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# Management of Diabetes During a Dual Pandemic

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### ABSTRACT

The dual pandemics of coronavirus disease-19 (COVID-19) and diabetes among patients are associated with 2- to 3-times higher intensive care admissions and higher mortality rates. Whether sheltering at home, quarantined with a positive COVID-19 test, or hospitalized, the person living with diabetes needs special considerations for successful management. Having diabetes and being COVID-19–positive increases the risk of poor outcomes and death. Providers need to give anticipatory pharmacologic guidance to patients with diabetes during COVID-19 lockdown. Patients with diabetes need to be more observant than others and to use self-protective actions. This review (1) discusses the clinical observations of COVID-19, diabetes and underlying mechanisms, (2) describes special considerations in caring for patients with diabetes in a COVID-19 environment, and (3) reviews clinical implications for the health care provider. This review highlights current evidenced-based knowledge. Additional research regarding clinical management is warranted

Diabetes continues to grow at an alarming rate, not only in the United States (US) but worldwide. Currently, 463 million people (9.3%) aged 20 to 79 years globally are living with diabetes.<sup>1</sup> Global projection estimates 578 million adults will be affected by diabetes by 2030 and 700 million by 2045.<sup>1.2</sup> Moreover, diabetes affects individuals across race/ethnicity and at various ages, reduces productivity and life expectancy, and increases health expenditures, including short- and long-term complications.<sup>3</sup> Thus, diabetes is the silent pandemic.<sup>2,4,5</sup> Policy experts predict that the escalating incidence of diabetes can overwhelm health care systems and

global economies without urgent multilevel preventive measures.<sup>5</sup> Recently, these overwhelming effects occurred within another pandemic, severe acute respiratory syndrome coronavirus (SARS-CoV-2), a novel coronavirus first identified in a December 2019 pneumonia case of unknown origin in China.<sup>6</sup> As cases quickly spread throughout provinces in China, a newly recognized infectious disease began to make its way to other countries, with the death toll quickly rising. On February 11, 2020, the World Health Organization named the disease coronavirus disease of 2019 (COVID-19) caused by SARS-CoV-2.<sup>7</sup> On March 11, 2020, the World Health Organization declared COVID-19 as a pandemic.<sup>7</sup> On March 13, 2020, the US declared COVID-19 a national emergency and released federal money to combat disease spread.<sup>8</sup> As of September 12, 2020, COVID-19 had spread to  $\geq$  200 countries and territories, infected 28.9 million individuals, and resulted in > 920,233 deaths worldwide.<sup>9</sup> COVID-19 has imposed momentous challenges for the public health and medical communities.

Additionally, these challenges are mainly experienced by the diabetes health care community now confronted with dual

pandemics, providing care for patients with diabetes amid COVID-19. While this information continues to evolve, in this narrative review, we discuss (1) the clinical observations of COVID-19 and diabetes and underlying mechanisms, (2) special considerations in caring for patients with diabetes in a COVID-19 environment, and (3) clinical implications for the health care provider.

### **Clinical Observations of COVID-19 and Diabetes**

Although data vary by country, the prevalence of diabetes with COVID-19 was first reported to range from 3% to 21% in Chinese studies.<sup>10,11</sup> In a meta-analysis of 8 trials in China, diabetes was present in 8% of 46,248 patients with COVID-19.<sup>11</sup> Preliminary data from the Centers for Disease Control and Prevention (CDC) demonstrated a prevalence rate of 10.9% among patients with laboratory-confirmed COVID-19.<sup>12,13</sup> Additionally, although data are still limited, clinical observational studies suggest a higher mortality rate among individuals with diabetes.<sup>10,11,14,15</sup> Among 191 hospitalized patients with confirmed COVID-19 in China, almost half of these patients had an underlying health condition, 19% had diabetes, and the mortality rate was 28%.<sup>14</sup> Multivariate analysis suggested older age, organ failure, and a D-dimer level > 1  $\mu$ g/L on admission were significant risk factors for in-hospital mortality.<sup>14</sup> Overall, however, studies reveal that individuals with diabetes are not more susceptible to COVID-19 but, rather, are at higher risk for poor prognosis and outcomes most likely due to multifactorial reasons such as age, sex, ethnicity, additional chronic conditions, such as cardiovascular disease and hypertension, and a proinflammatory and procoagulative state.<sup>16</sup>



Keywords:

COVID-19

insulin therapy

diabetes

continuous glucose monitoring

new-onset diabetes mellitus

coronavirus disease 2019 (COVID-19)





Emerging evidence also suggests that obesity is a risk factor for poor outcomes and death associated with COVID-19. Among 383 patients hospitalized with COVID-19, those who were obese had higher rates of diabetes (7.3% vs 5.4%) and more severe illness requiring intensive care compared with the normal-weight group.<sup>17</sup> These findings were supported by Gao et al.<sup>18</sup> who examined data for 75 patients hospitalized with COVID-19 infection and matched controls. Body mass index (BMI  $\geq$  25 kg/m<sup>2</sup>) was considered obese. After adjusting for multiple characteristics, including diabetes, the obese group had a 3-fold more significant likelihood of progressing to severe illness.<sup>19</sup>

In the first study dedicated explicitly to studying individuals with diabetes and hospitalized with COVID-19 among 53 French hospitals, results showed increased BMI was associated with mechanical ventilation and death 7 days after admission.<sup>15</sup> Additional factors also included the presence of comorbidities, including obstructive sleep apnea and microvascular and macrovascular complications.<sup>15</sup>

An equally significant area of study is whether glucose control serves as a prognostic factor for COVID-19 severity. Sardu et al<sup>19</sup> examined data for 59 patients hospitalized with COVID-19. Admission glucose levels were used to stratify patients into hyperglycemic and euglycemic groups; of these, 34 (57%) were euglycemic and 25 (42.4%) were hyperglycemic. Patients were treated with and without intravenous insulin infusions. In multivariate analysis with adjustment for risk factors, the intravenous insulin infusion. Although this finding is from a nonrandomized trial, results suggest that insulin infusion with tight glycemic control may improve COVID-19 outcomes. If this finding is confirmed in larger, randomized trials, optimal glucose control will be needed in hospitalized patients.

