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EDITORIAL

Impacts and Lessons Learned From the COVID-19 Pandemic

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The COVID-19 pandemic has impacted everything from our food buying practices to how the health-care system functions. We have had to learn to navigate a world with COVID-19 in it and to be in personal, school and work spaces. This edition of *The Diabetes Communicator* explores what we have learned from COVID-19 and how it has impacted us all.

Meghann Henderson describes how our mental health has been impacted by the lockdowns during the pandemic. The article describes how being together constantly with those with whom we live changes family dynamics and provides evidence for the increased incidence of anxiety and depression reported since the onset of the pandemic.

Kit Yan Christie Chung, Parinaz Parhizga and Angela M. Cheung discuss the mechanisms that could be at play with the increased rates of type 1 and type 2 diabetes being diagnosed since the onset of the pandemic. At this time, it is believed that COVID-19 has an impact on pancreatic beta cells and contributes to insulin resistance.

Next, in "Survival Guide: Outpatient COVID-19 Therapeutics," Jonathan Nhan gives a comparison of treatment options for COVID-19 in Canada and across the world. The survival guide includes what people with diabetes need to know to navigate a world with COVID-19. We then learn about the bivalent COVID-19 booster from Michael Boivin. This article is a great resource to help answer your patients' vaccine questions.

Elaine M. Cooke and Susan Harris review glucagon-like peptide-1 receptor agonist use, including benefits and possible side effects. The update to this class of medications in the guidelines includes a focus on reviewing and assessing not only glycemic management but also cardiovascular and renal status when deciding what glucose-lowering medication to add on.

The challenges and advances that emerged in our health-care system are discussed by a patient and health-care professionals. First, Susie Jin and Ilana Halperin answer a patient's question about how continuous glucose monitors are being used in both

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inpatient and outpatient settings since the onset of COVID-19. Next, Erin Krusky interviews a University Health Network patient partner, Snehal Kamath, to gain insights into how receiving diabetes care during COVID-19 looked and felt.

This issue wraps with an important glimpse into the "Potential for Virtual Diabetes Care in Indigenous Communities," written by Jessica (t'łisala) Guss, Barbara MacDonald and Rebecca Sovdi. As the world moved to virtual spaces for health care, work and education, the issue of digital equity became even more immediate. Digital equity includes internet access, software and hardware, and bandwidth to accommodate the increased demands. This article acknowledges that specific strategies are needed to address the colonial legacy of health care. However, the quality of the relationship between the care provider and the person living with diabetes is discussed as essential to producing positive patient outcomes.

As we reflect on how COVID-19 has impacted our personal life, work life and the health-care system, we know that while COVID-19 has brought changes that are challenging, it has also brought advancements that are hopeful. The pandemic has been both a great pause and a time of hectic change. We have come together in new and exciting ways, such as having more options to work, learn and play virtually. However, nothing can replace being able to be in the same physical space with others.

FROM THE CHAIR'S DESK

Bidding Farewell to 2022

Lynn Baughan, RN, BScN, MN, CDE
Chair, Professional Section National Executive

It's hard to believe that the year is almost over! It has been an interesting one, especially with COVID-19 still playing a large part in our everyday lives. In this issue, the editors have compiled a wonderful collection of articles all about COVID-19 and its effects on the care of people living with diabetes. Be sure to read them all! They're timely and informative, and give great insight into the practical care of COVID-19 and diabetes.

Thankfully, in some ways, despite COVID-19, we've been able to get back to some normal activities. For instance, the Diabetes Canada/CSEM Professional Conference in Calgary was a great success. There were 1,721 delegates in total, with 1,010 who attended in person and 711 who attended virtually. The lineup of speakers was amazing—Dr. Alice Cheng spoke about diabetes and chronic kidney disease; Dr. Harpreet Bajaj chaired an exciting clinical practice guidelines update session, showcasing the new "Remission of Type 2 Diabetes" chapter and accompanying "User's Guide"; Dr. Nicole Cardinal spoke about the barriers to diabetes care for Indigenous communities; and so many others who led educational sessions and symposia. Stay tuned for our Winter 2023 issue, which will showcase some of these great topics and speakers, as well as the award winners who were honoured in Calgary.

As this is the last issue of 2022, I'd like to take this opportunity to thank all of our professional members and volunteers who work so diligently and give so generously of their time to help Diabetes Canada and, in doing so, help to improve the lives of people living with and affected by diabetes. The selfless lending of your time and expertise is extremely important and so appreciated. You always go above and beyond and we thank you very much.

I hope you all enjoy the holiday season and have a very happy new year!

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What We've Come to Learn: The Effects of COVID-19 on Mental Health

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The past two and a half years have shaken up the way people communicate and interact, both personally and professionally. Many have experienced isolation, increased home/family demands, uncertainty and a decrease in face-to-face contact. We've also seen an increased reliance on virtual communication, as well as dramatic changes to daily routines. Many of us had to significantly change the ways in which we carried out our work and supported our patients, all while trying to navigate a looming pandemic and its implications on business and play, not to mention the anxiety and fear that came with the unknowns: how long would the pandemic last?, when might you or a loved one become sick? and would life ever return to "normal"?

There have been many opinions regarding COVID-19, and there never seems to be a shortage of emerging information on the virus. However, as a mental health professional, I'm sure that the past two and a half years have caused a collective trauma. As with any trauma, significant mental health consequences remain.

Alongside COVID-19 headlines, discussions about mental health have also taken the forefront throughout the pandemic. We have seen it in the news or perhaps through a more personal lens—seeing it firsthand in ourselves, family members or friends. From the perspective of a mental health professional, the concerns about mental health and increased conversations on the subject are not all that surprising.

In mid-March 2020, COVID-19 hit, and social distancing (and masks) were quickly encouraged. For many families, March break had just begun, and the possibility of an extended March break was on the horizon. Within weeks, those possibilities became a reality when schools were shut down and moved to virtual platforms. Likewise, workplaces were forced to close and pivot to remote working models. Masking was no longer recommended—it became mandatory. The previously encouraged social distancing turned into isolation/quarantining, and new information emerged daily (at times conflicting with the previous information). Handwashing, disinfectants, masks and hand sanitizer became necessities. The pandemic's beginning was marked by fear, confusion, questions, conflicting information and, in all honesty, chaos.

Naturally, many people became very anxious about the possibility of themselves or a loved one contracting COVID-19 and the potentially deadly consequences of the virus. These fears and anxiety were further fed by a lack of concrete information about the virus, not to mention the constant stream of fear-based media coverage.

