps hyperglycaemia may reflect consequences of a counter-regulatory state during severe COVID-19 infection [71]. Similar outcomes have been observed in retrospective studies in the USA. Among hospitalized patients with COVID-19, those with diabetes and/or uncontrolled hyperglycaemia had a four-fold increase mortality rate than those without (28% vs 6.2%, P < 0.001). Patients with diabetes and/or uncontrolled hyperglycaemia who survived and were discharged from hospital, had a significant increase length of stay compared to their counterparts (median 5.7 vs 4.3 days, P < 0.001) [72].

Recently, Ren et al (2020) investigated the association between the triglyceride and glucose index (TyG) with severity and mortality of COVID-19 [73]. They found that TyG index levels were significantly higher in the severe cases and death group after controlling for confounding variables. The TyG index has been positively associated with arterial stiffness, nephric microvascular damage and coronary artery disease, however is not a direct marker of metabolic control [73].

Whilst there is substantial evidence to suggest a strong association between hyperglycaemia, irrespective of diabetes status, and poorer prognosis, it is difficult to prove cause and effect based on the available observational studies. Further interventional studies are required to draw definitive conclusions.

7. Consequences of COVID-19 for people with diabetes

7.1. *Financial implications and food security*

The International Monetary Fund (IMF) has projected the global economy to contract sharply by approximately three percent, surpassing that of the 2008 global financial crisis [74]. In Australia, unemployment rates are expected to rise to 10%, almost doubled from rates in February this year [75]. The Australian government has responded quickly with stimulus packages of almost $320 billion dollars, providing financial support to businesses and employees, education providers and other community services including the “JobKeeper” and “JobSeeker” packages [76].

According to the Department of Agriculture, approximately 90% of Australia’s’ food supply is sourced locally with Australia producing substantially more food than it consumes [77]. Despite this, uncertainties around the impacts of COVID-19 initially triggered panic buying and stockpiling of staple goods resulting in temporary disruption in supermarket supply [77]. It is unclear what the impact of social isolation, home schooling and financial instability will have on healthy eating behaviours and glycaemia management. The disruption to work, school and social routine may lead to “stress and emotional eating” of high-calorie and high glycaemic index foods [78].

7.2. *Mental health and wellbeing*

Reduction in international travel, domestic movement, social distancing measures and various public health action have been successful at declining rates of infection since peak on the 29th of March [30] (*see* Fig. 1). However, these essential restrictions have been associated with rising anxiety, depression and disenfranchised grief due to loss of autonomy, occupational identity, capacity to earn an income, social connections and participation in purposeful activities [79]. Beyond Blue, an Australian non-profit organisation, has

reported a 30% increase in community calls since the implementation of social restrictions [80]. Anxiety and depression have previously been associated with poor glycaemic management in people with diabetes [81,82].

7.3. *Impact on health care delivery*

Telehealth, defined as the delivery of health care through the use of telecommunications and virtual technology, has been heavily utilised since the outbreak of the COVID-19 pandemic. Ninety-two new Medicare Benefits Schedule (MBS) telehealth items have been made available to medical, nurse and allied health practitioners as well as mental health providers to enable bulkbilled telehealth consultations [83]. Legislative changes have also been introduced to legalise electronic prescriptions and home delivery of medications for vulnerable patients and those in isolation [84].

Hospitals have converted the majority of face to face outpatient appointments to telehealth consultations, with the main provider of telehealth consultations reporting increased usage from 400 consultations to over 10,000 a day [85]. The use of telehealth in the management of diabetes prior to the pandemic has been well documented with evidence to support improved glycaemic management [86,87] and patient satisfaction [88] compared to conventional health services. Although long-term outcomes from telehealth are lacking, short to intermediate term improvement in hyperglycaemia and patient engagement makes telehealth a viable way to deliver health care during periods of pandemic and natural disasters. There are however potential barriers to telehealth such as internet connectivity, age, fear and lack of support to use technology, access to devices, patient preference for face-to-face encounters and patients with hearing and/or vision impairments [89].