In summary, findings suggest that diabetes is a risk factor for poor outcomes of a COVID-19 infection. Patients with diabetes, for multifactorial reasons, have 2- to 3-times higher intensive care use than the overall population. Mortality rates are higher in those with diabetes. Findings also highlight the need for further research to understand diabetes with COVID-19.

#### Underlying Mechanisms of Diabetes, COVID-19, and Outcomes

An increased synthesis of glycosylation end products is believed to result from hyperglycemia and insulin resistance. Likewise, proinflammatory cytokines and oxidative stress lead to a cascade of events that set up conditions that foster tissue inflammation and stimulate adhesion molecules that mediate inflammation and dysfibrinolysis.<sup>20-22</sup> Hence, patients with diabetes are susceptible to dysfibrinolysis, the propensity to form blood clots. Likewise, Guo et al<sup>23</sup> found significantly higher blood levels of inflammationrelated biomarkers, including interleukin (IL) 6, C-reactive protein, serum ferritin, coagulation index, and D-dimer, in COVID-19 patients with diabetes. In short, COVID-19 fosters an inflammatory progression leading to a higher susceptibility for infections and poor outcomes among patients with diabetes.<sup>20</sup>

#### Special Consideration for Patients with Diabetes in the COVID-19 Environment

Whether sheltering at home, quarantined, or hospitalized with a positive COVID-19 test, the person living with diabetes needs special considerations for successful participatory management. In particular, mental health is an often overlooked area for successful diabetes management. There are limited studies of the psychologic profile of people living with diabetes during disasters or epidemics. In general, supporting any natural disaster or pandemic will lead to psychologic and diabetes-related distress among affected individuals when a social contact is limited.<sup>24</sup> Psychologic findings of a person living with diabetes through such issues as lockdown during a pandemic have caused increased psychologic distress. Publicized threats to physical health often foster mental health crises. Persons living with diabetes, when singled out as being a "vulnerable population" or at "higher risk" for COVID-19–related death, reported experiencing fear, anxiety, stress, depression, insomnia, denial, and anger.<sup>24-26</sup> It is concerning that a subset of persons living with diabetes may already have comorbid mental health issues secondary to being administered atypical antipsychotics, which foster type 2 diabetes.<sup>27</sup>

One study focused on diabetes self-care behaviors and coping difficulties during the COVID-19 pandemic. The Summary of Diabetes Self-Care Activities Tool (SDSCAT) was used before and during the pandemic lockdown on a sample of 212 individuals.<sup>25</sup> In the posttest, scores of global diabetes self-care behaviors decreased from  $5.15 \pm 0.9$  to  $4.49 \pm 1.02$ . (P < .001). This reduction in self-care was contributed to psychologic and diabetes-related distress coupled with food insecurity worsened by restraints of leaving home for diabetes-related supplies, food, and exercise, and potential loss of wages, all of which led to poor self-care management. Mental health issues permeate in COVID-19 and present special considerations regardless of whether at home or hospitalized.

#### Patients With Diabetes Sheltering at Home

A significant impact of being quarantined at home during a pandemic is a change in eating behaviors. Less access to fresh and quality food fosters a propensity to obtain calorie-laden shelf-stable foods. Coupled with a previous experience of food insecurity, quarantining may lead to hoarding of food and eating disorders such as binge eating.<sup>28</sup> At particular risk for eating disorders are low-income populations, those who live alone, and those residing in food deserts.<sup>28</sup> Patients with eating disorders are at substantial risk for increases in symptoms and reduced treatment access during the COVID-19 pandemic.

Environmental precautions to limit coronavirus spread have affected food availability and access to healthy coping mechanisms and have contributed to weight-stigmatizing social media messages that may be uniquely harmful to those experiencing eating disorders.<sup>28</sup> Providers proactively need to identify at-risk individuals and plan interventions. Tools and interventions such as telehealth, guided self-help sessions apps, and emails to maintain provider-patient communications, are imperative.

#### Providers Need to Give Anticipatory Guidance to Patients With Diabetes During Lockdown

Patients with diabetes need to be more observant than others and take self-protective actions, particularly handwashing, wearing masks, and physical distancing. Review sick day rules and encourage ketone testing when ill and at risk for diabetic ketoacidosis. Discuss early signs and symptoms of COVID-19 and advise patients to call before coming to the office or emergency department. Depending on patients' comorbidities, describe actions to be taken and develop an emergency medical plan with patients.

Determining whether patients are appropriate for face-to-face or remote follow-up must be based on their risk assessment. For example, patients who are pregnant, newly diagnosed with diabetes, and those with foot ulcers or injury may require closer monitoring.<sup>29</sup> Uncomplicated foot ulcers may be managed at home using a smartphone application upload of digital pictures (eg, https://healthy.io/wound).<sup>30</sup> When a patient must be examined in person, certain precautions must occur, including masks for all patients and staff. The office policy should only allow a few patients in waiting areas at a time to permit social distancing. Have patients wait in the car until the provider can see them.

#### **Health Maintenance**

Ensure routine vaccinations (pneumococcal and seasonal influenza) are up to date. Advise patients to maintain enough glucose testing materials and diabetes medications to last at least 2 weeks, preferably 1 month. Encourage them to sign up for home delivery of supplies, medications, and groceries, and plan for phone or telemedicine follow-up.