While much of the anxiety and fear surrounding the COVID-19 virus is entirely understandable (valid even), mental health professionals (and anyone who has sought professional help for anxiety) know that anxiety feeds off of fear. Specifically, avoidance and giving in to the anxiety/fear, including making overt efforts to avoid the anxiety (provoking stimuli to protect oneself from a perceived threat), actually cause an increase in anxiety. Likewise, depression and depressive feelings feed off of, and are made worse by, all of the actions and behaviours that depressed individuals engage in, such as socially isolating one's self; withdrawing from people and things that used to bring joy; losing interest/engagement in hobbies, sports and activities; pulling away from friends and family; and not leaving the house. When we consider those descriptions, they start to sound eerily similar to how many would describe their experience during the pandemic—socially isolating, spending more time at home, decreased participation in things one used to enjoy, avoiding certain situations or engaging in overt actions and behaviours to keep ourselves safe from contracting COVID-19.

When we lay it out, the perfect storm becomes clear: how the conflicting media reports and increased use of social media to share assumptions, fears and worries, daily uncertainty, unanswered questions, increased family/home demands, and following (necessary) recommendations of masking, isolating, social distancing, sanitizing, etc., quickly led to increased rates of anxiety and depression.

As if that weren't enough, many parents, kids and families were forced to be together 24/7. Parents and caregivers suddenly got an inside look into their children's and teens' day-to-day lives, moods and thinking. They had no alternative

but to see behind the curtain into the thoughts, feelings and stresses their children and teens were experiencing daily. For many families, the situation inadvertently facilitated a version of "helicopter parenting" that didn't previously exist—a version of parenting and family life where the parents are always around, always watching and noticing things, further adding to the already increased stress levels that both caregivers and children/teens were experiencing.

Through this new, 24/7, inadvertent helicopter style of parenting that was thrust upon us, many caregivers started to notice potential symptoms in their children and teens (anxiety/anxious tendencies, depression/depressive tendencies, strained social relationships and poor mental health in general). In other cases, anxious/depressive tendencies were emerging because of the situational factors of the pandemic. This noticing and increased awareness of their children's struggles caused many parents to become more and more concerned, which became further amplified as they read and saw the media's focus on and coverage of the "mental health crisis." Parents and caregivers were hearing catastrophic news coverage regarding the "youth mental health crisis," which caused more panic and worry. In many cases, parents and caregivers began to closely monitor and hover over their children and teens, only exacerbating the stress and anxiety levels within many households.

Over the pandemic, the converging of environmental, social, emotional, situational and behavioural factors have come together and facilitated a decrease in overall emotional well-being, as well as increased concern and awareness of mental health in general.

While we begin to adapt to a new normal and live with/post COVID-19, collectively, we will continue to face its effects. This presents some people with increased anxious or depressive tendencies, more health-related anxiety, decreased social skills and difficulty re-entering life outside one's home. For some individuals, a formal diagnosis of anxiety or depression might be fitting, while, for others, the term "anxious tendencies" or "depressive tendencies" might be a better description. However, regardless of whether a formal diagnosis is warranted, some people may benefit from engaging in psychotherapy sessions with a registered psychotherapist, registered social worker or psychologist to assist them in managing those feelings throughout the transition to a new normal/world post-COVID-19.

Despite the many difficulties of the pandemic, one of the good things to come out of COVID-19 is that, as a society, we have an increased understanding and awareness of the importance of mental health and mental health care, including the importance of proactive mental health care.

As professionals, we can help maintain this new focus on the need for mental health care (proactive care as well as treatment) by encouraging individuals to prioritize and care for their mental health just as they prioritize and care for their physical health and well-being.

COVID-19 and New-Onset Diabetes

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Over 605 million confirmed cases of COVID-19 and more than 6.4 million severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)–related deaths have officially been recorded by the World Health Organization (1). Individuals diagnosed with either type 1 or type 2 diabetes mellitus are associated with higher hospitalization and mortality rates when infected with SARS-CoV-2 (2). Although the majority of the literature has focused on diabetes as a significant risk factor for COVID-19 infection and hospitalization outcomes, recent studies have started exploring the relationship between COVID-19 infection and the development of new-onset diabetes.

Viruses such as enteroviruses, rubella, cytomegalovirus and hepatitis C viruses have been shown to contribute to the development of diabetes via molecular mimicry or cytolysis (3). From the 2002–2004 outbreak of SARS-CoV-1, it was understood that angiotensin-converting enzyme 2 (ACE2) receptors are present on pancreatic beta cells, facilitating the entry of the virus into its host (4). A longitudinal study from China conducted in 2006 found that 10% of individuals with SARS-CoV-1 continued to have diabetes three years post-recovery (5). As both SARS-CoV-1 and SARS-CoV-2 are genetically similar, the data suggested that COVID-19 could induce new-onset hyperglycemia (3).

Pancreatic Beta-Cell Damage Caused by SARS-CoV-2 Infection

ACE2 proteins are expressed on pancreatic islet cells, allowing the direct binding and entry of SARS-CoV-2, leading to beta-cell cytolysis and impaired function (6). The mechanism and outcome of this is comparable to that of type 1 diabetes, as pancreatic beta cells are damaged and, occasionally, fully destroyed, resulting in a lack of insulin secretion (6).

Alternatively, viral infection can precipitate the body to release cytokines and chemokines causing inflammation, which can then prompt pancreatic beta-cell death and results in the decreased ability to detect blood glucose levels and the release of insulin accordingly (6). Studies have suggested that severe cases of COVID-19 inducing pancreatic tissue damage, in the setting of acute pancreatitis, can cause increased amylase and lipase levels, and focal enlargement and dilation of the pancreatic duct on computed tomography scans (7).

COVID-19 infection may also trigger an autoimmune response through molecular mimicry of the enzyme glutamic acid decarboxylase (GAD) released by islet cells (8). CD8+ T cells are activated and may mistakenly recognize GAD as a viral protein, triggering autoimmune and autoinflammatory cascades, inducing islet cell injury (8).

A 2021 study discussed the impact of COVID-19 on the endocrine and exocrine functions of the pancreas (9). Postmortem investigations of people with COVID-19 established the presence and replicating capability of the SARS-CoV-2 virus in the pancreatic beta cells (9). Ex-vivo experiments were performed on four human pancreatic islet donors by exposing the cells to COVID-19 virus (9). Nucleocapsid and spike proteins were detected on days three and five, post–ex-vivo exposure to COVID-19 (9).