7.4. *Access to medications and diabetes technology*

Measures to prevent medication stockpiling have been introduced since the 19th of March to ensure people have adequate access to pharmaceuticals. Pharmacies have been limited to dispensing and supplying only one month of medications for certain prescriptions and over-the-counter medications [90]. In Australia, there is currently no shortage in the ability to manufacture and supply insulin [53].

To reduce the burden on primary care and general practitioners, pharmacists have also been given interim authority to continue supply of usual medications for up to one month on Pharmaceutical Benefit Schedule without prescription. These emergency measures were initiated following the widespread bushfires in Australia in January and are set to continue until at least the end of June 2020 in light of COVID-19 pandemic [90]. Since 2017, over $354 million dollars has been invested to provide subsided continuous glucose monitoring (CGM) products to people with type 1 diabetes who are pregnant, planning for pregnancy, aged 21 or older with concession cards or individuals with similar condition requiring insulin [91].

With the increasing use of insulin pump therapy and CGM devices, telemonitoring of diabetes management can be improved to help support individuals with diabetes and avoid prolong hyperglycaemia and its complications. This increase in technology will also greatly complement telehealth by providing invaluable, real-time data and improve patient engagement and contact through the COVID-19 pandemic and beyond. Clinicians can access the uploaded reports and assist people with diabetes remotely leading to collaborative decision making to improve outcomes including reducing hypo and hyperglycaemia [92].

8. Summary

People with diabetes are more likely to experience severe infection and death from COVID-19. Frailty, pre-existing comorbid conditions and underlying immune system dysfunction may contribute to poorer outcomes. We suggest the continuation of usual care for people with diabetes incorporating telehealth, with a larger focus on sick day management, early detection and testing for SARS-CoV-2 where permissible and increased blood glucose testing to account for changes in daily routine, diet and mental health. Health care practitioners should encourage people with diabetes to engage in uptake of technology to improve and add value to telehealth services during COVID-19. The efficacy and problems of telehealth during the COVID-19 pandemic should be evaluated in detail with other modalities and warrant more research.

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Appendix 1. Principles of management of diabetes for healthcare professionals through the COVID pandemic

General principles

1. Advise patients to increase the frequency of glucose monitoring through capillary glucose testing, continuous or flash glucose monitoring. Most individuals living with diabetes have significantly changed their working environments, diet and physical activity patterns. Increased frequency of glucose monitoring is recommended to determine the impact of these changes in daily routine on glycemia, particularly for those on insulin therapy.

2. Insulin dosing should be reviewed. For individuals using insulin pump therapy, temporary basal rates may need to be trialled and then incorporated into new settings. For individuals using multiple daily injections, basal or bolus insulin requirements may differ from usual and individuals should contact their health professionals (certified diabetes educators, diabetes nurse practitioners, endocrinologists) if assistance is required.
3. Sick Day management should be discussed. All patients should be advised to present for COVID-19 testing if they develop a fever or respiratory symptoms according to state guidelines [10].
   a. For individuals with type 1 diabetes: ketone testing should be encouraged and the usual principles of ensuring adequate hydration and increasing insulin doses should be emphasised. Patients should be reassured that hospitals in Australia are safe and the risk of contracting COVID-19 is low and patients should present to emergency departments for management of diabetic ketoacidosis if required.
   b. For individuals with type 2 diabetes: SGLT2 inhibitors should be withheld during intercurrent illness due to the increased risk of ketoacidosis, including euglycemic ketoacidosis [95]. Capillary ketone levels should be checked if a patient taking a SGLT2 inhibitor presents acutely unwell. When the acute illness has resolved, SGLT2i should be resumed as appropriate for their cardiovascular, renal and metabolic benefits. If oral intake is reduced, sulphonylureas should be reduced or withheld and insulin doses modified. We suggest that there be a low threshold for commencing insulin, which may be the safest medication class to use during acute illness.