#### Nutrition

Eating a healthy diet can be quite challenging during this time, particularly if under economic constraints. Long lines and bare grocery shelves may cause heightened anxiety; likewise, if previously reliant on a food pantry that now may be facing limited supply to increased demand. Encourage patients to follow a schedule set mealtime and be self-aware of internal hunger and satiety cues.<sup>28</sup> Frequently survey the patient's coping behaviors.

#### Physical Activity

Closure of fitness centers and mandates to maintain physical distancing has fostered the need for creative outlets to maintain physical activity. Establishing an exercise routine that is suitable for home is a necessary intervention. A positive correlation between physical activity and mental well-being (r = 0.07541, P = .0002) was found in Italy's population during the pandemic,<sup>31</sup> indicating that the lack of physical activity had a deleterious impact on psychologic health and well-being.

#### Medications

Review medications for proactive adjustments. If the patient is at home and stable, most medications can be continued, but specific considerations should occur. Discontinue metformin when at risk for dehydration, which often leads to lactic acidosis and will require hospitalization. Once admitted to the hospital, metformin is contraindicated due to tests requiring contrast medium or propensity for kidney injury. Exchanging metformin with a dipeptidyl peptidase 4 (DPP-4) inhibitor, such as sitagliptin (Januvia, Merck), lowers the risk profile and is less likely to cause adverse effects (lactic acidosis during studies with contrast dye or hypoglycemia).<sup>22,32</sup> DPP-4 inhibitors have been shown to provide favorable influence outside of their lowering glucose and manifest an antiinflammatory effect. In a meta-analysis, prescribing DPP-4 inhibitors was found to decrease the associated risk of respiratory infections.<sup>33</sup> In short, the exact immune response of DDP-4 inhibitors is not fully understood.

Consideration should be given to the patient's clinical picture and risk of dehydration and/or ketoacidosis. As when COVID-19 positive and symptomatic, the literature supports discontinued use of sodium-glucose cotransporter 2 (SGLT2) inhibitors to minimize the occurrence of dehydration.<sup>34,35</sup> Individually consider maintaining or discontinuing other medications such as sulfonylureas and statins. Owing to the link of diabetes with cardiovascular disease, maintaining control of lipids is advisable. Likewise, because statins have an anti-inflammatory effect, there is concern that is abruptly stopping may elicit a cytokine storm (eg, the release of IL-6 and IL-1 $\beta$ ).<sup>36</sup>

Unless contraindicated, angiotensin-converting enzyme inhibitors(ACEI)/angiotensin II receptor blockers (ARBs) should be continued.<sup>37,38</sup> Transitory, there was concern that ACEI and ARBs could accelerate the virus's entry into the cells via the increased expression of ACE2.<sup>39</sup> However, expert consensus panels have theorized that ACEI/ARBs may protect against severe lung injury in the wake of infection.<sup>37</sup> ACEI/ARBs have been postulated to have significant immunomodulatory influences by decreasing cytokines and consequently decreasing pulmonary and systemic inflammatory reactions.<sup>40-42</sup>

#### Mental health

For those who are highly anxious regarding COVID-19, encourage them to take periodic breaks from COVID-19 news. Staying active, such as brief walks or only doing chair exercises, is essential to maintain physical activity levels during this time. Additionally, encourage the use of technology to avoid social isolation and maintain contact with family and friends via social media and electronically. Staying connected, whether through an online peer support group or eating with family members in person or via the internet, will reduce stress and promote well-being. Encourage individuals to find ways to reduce stress, strengthen coping skills, and encourage enough sleep to allow for adequate rest time.

### COVID-19 Testing

Advise patients when they need to be COVID-19 tested and where to be tested (see the Box).<sup>43</sup> When a patient with diabetes needs to be tested for COVID-19, considerations should be given for the test type (Table 1).<sup>43-45</sup> Likewise, consideration should include the expected time frame for reporting of results. If a patient with diabetes is symptomatic, time may be a safety factor. Based on the patient's clinical picture, the provider may individualize recommendation of testing type for COVID-19.

#### Patients With Diabetes Hospitalized for COVID-19

Inpatient providers should be aware that diabetes is associated with more severe respiratory outcomes. Wu et al<sup>45</sup> stratified patients with COVID-19 with and without acute respiratory distress syndrome (ARDS) and discovered that diabetes was a significant predictor of ARDS (hazard ratio, 2.34; 95% confidence interval, 1.35-4.05) but not of death (hazard ratio, 1.58; 95% confidence interval, 0.80-3.13). However, a small sample size adjustment for confounding factors was not performed. Patients with both COVID-19

## Box

Reasons to be Tested for COVID-1943

- **Surveillance:** Monitoring infection rates and trends to determine whether public health measures are effective. Commonly includes a random sample of people in the population to be tested. Allows determination of how extensive a virus has become.
- Screening: Testing people even if they are not symptomatic or unaware of being exposed to the virus. Enables scientists to identify who might be carrying the virus and to prevent it from spreading.
- **Diagnostic:** Testing when there is suspicion that a person may be infected. This is a symptomatic person or one who knows they have been exposed to the virus, and is also a test of cure to verify they no longer have the virus.