COVID-19's Contribution to Insulin Resistance

The SARS-CoV-2 virus invades the host via the ACE2 receptors and induces the downregulation of this receptor by promoting the overexpression of angiotensin II (10). An imbalance of ACE2/angiotensin II disrupts the insulin-signalling pathway, and the overexpression of angiotensin II contributes to the development of insulin resistance (10).

Another factor that contributes to insulin resistance involves the adipose tissue, which plays an important role in releasing proteins and cytokines, known as adipokines (11). Adipokines have a major function in regulating insulin sensitivity, and individuals with severe COVID-19 tend to express lower levels of adiponectin and have lower adiponectin-to-leptin ratios, which can also explain hyperglycemia in this population (11).

Individuals with COVID-19 may also develop insulin resistance through the widespread use of glucocorticoids for their immunosuppressive properties during the acute phase of the infection (12). Glucocorticoids such as dexamethasone can be a lifesaving intervention during the acute phase; however, a well-known side effect of their use is hyperglycemia, which can contribute to the development of diabetes (12). They can promote insulin resistance through disruption of muscle and adipose tissue's uptake of blood glucose and can increase inflammatory cytokine levels (12). Although most people who experienced hyperglycemia while receiving glucocorticoid therapy return to their baseline, some people do go on to develop new-onset diabetes (12).

Outcomes Data in Individuals With COVID-19

A children's hospital in Alabama, United States, reported an alarming increase of 205.3% in diabetes admissions relating to new-onset diabetes between April and November 2020, in contrast to a 1.9% and 4.8% average annual increase for type 1 and type 2 diabetes, respectively, from 2002 to 2015 (13). However, it is unclear whether the increase in cases of new-onset diabetes can be directly linked to COVID-19 infection. Another study in China found that 27 of 658 individuals with acute COVID-19 without a previous diagnosis of diabetes presented with ketoacidosis (14). In a third study, 46% of 551 individuals hospitalized with COVID-19 presented with hyperglycemia (15). Among those with hyperglycemia, 35% continued to have hyperglycemia after six months and approximately 2% were diagnosed with new-onset diabetes (15). A prospective study of 64 individuals with COVID-19 without a prior diagnosis of diabetes examined C-peptide and fasting blood glucose levels at various time points (16). While there was a significant increase in C-peptide levels (an indicator of innate insulin production) at the three- and six-month follow-ups compared to baseline, fasting blood glucose levels at six-month follow-up were significantly higher than at three months, suggestive of insulin resistance in people with COVID-19 (16). Finally, a recent systematic review and meta-analysis of seven studies concluded with a 20% incidence for COVID-19–related new-onset diabetes and 25% incidence for COVID-19–related hyperglycemia (17).

Summary

There is evidence to suggest that a COVID-19 infection can increase the risk of developing diabetes. Various mechanisms are responsible for this phenomenon. Clinicians should be aware of this potential relationship between COVID-19 and new-onset diabetes and provide appropriate care plans for individuals who have had a COVID infection. Long-term outcomes should be further studied in this population.

Declaration of Conflicts of Interest

A.M. Cheung has served as a consultant for Roche, and is a Principal Investigator on the CIHR-funded RECLAIM trial for which MediciNova is providing a drug. All other authors have no potential conflicts of interests to declare.

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Survival Guide: Outpatient COVID-19 Therapeutics

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Introduction

Although miraculous progress has been made since the beginning of the pandemic, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) continues to be a global challenge to public and personal health. COVID-19 is the disease that encompasses a spectrum of illnesses from mild respiratory symptoms to severe pneumonia, multiorgan failure and death (1,2). Some will experience long COVID, which may be physical or psychological symptoms that persist after the initial infection. Individuals who are unvaccinated, immunocompromised, older or who have chronic conditions are at higher risk for severe outcomes, including hospitalization and death (3).

How COVID-19 Affects Those Living With Diabetes

It is well documented that people living with diabetes are at high risk. These individuals may have other risk factors (i.e. advanced age, hypertension, obesity) that also increase the risk of severe outcomes. A recent meta-analysis found that diabetes approximately doubles the risk of disease severity and mortality (4).

What Should People Do?

It is important to prepare for isolation and if feeling unwell from COVID-19. Individuals are encouraged to proactively do the following:

- be up-to-date on COVID-19 vaccinations;
- have sufficient glucagon (if at risk of significant hypoglycemia), ketone strips (type 1 diabetes) and blood glucose monitoring supplies;
- routinely monitor blood glucose, and more frequently, if needed;
- continue taking medications and practice sick-day management if unwell and/or dehydrated; and
- keep a list of all prescription and nonprescription medications.

If patients are symptomatic or were a close contact with a person known to have COVID-19, they are recommended to

seek a test (i.e. rapid antigen) as soon as possible. If positive, they should contact their preferred health-care provider or visit a COVID-19 assessment centre to assess treatment eligibility, as timely access is important to ensure optimal efficacy.

What Treatment Options Are Available?

It is important to note that the COVID-19 literature and recommendations rapidly evolve over time. As of December 2022, several treatment options exist for mild-to-moderate COVID-19.

Nirmatrelvir/ritonavir (Paxlovid) is an antiviral used for adults ≥18 years old. Paxlovid inhibits an enzyme that renders the virus incapable of processing its proteins, preventing replication. It is a five-day regimen given within five days of symptom onset. The dose may need to be adjusted if kidney function is impaired. Pharmacist collaboration is strongly encouraged to manage drug interactions, as this poses a significant challenge to its use. Patients may need to adjust the doses of their antihyperglycemic, antihypertensive, cholesterol and other chronic medications. Consequently, certain drug interactions will contraindicate its use, and another treatment should be considered.

Remdesivir (Veklury) is another antiviral medicine that can be used for adults ≥18 years of age. Remdesivir is metabolized to form a substrate that ultimately prevents viral replication and RNA synthesis. Remdesivir is a three-day regimen given intravenously at a hospital or clinic within seven days of symptom onset. Patients need to return each day for treatment. Drug interactions are minimal with this medication.

Sotrovimab is a monoclonal antibody used to treat adults and children ≥12 years old and who weigh at least 40 kg. Sotrovimab binds to a highly conserved portion of the SARS-CoV-2 spike protein, neutralizing the virus, and elicits immune processes to promote viral destruction and clearance. It is a one-dose treatment given intravenously in a hospital or clinic setting within seven days of symptom onset. Sotrovimab has no known drug interactions.