Appendix 2. Recommendations for individuals with diabetes

1. General measures:
   - Wash your hands frequently with soap and running water and dry properly.
   - Cover mouth and nose with bent elbow or tissue when coughing or sneezing.
   - Avoid touching mouth, nose and eyes.
   - Stay home as much as possible. Avoid crowds, non-essential travel and public areas.
   - Avoid touching surfaces in public (including elevator buttons, door handles, handrails). Try to cover your hand or finger with a tissue or your sleeve and wash your hands after.
   - Smoking and alcohol cessation – speak to your doctor if you would like assistance.
   - Remain up-to-date with the Influenza and Pneumovax vaccinations.

2. Preparation of supplies
   - Collect a supply of simple carbohydrates (such as soft drinks, jam, honey, lollies) for if you have a hypoglycaemic episode and are too ill to tolerate other food.
   - Have enough household items and groceries on hand so that you will be prepared if required to quarantine for a period of time.
   - Write down the phone numbers of your doctor, diabetes educator and local pharmacy.
   - Write down a list of your usual medications and doses.
   - You should have a 30-day supply of insulin and other diabetes medications, in the unlikely event that you are quarantined.
   - Ensure you have supply of insulin pump consumables and continuous glucose monitoring device.
   - All patients with type 1 diabetes should have sufficient supply of ketone testing strips (and glucagon if prescribed by your doctor).

3. Ongoing diabetes management

   People with type 1 diabetes
   - Engage with your diabetes team and your pump supplier and learn how to upload pump data to your diabetes nurse educator, endocrinologist or doctor while in isolation.
   - Continue to monitor your blood glucose level (BGL). If your glucose management is unsatisfactory (BGLs consistently more than 12 mmol/l, or less than 5 mmol/l) speak to your doctor or diabetes nurse educator for assistance with medication adjustments.
   - Ketone levels should be checked every 1-2 hours when BGLs are more than 15 mmol/l. Call your doctor immediately if you have raised ketones.
   - If you experience a hypo (BGL less than 4 mmol/l), eat 15 g of simple carbohydrates (5 jelly beans or ½ can of full strength soft drink) and recheck your BGL in 15 minutes to ensure your levels are rising.
   - Develop a "sick day management plan" with your doctor or diabetes nurse educator.

   People with type 2 diabetes
   - Continue to monitor your blood glucose level (BGL). If your glucose control is unsatisfactory (BGLs consistently more than 12 mmol/l, or less than 5 mmol/l) speak to your doctor or diabetes nurse educator for assistance with medication adjustments.
   - If you experience a hypo (BGL less than 4 mmol/l), eat 15 g of simple carbohydrates (5 jelly beans or ½ can of full strength soft drink) and recheck your BGL in 15 minutes to ensure your levels are rising.
   - Continue taking your usual oral medications and insulin as prescribed by your doctor.
   - If you are unwell with nausea and vomiting, or unable to tolerate oral intake, stop taking your SGLT inhibitor (empagliflozin, dapagliflozin, ertugliflozin) to prevent ketoacidosis.
   - Develop a "sick day management plan" with your doctor or diabetes nurse educator

Appendix 3. Reported prevalence of diabetes in COVID-19 cases in China

Reference	Total number (n=) of patients	Data collection period	Age; mean (range)	Diabetes (%)
Huang et al. [15]	41	12.1.19–2.1.20	49 (41–58)	20
Chen et al. [16]	99	1.1.20–20.1.20	55.5 (21–82)	12
Zhou et al. [21]	191	29.12.20–31.1.20	56 (18–87)	18.8
Guan et al. [17]	1099 (552 hospitals in China)	11.12.19–31.1.20	47 (35–58)	7.4
Wang et al. [18]	138	1.1.20–28.1.20	56 (42–68)	10.1
Zhang et al. [20]	140	16.1.20–3.2.20	57 (25–87)	12.1
Wu et al. [19]	44 672 (All cases reported to China's Infectious disease information system)	12.1.19–11.2.20	Not specified (approx 9–80)	5.3

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