Table 1Types of COVID-19 Testing43-45,a

Type of Test	Diagnostic	Antibody	Saliva
Specimen Mechanism	Nasopharyngeal swab Antigen test: Detects viral proteins (less accurate and may need further testing). Molecular test: Uses PCR to detect virus RNA.	Blood Indirectly detects virus by measuring immune response (IgM, IgG).	Saliva Dose not use nucleic acid extraction. Adapted from loop-mediated isothermal amplification (LAMP), previously used to detect outbreaks of Zika and Ebola.
Time Frame	Rapid (Antigen) version less than an hour. Molecular a few days to a week. Point-of-care rapid testing was released Fall 2020.	Few days	90 samples in less than 3 hours
When to obtain	Symptoms of COVID-19 (3-5 days after exposure or onset of symptoms).	If you had COVID-19 and have recovered. (First 2 weeks after onset of symptoms.)	Symptoms of COVID-19 (3-5 days after exposure or onset of symptoms). Sample can be easily obtained by patient.
Where to be tested	Drive-through or urgent care	Local hospital	On site (point-of-care testing) or mailed to laboratory.
Distinctions	Molecular test: Identifies early onset of infection and is most accurate. Antigen test: Positive results highly accurate, but negative results may need confirmation with PCR molecular test.	Quicker results, not as sensitive as PCR	Minimally invasive, can reliably be self- administered, and has shown similar sensitivity to nasopharyngeal swabs.

COVID-19 = coronavirus disease 2019; Ig = immunoglobulin; PCR = polymerase chain reaction.

Abbott Laboratories. Helping Slow Spread Of Coronavirus. https://www.abbott.com/IDNOW.html

<sup>a</sup> Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19: Serologic Testing. https://www.idsociety.org/practice-guideline/covid-19-guideline-serology/

and diabetes are at risk for precipitous deterioration, and this merits close monitoring.<sup>45</sup>

Maintaining glycemic control may be more challenging when caregivers need personal protective equipment, and continuous glucose monitoring (CGM) may reduce the care burden. Tight glycemic control is imperative among all patients with COVID-19. The nurse's frequency of exposure to the virus during needed interactions with patients receiving insulin therapy is significant.<sup>46</sup> Therefore, the contact frequency should be considered along with glycemic control, glycemic variability, and risk of hypoglycemia before choosing the optimal mitigation strategy.

As of April 2020, the US Food and Drug Administration has allowed for the availability and capability of noninvasive remote monitoring devices during the COVID-19 pandemic.<sup>47</sup> This modification was made to improve the capacity of in-hospital caregivers to monitor their patients while minimizing their exposure to COVID-19. This guideline applies to noninvasive patient monitoring technology, plus CGMs, and expands their indications to inpatient hospital settings. Consequently, the American Diabetes Association, Insulin for Life, and the Diabetes Disaster Response Coalition have partnered with Abbott to donate CGM sensors to US hospitals.<sup>47</sup>

The FreeStyle Libre 14-day system is now being used on the frontlines for people living with diabetes. The FreeStyle Libre is the only CGM system on the market with no acetaminophen interference, as other products provide falsely elevated glucose measurements when the patient is administered acetaminophen.<sup>48</sup> This is of utmost importance because acetaminophen is an antipyretic commonly administered to patients with COVID-19.

In short, CGM should be correlated with laboratory glucose, but the providers can monitor their patients from a distance, minimizing exposure to COVID-19 and conserving the consumption of personal protective equipment. Another advantage of CGM is that it clearly illustrates the patient's "time in range" of normal glucose levels vs a one-time average measurement such as hemoglobin A<sub>1c</sub>. Increasing time in range serves to optimize glycemic control while minimizing hypoglycemia. CGM can be used in any type of patient care area.

Insulin therapy is a mainstay among patients with COVID-19 who require intensive level care. However, many considerations need to occur. Commonly, continuous tube feeding is used for ventilated patients. The risk of interrupted tube feeding is hypoglycemia. So, interventions for the treatment of hypoglycemia must be anticipated in advance. If tube feeding is interrupted short-term (< 2 hours) and results in hypoglycemia, the standard ampule of 50% dextrose may restore euglycemia. When the tube feedings must be discontinued for a prolonged period (> 2 hours), infusing 10% dextrose in water may be necessary to maintain euglycemia.

Continuous intravenous insulin infusion, without the use of CGM, may offer the most optimal glycemic control, less glycemic variability, and the lowest risk of hypoglycemia (when tube feeding is stopped) but requires the most frequent nurse's exposure of every 1 hour.<sup>46</sup> Therefore, without CGM, continuous intravenous insulin infusion may not be the optimal option. The glucose target goal is relaxed, and the provider orders reduced contact monitoring frequency to every 2 to 4 hours.

Another insulin regimen offers the second-best glycemic control, but more glycemic variability, moderate risk of hypoglycemia, and monitoring frequency of every 6 hours (4 times daily). This regimen consists of subcutaneous basal insulin every 12 hours and regular insulin correction every 6 hours.<sup>46</sup> An alternative strategy to reduce monitoring is to lower the dose of basal insulin and add fixed-dose regular insulin every 6 hours along with correctional dose of regular insulin every 6 hours.

A third regimen is the use of neutral protamine Hagedorn (NPH) every 8 hours with regular correctional insulin every 8 hours. NPH offers moderate glycemic control, moderate glycemic variability, and moderate risk for hypoglycemia. The frequency of monitoring is every 8 hours (3 times daily).<sup>46</sup>

A fourth regimen is regular insulin every 6 hours. These last 2 regimens offer only mild to moderate glycemic control, moderate glycemic variability, and hypoglycemia risk. Monitoring frequency is 3 to 4 times daily. It is clear without CGM that any insulin regimen choice has its limitations when trying to limit caregiver exposure to the virus.

Glucocorticoid therapy is a mainstay treatment for ARDS and can foster hyperglycemia among patients who do not have diabetes. For recalcitrant hyperglycemia, combing NPH with basal insulin has been recommended.<sup>49</sup> The rationale is the pharmacokinetics of intravenous cortisol at 50 mg every 6 hours mimics NPH's peak, trough, and duration pattern.