Tixagevimab/cilgavimab (Evusheld) is a monoclonal antibody for adults and children ≥12 years old and weigh at least 40 kg. It neutralizes the virus, preventing viral attachment, and has utility as pre-exposure prophylaxis for COVID-19. Recently, it received authorization for treatment as two intragluteal injections within seven days of symptoms.

Table 1 summarizes the availability of provincial treatment options. Previous waves of COVID-19 had one predominate variant, whereas several are now circulating simultaneously. Recommendations differ due to the interpretation of data regarding variants of concern (VOCs). Paxlovid and remdesivir are effective against the circulating VOCs (5). Although sotrovimab maintained effectiveness to a broad range of variants, it is not widely used across Canada because laboratory studies suggested early omicron sublineages reduced its activity (5,6). However, recent real-world observational studies demonstrate that Paxlovid, remdesivir and sotrovimab remained effective in high-risk patients during early omicron variants

Table 1: Treatment options by province

Province	Paxlovid	Remdesivir	Sotrovimab	Evusheld
British Columbia	✓	✓	✓	✓
Alberta	✓	✓		
Saskatchewan	✓	✓		
Manitoba	✓	✓		
Ontario	✓	✓		
Quebec	✓	✓	✓	✓
New Brunswick	✓			
Newfoundland and Labrador	✓			
Nova Scotia	✓	✓	✓	
Prince Edward Island	✓			

(7-9). There is currently no real-world data to characterize the performance of Evusheld treatment to any omicron variant. Interestingly, similar concerns arose around Evusheld and suggest that current VOCs may be associated with resistance and recommendations against its use are being published (6,10).

Unproven, Ineffective Therapies

There is insufficient evidence to support colchicine, vitamin C or zinc (11-13). There is no robust evidence for ivermectin and hydroxychloroquine (14-16).

Potential Treatment Options

Bebtelovimab was an antibody used in the United States with much promise. However, the data came from a single phase 2 randomized placebo-controlled trial. Recent changes in United States Food and Drug Administration guidance paused its use because it is expected to be ineffective against the predominant BQ variants. It may make a comeback with future VOCs.

Molnupiravir is an antiviral medication that was submitted to Health Canada for review but has yet to be available. This may be due to the lacklustre results seen in the complete analysis of the trial, which demonstrated poorer efficacy than initially reported (17).

Other antivirals are on the horizon with oral remdesivir currently in clinical trials and ensitrelvir recently approved in Japan.

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Answering Your Frequently Asked Questions About the Bivalent COVID-19 Booster

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In the fall, Health Canada approved the bivalent COVID-19 boosters. These boosters are a new option in reducing the risk of contracting the COVID-19 virus, and they are especially important for people living with diabetes, who are at an elevated risk of severe COVID-19 outcomes, such as hospitalization and death (1).

Health-care professionals should be able to address some of the common questions that people will have regarding these new booster options. This article covers eight of the most frequently asked questions about these new boosters.

1. What is in these new boosters?

The original mRNA vaccines contained mRNA that codes for the spike protein of the ancestral (original) COVID-19 virus. The bivalent boosters contain mRNA that codes for the spike protein of the original ancestral strain and mRNA that codes for the spike protein of omicron (2). This leads to the production of antibodies targeting both the original ancestral spike protein and the omicron spike protein.

2. Why do we need this type of booster for omicron and not other previous variants, like delta?

Omicron has approximately 50 mutations, with 30 occurring in the spike protein. With vaccines targeting the spike protein, this number of mutations can decrease the ability of the generated antibodies to bind to the omicron spike protein. This puts people at risk of breakthrough infections from omicron.

Data show that the omicron subvariants are the most evolved away from the ancestral strain compared with other variants to date (3). Although current data have shown that the original vaccines and boosters are effective against omicron, their antibody levels drop significantly faster than with other variants (4).

3. I have already received two boosters; do I really need this one?

The primary series (two doses) and additional booster doses have protected people from COVID-19. The National Advisory Committee on Immunization (NACI) recommends that all people ≥12 years of age who are at risk of serious illness from COVID-19 (which is all people with diabetes) should be offered a fall COVID-19 vaccine booster dose regardless of the number of booster doses previously received (2). For adults 12 years of age and older, this would preferentially be a bivalent booster (2). One key point is that the bivalent boosters are only recommended in people who have completed their two-dose primary series (2).

A way to explain the recommendation for a fall booster to people is that the fall is a reset in the COVID-19 vaccine strategy. We are building on what they have done in the past and this new strategy is to help protect them moving forward.

4. Do these new boosters actually work?

In a study measuring antibody response, not only did the new boosters lead to significantly higher protection against the omicron BA.1 variant, they also boosted the antibodies to all previously circulating variants (5). Real-world evidence from the United States found that the bivalent boosters provided significant additional protection against symptomatic severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection in persons who had previously received two, three or four monovalent vaccine doses (1).

5. There are multiple versions of the bivalent booster; which one should I get?

There are now three bivalent boosters authorized by Health Canada. These include the following:

- mRNA-1273.214 (Moderna)—contains 25 µg of mRNA that codes for the BA.1 omicron strain spike protein and 25 µg of mRNA that codes for the ancestral strain spike mRNA
- BNT162b2 (Pfizer)—contains 15 µg of mRNA that codes for the BA.4/5 omicron strain spike protein and 15 µg of mRNA that codes for the ancestral strain spike mRNA
- mRNA-1273.222 (Moderna)—contains 25 µg of mRNA that codes for the BA.4/5 omicron strain spike protein and 25 µg of mRNA that codes for the ancestral strain spike mRNA

Some people may ask which bivalent booster they should receive. NACI recommends the following:

- Bivalent omicron-containing mRNA COVID-19 vaccines are the preferred booster products for the authorized age groups.
- The Pfizer bivalent booster is indicated for people 12 years of age and older. The Moderna bivalent boosters are indicated in people 18 years of age and older.
- Bivalent omicron-containing mRNA vaccines are expected to broaden the immune response and provide improved protection against the omicron variant and subvariants compared to the original mRNA COVID-19 vaccines, with a similar safety profile.

To answer the question, either booster option would be appropriate for people with diabetes. The fundamental issue is the sooner they can be boosted, the sooner they will have enhanced protection against the omicron variant.

6. I have already had COVID-19, so I should be protected, right?

Unfortunately, many Canadians have had breakthrough infections during the omicron wave. Just as with vaccines, the antibodies generated by these infections will tend to wane over time. A bivalent booster is recommended by NACI at six months after a previous COVID-19 infection (2). They suggest that this can be changed to three months, depending on the amount of circulating virus and the individual's risk (2). Current studies have shown that when the bivalent booster was given to people with a previous infection, the antibody response was very high and may offer significant protection (5).

7. I just had my last booster; when should I get my bivalent booster?

NACI recommends that people should receive a bivalent booster at least six months after their last booster, or can be considered at three months, depending on the individual's risk (2). It is important to note that the recommendations on booster timing of provinces or territories may be different from those of NACI.

8. Are the bivalent boosters safe?

The side effects of the bivalent boosters are generally equal to or less than the second dose of the primary series (2). Of special note is that the risk of myocarditis/pericarditis is lower with booster doses than with the second dose of the primary series (2). There are no differences between the risk of myocarditis between the Pfizer and Moderna boosters, and, thus, the bivalent Moderna booster is recommended for adults ≥18 years and the Pfizer bivalent booster can be used in those ≥12 years old (2).

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Using Glucagon-like Peptide-1 Receptor Agonists in Practice

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The 2020 pharmacologic update to Diabetes Canada clinical practice guidelines (CPG) brought a change to the type 2 diabetes (T2D) treatment algorithm with an emphasis on reviewing and assessing not only glycemic management but also cardiovascular (CV) and renal status when considering adding, replacing or adjusting pharmacotherapy (1). Glucagon-like peptide-1 receptor agonists (GLP-1 RA) and sodium-glucose cotransporter-2 inhibitors (SGLT2i) at doses that have demonstrated cardio-renal benefits became the agents of choice when adjusting or advancing therapy. This article focuses on the GLP-1 RA class of medications.

Multiple GLP-1 RA have proven CV risk reduction at specific doses, and all show effective glycemic management, the potential for weight reduction and a low risk of hypoglycemia when not used with insulin or a sulfonylurea.

When selecting the appropriate GLP-1 RA for an individual, clinicians need to be aware of differences in the agents' CV risk reduction, glycemic management, weight reduction, incidence of side effects and suitability for special populations.

Liraglutide study also showed a significantly lower incidence (22%) of CV death (1). The majority of participants (68.5%) in the dulaglutide trial were over 60 years of age with a minimum of two CV risk factors only (1). The outcome of major adverse cardiovascular events was the same for all study participants, leading to the recommendation of a GLP-1 RA for primary prevention in the over 60 years age group with at least two CV risk factors (1). The evidence for this primary prevention is grade A for dulaglutide, grade B for liraglutide and grade C for semaglutide (1).

Contributing to weight loss, GLP-1 RA reduce appetite and prospective food consumption, increase satiety and a feeling of abdominal fullness, and limit caloric intake under conditions of ad libitum feeding (2). Human studies have confirmed the ability of GLP-1 RA to influence food choices (toward a selection of less energy-dense, healthier foods) (2).

The most common adverse events are nausea and vomiting, both of which are usually transient and of mild or moderate severity, and people can develop tolerance to these adverse effects over time (3). The frequency of nausea among patients ranges from 13% with dulaglutide (0.75 mg); approximately

Table 1: Clinical benefits for glucagon-like peptide-1 receptor agonists

Medication	MACE (hazard ratio) (1)	Fasting plasma glucose reduction from baseline (mmol/L) (2)	Reduction from baseline of A1C (%) (2)	Weight loss (kg) (2)
Dulaglutide	0.88	2.0	1.4	3.0
Exenatide BID	0.91	1.1	0.9	3.5
Exenatide XR		1.7	1.25	2.8
Liraglutide	0.87	2.0	1.3	3.2
Lixisenatide		1.4	0.95	3.2
Semaglutide injectable	0.74*	2.8	1.8	6.5
Semaglutide oral	0.79†	2.0	1.2	4.2

A1C, glycated hemoglobin; *BID*, twice daily; *MACE*, major adverse cardiovascular event; *XR*, extended release.
*Evidence is graded lower because the hypothesis for MACE was not predefined.
† Indicated cardiovascular safety but did not demonstrate superiority because the trial was not designed to test superiority.

Table 2: Glucagon-like peptide-1 receptor agonist dosage recommendations (3)

Drug	Titration	Initial dosage	Recommended dosage	Administration in relation to meals	Missed dose
	Once or twice daily				
Exenatide	Yes	5 mcg BID for at least one month	5–10 mcg BID	Should be administered within 60 min before the two main meals of the day at least six hours apart	Continue with the next scheduled dose
Liraglutide	Yes	0.6 mg OD for at least one week	1.2–1.8 mg OD	At any time, without regard to meals	Take dose on the next day as usual. Do not take an extra dose or increase the dose on the following day to make up for the missed dose
Lixisenatide	Yes	10 mcg OD for 14 days	20 mcg OD	Should be administered within 1 hour prior to the first meal of the day	Administer the dose within one hour before the next meal
Semaglutide oral	Yes	3 mg for at least 30 days	7 mg for at least 30 days may be increased to 14 mg if necessary	Must be swallowed whole on an empty stomach with no more than 120 mL of plain water, at least 30 minutes before the first food, beverage or other oral medication	Skip missed dose and take next dose the following day
	Once weekly				
Dulaglutide	No	Not applicable	Monotherapy: 0.75 mg once weekly	At any time, without regard to meals	Three or more days until the next scheduled dose: administer the dose as soon as possible
			Add-on therapy: 1.5 mg once weekly		Less than three days until the next scheduled dose: skip the dose, wait and administer their next regularly scheduled weekly dose
Exenatide XR	No	Not applicable	2 mg once weekly	At any time, without regard to meals	Administer the next dose as soon as practical. Only one injection should be administered in a 24-h period
Semaglutide SC	Yes	0.25 mg once weekly for 4 weeks	0.5–2.0 mg once weekly (dose increase after 4 weeks if required)	At any time, without regard to meals	≥ 5 days until the next scheduled dose: administer the dose as soon as possible

BID, twice daily; *OD*, once daily; *SC*, subcutaneous; *XR*, extended release.

20% with liraglutide, extended-release exenatide, dulaglutide (1.5 mg) and semaglutide; 26% with lixisenatide; and 36% with once-daily exenatide (3).