#### COVID-19 Impact on Existing Diabetes and New-Onset Diabetes

All patients hospitalized due to COVID-19 should be screened for diabetes. The COVID-19 virus binds to ACE2 receptors expressed in many organs and tissues, including pancreatic  $\beta$ -cells.<sup>50</sup> Thus, it is theorized that COVID-19 may cause modifications of glucose metabolism that could compound the pathophysiology of existing diabetes or lead to new diabetes onset. There are several examples of a viral etiology of ketosis-prone and diabetes hyperosmolarity for which exceptionally high doses of insulin were merited from other coronaviruses that bind to ACE2 receptors.<sup>51</sup> Likewise, increased occurrences of fasting hyperglycemia and acute-onset diabetes have been found among patients with SARS COVID-19 pneumonia.<sup>51</sup>

The worsening of existing diabetes and the new onset of dysglycemia has led to the theory of a potential diabetogenic consequence of COVID-19, besides the recognized stress response.<sup>52</sup> This theory led to questions:

- Will the COVID-19 alterations in glycemic control improve or endure?
- Is COVID-19—associated diabetes classified as classic type 1 and type 2 diabetes or in need of a separate category?
- Will patients with COVID-19 remain at higher risk for diabetes or diabetic ketoacidosis?

To better characterize the impact of COVID-19 among both patients with preexisting or new-onset diabetes, an international group of researchers established the CoviDIAB Project as a worldwide registry of patients with COVID-19–related diabetes.<sup>53</sup>

Answering these questions will serve to inform clinical care, follow-up, and monitoring of affected patients.

#### Transitional Care From Inpatient to Home

Patient transitions from inpatient to home care are a vital area of focus for reducing costly hospital readmissions. These challenges are amplified when the patient carries a history of diabetes mellitus in the face of being COVID-19 positive. According to the CDC,<sup>54</sup> a clinically stable patient who is positive for COVID-19 may be discharged home even when they are still meeting the criteria for continuation of transmission-based precautions under the following conditions. The patient is cognitively capable of following transmission-based precautions and has access to appropriate caregivers, food, medicine, and a home environment conducive to self-isolating.<sup>54</sup> Criteria for a patient with COVID-19 for discontinuing transmission-based precautions are resolution of fever without antipyretics or 30 days since the last fever (when test is unavailable), improved symptoms (ie, cough and dyspnea), 2 negative nasopharyngeal swab tests 24 hours apart, and 7 days since the last symptom.<sup>54</sup>

Although the CDC only advises patients living with diabetes who are COVID-19 positive to follow "sick day rules" as appropriate, it does provide criteria about when to return to the emergency department.<sup>55</sup> Providers need to consider the following discharge management issues: glycemic control (ie, oral steroids), restarting oral hypoglycemic agents (ie, consideration of renal function), level of deconditioning, oxygenation (ie, Pao<sub>2</sub> > 92 mm Hg on room air) and psychologic.<sup>56</sup>

Initially, posthospital management of glycemic control may still require insulin, as patients who received 6 mg dexamethasone intravenously for 7 to 10 days are commonly transitioned to oral steroids upon discharge.<sup>56,57</sup> Providers therefore need to individualize the glycemic regimens based on the therapies the patient received acutely and is prescribed at discharge. Before oral diabetes

medications are restarted, consideration should be given to glycemic control and renal function.

Patients need to be frequently reassessed for adequate oxygenation depending on their baseline and post–COVID-19 lung function. In severe cases of COVID-19 pneumonia, a pulmonary embolism may have occurred. Anticoagulation for COVID-19–induced pulmonary embolism should be continued for 3 months and then evaluated by a contrast computed tomography angiography of the chest.<sup>57</sup> Home oxygen may be still needed if the patient is symptomatic and/or Pao<sub>2</sub> is < 92 mm Hg.<sup>54</sup>

Deconditioning due to prolonged convalesce is a common issue.<sup>58,59</sup> Older patients will often require inpatient rehabilitation. All patients should be evaluated by physical therapy before discharge. Consideration should be given to both home health nursing and in-home physical therapy. Research reveals only 40% of patients with COVID-19 with prolonged general weakness return to work 2 to 3 months after discharge.<sup>59</sup> In short, innovated models of monitoring and follow-up will be required.<sup>60,61</sup> Virtual methods of care, such as telemedicine and eConsultation, have become the new normal.

#### **Clinical Implications**

Providers have many considerations when managing patients with diabetes during the COVID-19 pandemic. Interventions range from anticipatory guidance to patients with diabetes during the lockdown or COVID-19 positive when at home to intensive care unit level care. An analysis of the patient's clinical picture and a decision, if possible, about medication adjustments may be made via telemedicine or may need to occur in person. The inpatient management of 2 pandemics-COVID-19 and diabetes-combined carries still an added burden. Provider concerns extend beyond that solely of the patient but include the direct caregivers' exposures frequency to the virus. Glycemic control may be more challenging when caregivers need personal protective equipment. The Food and Drug Administration has recently approved CGM for inpatient monitoring, reducing the care burden by limiting possible exposure to the virus. Without CGM, any insulin regimen choice has limitations when trying to limit caregiver exposure to the virus.

#### Conclusion

Patients with COVID-19 who receive intravenous insulin had less illness progression than the patients without insulin infusion. Although this finding is from a nonrandomized trial, results suggest that insulin infusion with tight glycemic control may improve COVID-19 outcomes. If this finding is confirmed in larger randomized trials, optimal glucose control will be needed in hospitalized patients. In summary, findings suggest that diabetes is a risk factor for poor outcomes of a COVID-19 infection. For multifactorial reasons, patients with diabetes have 2- to 3-times higher intensive care utilization than the overall population. Mortality rates are higher with those with diabetes. Findings also highlight the need for further research to understand diabetes with COVID-19.