Nausea and vomiting occur more frequently when a GLP-1 RA is combined with metformin or insulin (3). Since GLP-1 RAs reduce glucagon secretion, providing an action similar to metformin, a trial of lowering the metformin dose may be beneficial in minimizing gastrointestinal (GI) side effects (3). Recommendations to manage nausea include eating smaller meals, eating slowly and avoiding high-fat meals and spicy foods (3). However in the context of managing GI side effects, it is better to say that 80% to 90% of people do not experience any.

Special populations

All agents, except for liraglutide, are indicated for use in those 18 years of age and older. Liraglutide can be used in those ≥10 years of age as an adjunct to metformin with or without insulin when lifestyle plus maximum tolerated metformin does not provide adequate management.

There is no dose adjustment necessary for those 65 years of age and older. However, they may have greater sensitivity to the effects and require a lower dose (4). Avoiding hypoglycemia is especially important in older adults. GLP-1 RA have low risk of hypoglycemia, and are more effective for glycemic management and weight loss than dipeptidyl peptidase-4 inhibitors, which are often used in older adults (4).

Public drug coverage as of July 2021 for GLP-1 RA can be found on the Diabetes Canada website (5). Coverage for medications is indicated as "Not Listed" when there is no coverage; on the public drug plan, listed where the medication can be prescribed by any doctor; or restricted, with coverage restricted to those who meet eligibility criteria and receive prior approval from the provincial drug benefit plan. Cost in the "listed" or "restricted" category could be fully or partially covered according to the terms of the public drug plan.

Semaglutide injection is listed in Ontario, Nunavut, Northwest Territories, Yukon and for the Non-insured Health Benefits (NIHB) program. All other provinces cover on a restricted basis.

Lixisenatide injection is listed in Ontario, Nunavut, Northwest Territories and for the NIHB program, and on a restricted basis in Alberta, Saskatchewan and New Brunswick.

Liraglutide injection is covered on a restricted basis only in Quebec.

Dulaglutide injection coverage is available in Quebec on a restricted basis.

Other GLP-1 RA injectables or orals are not listed in all provinces.

Many private drug plans cover GLP-1 RA; individuals should check with their plan directly.

Although GLP-1 RA share the same general mechanism of action, they differ in terms of their formulations, indications (monotherapy and/or combined therapy), cardiorenal benefits, dosages, precautions and use in special populations. Being aware of these differences can help health-care providers match the most appropriate GLP-1 RA with the person's characteristics.

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The Diabetes Communicator: Call For Applications

Do you want to strengthen your writing skills and work with a collaborative group of Diabetes Canada multidisciplinary professionals across the country while reviewing the newest information on diabetes?

If so, *The Diabetes Communicator* Editorial Board may be a great fit for you! The Editorial Board is seeking new board members from medicine, nursing, nutrition, pharmacy or social work who are (or are willing to become!) Diabetes Canada members.

As an Editorial Board member, your responsibilities will include the following:

- **collaborating with other board members over regular teleconference meetings to determine issue themes;**
- **connecting with other members in the diabetes health-care community to seek authors for articles;**
- **reviewing and approving content for the journal's audience; and**
- **acting as an associate editor once or twice a year.**

Interested applicants should email the following to Jill Toffoli at jill.toffoli@diabetes.ca:

- **a current CV, along with two references,**
- **two short samples of professional writing, and**
- **a brief explanation of why you would be a great candidate to join us.**

Deadline for applications is January 31, 2023.

Ask the Experts:

"I am interested in knowing more about how COVID-19 has influenced the use of CGMs [continuous glucose monitors] in the inpatient setting."

Response 1:

Susie Jin, RPh, CDE, CRE
Clinical Pharmacist, Ont.

During the early months of the COVID-19 pandemic, a fervent effort was made to preserve inpatient and all hospital resources. So, although not in the inpatient setting, here is my community pharmacist's perspective on how continuous glucose monitoring (CGM) impacted care of people with diabetes.

Background setting: I live and work in a small town, and having personal relationships with other diabetes care team members has always supported collaborative care. I believe it was this pre-existing trusting relationship with the health-care teams of persons living with diabetes that enabled their positive outcomes.

A few times during the early months of the pandemic, I received urgent phone calls from local primary care providers. In each situation, they had either a person who was newly diagnosed with a glycated hemoglobin (A1C) above 12% or a person who was not newly diagnosed but whose previously at-target A1C was now above 11% on follow-up blood work (discovered during a routine follow-up virtual appointment). In all of these cases, the primary care provider explained to me that, depending on the urgency of the situation, they would normally have either directed the person to the hospital emergency department immediately or referred them to our local diabetes education program. However, in the early months of the pandemic, some people were, perhaps inappropriately, fearful of using hospital services, and diabetes education programs, similar to many health-care services, were temporarily unavailable until policies and procedures were quickly established.

Particularly where there was a concern that the person was (or was on the border of) experiencing an acute hyperglycemic emergency, rules were established and I, the diabetes educator pharmacist, agreed to provide care only if the person and/or caregiver agreed to stay in close virtual connection with me (after a shortened in-person meeting), and the person and/or caregiver had the capacity to perform a basic level of self-care (being able to communicate [i.e. to describe symptoms], capture CGM, and access and prepare agreed-upon foods). There was also open access between the pharmacist and primary care provider, and I would reach out, via text or email, to the primary care provider according to professional judgment. Of note, while texting is often convenient and quick, the advantage of an email is that communication is more readily retrievable in future (if necessary) and the primary care provider can more easily capture email communication and store it on an electronic medical record to support documentation.

In these situations, COVID-19 influenced the use of CGM technology in that it enabled people to safely care for themselves at home, rather than be cared for in the emergency department. In some instances, the person would come to the pharmacy for an initial shortened meeting where they would be connected to a CGM device and insulin was injected subcutaneously when indicated; other times, the person/caregiver did a curbside pickup of the CGM device (and insulin) and the CGM (and insulin) demonstration was done via a subsequent video call. Follow-up was usually done virtually via audio only (phone call) or on a video and audio platform, although pharmacies remained open, and, when it enhanced care, people did come into the pharmacy for shortened in-person meetings. Follow-up between the person/caregiver and pharmacist was open and determined based on the person's need—possibly, initially, every hour or even more frequently, particularly if rapid insulin was administered and there was a concern that an acute hyperglycemic emergency was imminent, and then decreased once the person/caregiver was more self-care confident and any acute risks of either hypo-or hyperglycemia were resolved. In each of these situations, the person had connectivity with CGM via a cloud-based platform. This enabled the pharmacist to keep the person with diabetes safe and have timely conversations about the person's CGM data.

As a direct result of the pandemic, health-care communities increased collaboration to keep both people needing care and providers safe. This is one example of how health care could be enhanced in the future wherein some people could care for themselves at home with increased access to health care that could support people in their homes, and possibly increased access to technologies, such as CGM.

Response 2:

Ilana Halperin, MD, MSc, FRCPC
Sunnybrook Health Sciences Centre and University of Toronto, Toronto, Ont.

The COVID-19 pandemic led to many innovations in how diabetes care is provided. A number of American hospitals started pilot projects using continuous glucose monitors (CGMs) in hospitalized individuals in order to minimize the number of times nurses needed to don personal protective

equipment and enter the room. The CGMs were found to be reasonably accurate compared with traditional capillary glucose monitoring and reduce the frequency with which the nurses needed to enter the individual's room. They also found that the use of CGMs helped to reduce the incidence of hypoglycemia in hospital. Based on this new evidence, the Endocrine Society published the following recommendation in 2022:

"In adults with insulin-treated diabetes hospitalized for non-critical illness who are at high risk of hypoglycemia, we suggest the use of real-time continuous glucose monitoring (CGM) with confirmatory bedside point-of-care blood glucose (POC-BG) monitoring for adjustments in insulin dosing rather than POC-BG testing alone in hospital settings where resources and training are available" (1).

The last line of this recommendation is, in fact, the most important message for us in Canada, as currently resources are limited and the cost of CGM is prohibitory for hospitals on tight budgets. Many hospitals, including my own, have instituted policies to support individuals who have their own glucose sensors to continue wearing them in hospital; however, practices vary regarding how the sensor glucose is used by the nurse. At my institution, only those who have been seen by someone in the Endocrinology Division and deemed safe and suitable for self-management of their diabetes can use the sensor glucose to adjust insulin; if the nurse is administering the insulin, then point-of-care glucose testing on the hospital-calibrated machine is expected. I have heard of other institutions where the nurses are able to dose insulin based on the individual's sensor readings if the sensor is compared once daily to a capillary glucose value and the two results are within 15% of each other. As with many innovations, Canada does lag behind the United States in implementing newer technologies, but, in this case, I think a cost-effectiveness analysis would have to be conducted before we see more widespread use of glucose sensors in hospitalized individuals.

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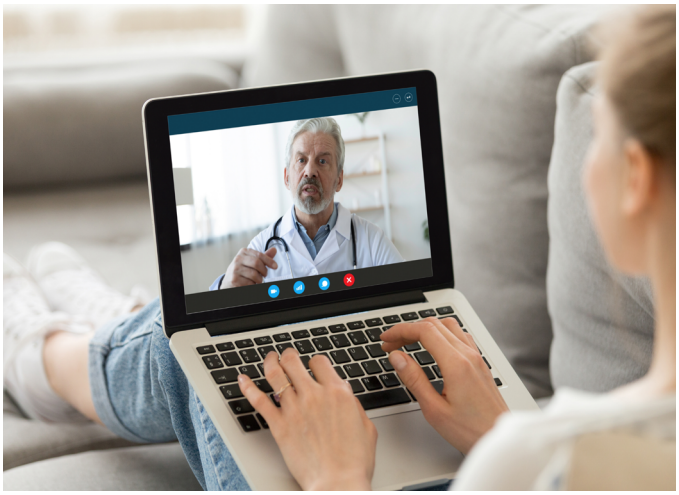
Virtual Diabetes Care During the COVID-19 Pandemic: A Patient's Perspective

Snehal Kamath[1]; Erin Krusky, MHSc, RD, CDE[2]

[1]Patient Partner, University Health Network, Toronto, Ont.; [2]Capacity Building Coordinator, Patient Education and Engagement Department, University Health Network, Toronto, Ont..

Receiving care changed during the COVID-19 pandemic and continues to evolve and change. Snehal, a patient partner at University Health Network, shares her perspective on accessing health care for her diabetes during the COVID-19 pandemic. The UHN Patient Partner Program is a community of patients and caregivers who are interested in contributing their experiences and expertise to improving and transforming health care. The program supports patients, staff and leaders to partner and work together meaningfully toward common goals that are aimed at improving quality, safety and care.



Erin: What are some experiences you have had accessing virtual care since the COVID-19 pandemic began?

Snehal: My experiences accessing virtual care were quite positive. I felt good about virtual care because I was able to receive care in the comfort of my home and not risk exposure to COVID-19. Appointments with my endocrinologist have been by telephone for the past two years. He sent a requisition, via secure messaging, to have my blood drawn every three months and we reviewed the results together during our call. We covered similar information that he does in our in-person appointments, apart from a physical examination. I needed to be ready to share my weight, waist circumference and glucometer averages.

Having a previous relationship with my doctor before virtual care began was helpful. Open two-way communication is important. I found that with virtual appointments they did not feel rushed.

One huge advantage with virtual care is time saving. It was great that I didn't have to waste time travelling to and from appointments, paying for parking and sitting in a waiting room to be seen. I was told my doctor will call between a certain time frame, and I waited comfortably at home for the call. My 15-minute appointments were just that and I was able to continue with my day.

Erin: Are there any virtual care experiences that were not positive?

Snehal: The most important thing that virtual care cannot replace is a physical exam. For instance, people with diabetes should have their feet checked regularly for neuropathy or sores. Virtual appointments also do not allow for blood pressure to be taken and for examining your abdomen for enlarged liver or possible fluid in the belly cavity.

If you don't have a previous relationship with your health care provider, it can be hard to develop a connection virtually. As well, if you have poor communication, it could result in misunderstanding and errors in treatment or diagnosis.

Erin: Are you getting more choices now about how you access health care? Is there anything lacking still about your care?

Snehal: I am part of a walking group that could not continue in the beginning of the COVID-19 pandemic. I missed the social interaction and connecting with others because we really helped motivate each other. We have been able to start walking together again now since vaccines became available.

The choice of how I access my health care will ultimately be up to the doctor's office. My preference would be to meet new health-care providers in person to establish a relationship first and then, where possible, be offered a choice between in person and virtual.

Erin: Sounds like you also make your preference clear for how you want to access health care.