Having diabetes, especially with poor glycemic control, and being COVID-19 positive increases the risk of poor outcomes and death. Worsening of existing diabetes and the new onset of dysglycemia has led to the theory of a potential diabetogenic consequence of COVID-19. To better characterize the impact of COVID-19 among patients with preexisting or new-onset diabetes, an international group of researchers established the CoviDIAB Project as a worldwide registry of patients with COVID-19—related diabetes. At the time this article went to press there were 2 vaccines approved for emergency use. Table 2 describes how to speak with your patients concerning vaccination.

#### Table 2

Talking to the Person Living with Diabetes regarding the Importance of Receiving the COVID-19 Vaccination

Concerns	Considerations	
Safety	Based on data that exists now, both current vaccines appear to be extremely safe.	
Speed of development	From knowledge and technology developed over the past 15 to 20 years of HIV research and drug development. Scientist were able to build on their knowledge of viruses and shift expertise to the making of COVID vaccine. What was fast-tracked was not safety, but production of vaccine. As the manufactures started producing the vaccines when the usual clinical safety trials were being conducted	
	If the vaccine had not worked the supply would have been discarded.	
Will I still need a mask	Although the vaccine prevents symptoms of COVID infection, its not know if it prevents asymptomatic infection.	
	symptoms can transmit the virus mask and physical distancing are needed.	
How often will I need the vaccine	It is not known how long immunity is conferred. Research will determine if it is annually or every few years that re-inoculation will be required.	
Will safety and effectiveness be monitored	Together the CDC and FDA are committed to monitoring outcomes. Vaccinated people will be monitored for both short- and long-term outcomes. These findings will be openly reported to the public.	

 $\mathsf{CDC}=\mathsf{Centers}$  for Disease Control and Prevention;  $\mathsf{FDA}=\mathsf{Food}$  and Drug Administration.

In December of 2020 the Food and Drug Administration approved 2 vaccines via Emergency Use Authorization (EUA). Table 2 outlines concerns and considerations when talking to patients living with diabetes about the vaccine (https://www.fda.gov/ news-events/press-announcements/fda-takes-additional-actionfight-against-covid-19-issuing-emergency-use-authorizationsecond-covid).

#### References

- International Diabetes Federation. Diabetes prevalence in 2019 and projections to 2030 and 2045 (65-99 years). *IDF Diabetes Atlas*. 9th ed. IDF, 2019: 40-43.
- Cho NH, Shaw JE, Karuranga S, et al. IDF Diabetes Atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res Clin Pract.* 2018;138:271-281. https://doi.org/10.1016/j.diabres.2018.02.023.
- International Diabetes Federation. Diabetes complications and co-morbidities. IDF Diabetes Atlas. 9th ed. IDF, 2019:78-105.
- Toniolo A, Cassani G, Puggioni A, et al. The diabetes pandemic and associated infections: suggestions for clinical microbiology. Virology. 2019;30:1-17. https://doi.org/10.1097/MRM.00000000000155.
- Hu FB, Satija A, Manson JE. Curbing the diabetes pandemic: the need for global policy solutions. JAMA. 2015;313(23):2319-2320. https://doi.org/10.1001/ jama.2015.5287.
- Fadini GP, Morieri ML, Longato E, Avogaro A. Prevalence and impact of diabetes among people infected with SARS-CoV-2. J Endocrinol Invest. 2020;43(6): 867-869. https://doi.org/10.1007/s40618-020-01236-2.
- World Health Organization. Rolling updates on coronavirus disease (COVID-19); Updated July 31, 2020. Accessed September 12, 2020, https://www.who. int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen.
- American Journal of Managed Care. A timeline of COVID-19 developments in 2020; Published July 3, 2020. Accessed September 12, 2020, https://www. ajmc.com/view/a-timeline-of-covid19-developments-in-2020.
- John Hopkins University of Medicine. Coronavirus Resource Center. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins; Published September 12, 2020. Accessed September 12, 2020, https://coronavirus.jhu.edu/map.html.
- Tadic M, Cuspidi C, Sala C. COVID-19 and diabetes: Is there enough evidence? J Clin Hypertens (Greenwich). 2020;22(6):943-948. https://doi.org/10.1111/ jch.13912.
- Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *Int J Infect Dis.* 2020;94:91-95. https://doi.org/10.1016/j.ijid.2020.03.017.