Snehal: I sometimes ask for virtual because it is more convenient. I see the benefits of both virtual and in-person visits. It really depends on the situation and health issue. There are many people who don't have a primary care doctor and end up at urgent care. Also, remote parts of our country, where people are underserved, could receive health care without having to travel long distances by accessing virtual care.

The hybrid model of care that has evolved from the pandemic offers the option of both in-person and virtual care, including phone or video communication. Each model of care has a place. Allowing for individuals to make the choice to access the type of care they need is important in making health care accessible.

COVID-19 Pandemic Shifts Potential for Virtual Diabetes Care in Indigenous Communities

Jessica (t'łisala) Guss, Indigenous Advisor, IDEA Diabetes; Barbara MacDonald, Diabetes Consultant and Co-founder, IDEA Diabetes; Rebecca Sovdi, Diabetes Consultant and Co-founder, IDEA Diabetes

As the world shifted and adapted in response to the global COVID-19 pandemic, the provision of virtual care became the mainstay between service providers and individuals requiring care. Indeed, in many remote and isolated Indigenous communities, there were situations where fly-in nursing programs completely halted, and many personal support workers accessed physicians and nurses to provide virtual care as the only option for health care (1). While virtual care was thought of as a stopgap rather than an ideal option of health-care service provision during the pandemic (2), there are many people from coast to coast to coast, including those living in Indigenous communities, for whom virtual care has the potential to increase access to high-quality, timely and culturally safe health care.

Not only did health care transition to virtual care, so did practically all programs and services in Indigenous communities, including communications, some employment and education, which moved to online or virtual platforms because of the COVID-19 pandemic (1). This put an immediate emphasis on improving digital equity associated with internet access, software and hardware, and bandwidth to accommodate the immediate demands.

However, as the demands of COVID-19 moved to front and centre, other care needs, including diabetes, were forced to the background. Maybe, in time, the consequences of this will be more clearly understood. What has emerged is perhaps an acceptance and possible reliance on virtual care to augment or provide the basis of diabetes care in Indigenous communities.

Additional benefits of virtual care are associated with people not having to travel or, at least, having their travel reduced. This may contribute to a decrease in the risk of weather-related interruptions, a positive impact on the environment by reducing emissions created during transportation, and the

funds for travel can be redirected toward other aspects of care. Virtual care also offers an opportunity to restructure the schedule, timing and purpose of each encounter, to achieve specific outcomes on a continuum toward optimal diabetes self-management in ways that are more meaningful and designed for the person with diabetes.

With this shift, there needs to be some consideration about meeting the needs of people with diabetes in Indigenous communities through virtual care compared with in-person care, with some criteria for outcome tracking to determine effectiveness and to understand and guide decisions. Is it possible that outcomes from virtual encounters are better than usual care? Metrics need to be applied to demonstrate and offer insight into when in-person care is essential relative to the cost and other factors compared with virtual care. Consistent with key learnings from the COVID-19 pandemic (1), outcome measures need to be determined in conjunction with the Indigenous community members and leaders to ensure that Indigenous ways of knowing and being form the foundation for the approaches to diabetes care and management and are also aligned with the Diabetes Canada clinical practice guidelines.

Whether care is delivered virtually or in person, creating a safe environment and developing a relationship of trust is fundamental. This is done by preparing in advance, acknowledging and striving to eliminate systemic racism, understanding the impacts of colonialism on Indigenous health and well-being, and creating space to listen and find solutions together for a positive health-care relationship that will improve diabetes outcomes and quality of life (3).

The quality of relationship between the care provider and the person with diabetes determines the level of success in all circumstances, including virtual encounters. Establishing a relationship of trust and respect creates a foundation to move toward an individualized care plan determined by both the person with diabetes and the care provider. The objective is to establish a sound and lasting relationship that will foster knowledge-sharing and autonomous, effective diabetes self-management, and to assume this is one of many encounters, not a one-time-only event. In these encounters, application of a trauma-informed lens and holistic approach may reveal experience of loss and trauma, as well as strengths and solutions that have worked in keeping them going despite sometimes major obstacles. Even during a telephone call, a genuine relationship can develop very quickly where compassion and concern for the person are conveyed through pace, tone of voice, language, and ensuring the person remains at the centre of the model where their interests take precedence over the schedule or agenda of the health-care provider.

Positive health-care relationships have long been considered central to mitigating harm to Indigenous peoples. Specific strategies are needed to address the colonial legacy of health care and the perpetuation of inequities and to reduce the structural barriers to care (4). With careful consideration and collaboration, monitoring of outcomes and successes, virtual diabetes care can play a significant role in addressing these gaps and identifying strengths and solutions. The starting point is to view and design diabetes virtual care strategies with these themes in mind, and with the person with diabetes at the centre of the model.

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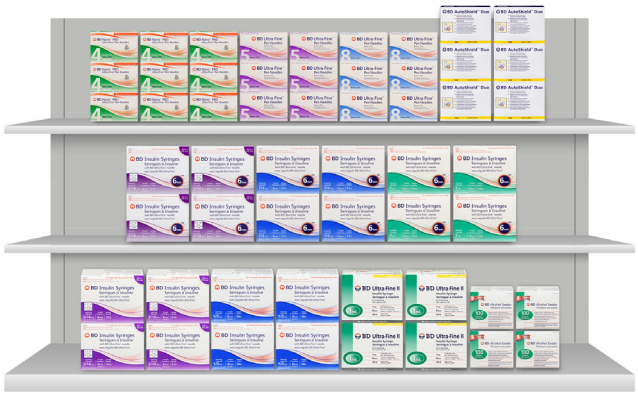
embecta formerly part of BD.
BD is manufacturer of the advertised products.

Diabetes has our undivided attention

embecta, formerly part of BD, is now a company singularly focused on diabetes care.

As one of the largest global diabetes companies, we will bring you the same trusted, broad BD product portfolio.



No immediate changes for you or your patients

- ☑ Same BD product packaging
- ☑ Same trusted products
- ☑ Same name in eRx system
- ☑ Same customer service and support

Advance every day together.

To develop and provide solutions that make life better for people living with diabetes.

Building on nearly a hundred years of experience in diabetes care:

~30 million
People living with diabetes trusting our products annually*

>7 billion
Units produced globally on an annual basis†

>100
Countries where our products are used to aid with the management of diabetes‡

*Data on file. embecta market model. 2021
†Data on file. embecta manufacturing. 2021
‡Data on file. 2021