- Chow N, Fleming-Durtra K, Gierke R, et al. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019 – United States, February 12-March 28, 2020. MMWR Morb Mort Wkly Rep. 2020;69(13):382-386. https://doi.org/10.15585/ mmwr.mm6913e2.
- Stokes EK, Zambrano LD, Anderson KN, et al. Coronavirus disease 2019 cases surveillance – United States: January 22-May 30, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(24):759-765. https://doi.org/10.15585/mmwr.mm6924e2.
- Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adults inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020;395:1054-1062. https://doi.org/10.1016/S0140-6736(20) 30566-3.
- Carlou B, Hadjadj S, Wargny M, et al. Phenotypic characteristics and prognosis of inpatients with COVID-19 and diabetes: the CORONADO Study. *Diabetologia*. 2020;63:1500-1515. https://doi.org/10.1007/s00125-020-05180-x.
- Apicella M, Campopiano M, Mantuano M, et al. COVID-19 in people with diabetes: understanding the reasons for the worse outcomes. *Lancet Diabetes Endocrinol.* 2020;8:782-792. https://doi.org/10.1016/S2213-8587(20)30238-2.
- Cai Q, Chen F, Wang T, et al. Obesity and COVID-19 severity in a designated hospital in Shenzhen, China. *Diabetes Care*. 2020;43:1392-1398. https:// doi.org/10.2337/dc20-0576.
- Gao F, Zheng KI, Wang X, et al. Obesity is a risk factor for greater COVID-19 severity. *Diabetes Care*. 2020;43(7):e72-e74. https://doi.org/10.2337/dc20-0682.
- Sardu C, D'Onofrio N, Balestrieri M, et al. Outcomes in patients with hyperglycemia affected by COVID-19: can we do more on glycemic control? *Diabetes Care.* 2020;43:1408-1415. https://doi.org/10.2337/dc20-0723.
- Knapp S. Diabetes and infection: is there a link?-A mini-review. *Gerontology*. 2013;59(2):99-104.
- Petrie JR, Guzik TJ, Touyz RM. Diabetes, hypertension, and cardiovascular disease: clinical insights and vascular mechanisms. *Can J Cardiol.* 2018;34(5): 575-584. https://doi.org/10.1016/j.cjca.2017.12.005.
- Kulcsar KA, Coleman CM, Beck SE, Frieman MB. Comorbid diabetes results in immune dysregulation and enhanced disease severity following MERS-CoV infection. JCI Insight. 2018;4(20):e131774. https://doi.org/10.1172/ jci.insight.131774.
- Guo W, Li M, Dong Y, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. *Diabetes Metab Res Rev.* 2020, e3319. https://doi.org/ 10.1002/dmrr.3319.
- Hillson R. COVID-19: psychological issues for people with diabetes and health care staff. Pract Diabetes. 2020;37(3):101-104. https://doi.org/10.1002/pdi.2278.
- Silva-Tinoco R. Effect in self-care behavior and difficulties in coping with diabetes during the COVID-19 pandemic (PDF). ResearchGate. https://doi.org/ 10.24875/RME.20000063
- Joensen LE, Madsen KP, Holm L, et al. Diabetes and COVID-19: psychosocial consequences of the COVID-19 pandemic in people with diabetes in Denmark—what characterizes people with high levels of COVID-19-related worries? *Diabet Med.* 2020;37(7):1146-1154. https://doi.org/10.1111/ dme.14319.
- Akinlade KS, Rahamon SK, Lasebikan VO. Beta-cell function and metabolic clearance rate of glucose in patients with major mental health disorders on antipsychotic drug treatment. J Natl Med Assoc. 2018;110(5):504-511. https:// doi.org/10.1016/j.jnma.2018.01.003.
- Cooper M, Reilly EE, Siegel JA, et al. Eating disorders during the COVID-19 pandemic and quarantine: an overview of risks and recommendations for treatment and early intervention. *Eat Disord*. Published online July 9 2020. https://doi.org/10.1080/10640266.2020.1790271
- National Health Service (NHS) London Clinical Network. Outpatient Appointment Prioritisation for Specialist Diabetes Departments during the Coronavirus. Approved March 26, 2010; Accessed April 11, 2020, https://www.england. nhs.uk/london/wp-content/uploads/sites/8/2020/04/4.-Covid-19-Diabetes-Outpatient-Appointment-Prioritisation-Crib-Sheet-27032020.pdf.
- Healthy.io. Wound care; Accessed December 18, 2020, https://healthy.io/ services/wound/.
- Maugeri G, Castrogiovanni P, Battaglia G. The impact of physical activity on psychological health during Covid-19 pandemic in Italy. *Heliyon*. 2020;6(6), e04315. https://doi.org/10.1016/j.heliyon.2020.e04315.
- Iacobellis G. COVID-19 and diabetes: can DPP4 inhibition play a role? *Diabetes Res Clin Pract*. 2020;162:108125. https://doi.org/10.1016/j.diabres.2020.108125.
- Yang W, Cai X, Han X, Ji L. DPP-4 inhibitors and risk of infections: a metaanalysis of randomized controlled trials. *Diabetes Metab Res Rev.* 2016;32(4): 391-404. https://doi.org/10.1002/dmrr.2723.
- Meyer EJ, Gabb G, Jesudason D. SGLT2 Inhibitor-associated euglycemic diabetic ketoacidosis: a South Australian clinical case series and Australian spontaneous adverse event notifications. *Diabetes Care*. 2018;41(4):e47-e49. https:// doi.org/10.2337/dc17-1721.
- Wilding J, Fernando K, Milne N, et al. SGLT2 inhibitors in type 2 diabetes management: key evidence and implications for clinical practice. *Diabetes Ther Res Treat Educ Diabetes Relat Disord*. 2018;9(5):1757-1773. https://doi.org/ 10.1007/s13300-018-0471-8.
- Shin Y, Min J, Lee J-H, et al. The effect of fluvastatin on cardiac fibrosis and angiotensin-converting enzyme-2 expression in glucose-controlled diabetic rat hearts. *Heart Vessels*. 2017;32(5):618-627. https://doi.org/10.1007/s00380-016-0936-5.

- European Society of Cardiology, de Simone G. Position statement of the ESC Council on Hypertension on ACE-inhibitors and angiotensin receptor blockers; March 13, 2020. Accessed April 15 2020, https://www.escardio.org/Councils/ Council-on-Hypertension-(CHT)/News/position-statement-of-the-esc-councilon-hypertension-on-ace-inhibitors-and-ang.
- Vaduganathan M, Vardeny O, Michel T, McMurray JJV, Pfeffer MA, Solomon SD. Renin-angiotensin-aldosterone system inhibitors in patients with Covid-19. N Engl J Med. 2020;382(17):1653-1659. https://doi.org/10.1056/NEJMsr2005760.
- Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *Lancet Respir Med.* 2020;8(4):e21. https://doi.org/10.1016/S2213-2600(20)30116-8.
- Henry C, Zaizafoun M, Stock E, Ghamande S, Arroliga AC, White HD. Impact of angiotensin-converting enzyme inhibitors and statins on viral pneumonia. *Bayl Univ Med Cent Proc.* 2018;31(4):419-423. https://doi.org/10.1080/ 08998280.2018.1499293.
- Mortensen EM, Pugh MJ, Copeland LA, et al. Impact of statins and angiotensin converting enzyme inhibitors on mortality of subjects hospitalised with pneumonia. *Eur Respir J.* 2008;31(3):611-617. https://doi.org/10.1183/ 09031936.00162006.
- Gullestad L, Aukrust P, Ueland T, et al. Effect of high-versus low-dose angiotensin converting enzyme inhibition on cytokine levels in chronic heart failure. J Am Coll Cardiol. 1999;34(7):2061-2067. https://doi.org/10.1016/ s0735-1097(99)00495-7.
- U.S. Food and Drug Administration. FAQs on Testing for SARS-CoV-2; Published online September 10, 2020. Accessed September 11, 2020, https:// www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/ faqs-testing-sars-cov-2.
- Wyllie AL, Fournier J, Casanovas-Massana A, et al. Saliva is more sensitive for SARS-CoV-2 detection in COVID-19 patients than nasopharyngeal swabs [preprint]. medRxiv; Published online April 22, 2020, https://doi.org/10.1101/ 2020.04.16.20067835.
- Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239-1242.
- Hamdy O, Gabbay RA. Early Observation and mitigation of challenges in diabetes management of COVID-19 patients in critical care units. *Diabetes Care*. 2020;43(8):e81-e82. https://doi.org/10.2337/dc20-0944.
- 47. U.S. Food and Drug Administration. Enforcement Policy for Non-Invasive Remote Monitoring Devices Used to Support Patient Monitoring During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency (Revised): Guidance for Industry and Food and Drug Administration Staff; Published June 5, 2020. Accessed July 15, 2020, https://www.fda.gov/regulatory-information/ search-fda-guidance-documents/enforcement-policy-non-invasive-remotemonitoring-devices-used-support-patient-monitoring-during.
- Maahs DM, DeSalvo D, Pyle L, et al. Effect of acetaminophen on CGM glucose in an outpatient setting. *Diabetes Care*. 2015;38(10):e158-e159. https://doi.org/ 10.2337/dc15-1096.

- Korytkowski M, Antinori-Lent K, Drincic A, et al. A pragmatic approach to inpatient diabetes management during the COVID-19 pandemic. J Clin Endocrinol Metab. 2020;105(9):3076-3087. https://doi.org/10.1210/clinem/ dgaa342.
- Hamming I, Timens W, Bulthuis MLC, Lely AT, Navis GV, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol. 2004;203(3):631-637. https://doi.org/10.1002/path.1570.
- Yang J-K, Lin S-S, Ji X-J, Guo L-M. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. *Acta Diabetol.* 2010;47(3):193-199. https://doi.org/10.1007/s00592-009-0109-4.
- Rubino F, Amiel SA, Zimmet P, et al. New-onset diabetes in Covid-19. N Engl J Med. 2020;383(8):789-790. https://doi.org/10.1056/NEJMc2018688.
- CoviDIAB Registry: Accessed July 15, 2020, https://covidiab.e-dendrite.com/.
  American Hospital Association. COVID-19: Checklist for Discharging Patients.
  With COVID-10: Distributed called Describes 0, 2020. Accessed Describes 0.
- With COVID-19; Published online December 8, 2020. Accessed December 8, 2020. https://www.aha.org/system/files/media/file/2020/04/COVID-19-Checklist-for-Discharging-Patients-Checklist.pdf.
- Centers for Disease Control and Prevention. Living With Diabetes: Managing Sick Days; Published online December 8, 2020. Accessed December 8, 2020, https://www.cdc.gov/diabetes/managing/flu-sick-days.html.
- Abdi A, Jalilian M, Sarbarzeh PA, Vlaisavljevic Z. Diabetes and COVID-19: a systematic review on the current evidences. *Diabetes Res Clin Pract.* 2020;166: 108347. https://doi.org/10.1016/j.diabres.2020.108347.
- Potus F, Mai V, Lebret M, et al. Novel insights on the pulmonary vascular consequences of COVID-19. *Am J Physiol Lung Cell Mol Physiol*. 2020;319(2): L277-L288. https://doi.org/10.1152/ajplung.00195.2020.
- Bellido V, Pérez A. Consequences of COVID-19 on people with diabetes. *Endocrinol Diabetes Nutr.* 2020;67(6):355-356. https://doi.org/10.1016/ j.endinu.2020.04.008.
- Disser NP, De Micheli AJ, Schonk MM, et al. Musculoskeletal consequences of COVID-19. J Bone Joint Surg Am. 2020;102(14):1197-1204. https://doi.org/ 10.2106/JBJS.20.00847.
- Jones MS, Goley AL, Alexander BE, Keller SB, Caldwell MM, Buse JB. Inpatient transition to virtual care during COVID-19 pandemic. *Diabetes Technol Ther*. 2020;22(6):444-448. https://doi.org/10.1089/dia.2020.0206.
- Agarwal S, Griffith ML, Murphy EJ, et al. Innovations in diabetes care for a better "new normal" beyond COVID-19. J Clin Endocrinol Metab. 2021;106(1): e377-e381. https://doi.org/10.1210/clinem/dgaa704.

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