January 14, 2021

Canadian Agency for Drugs and
Technologies in Health (CADTH)
865 Carling Ave.
Ottawa, ON K1S 5S8

Re: Diabetes Canada Feedback on the Hybrid Closed-Loop Insulin Delivery Systems for People with Type 1 Diabetes Technology Review

Thank you for the opportunity to provide feedback on the draft report *Hybrid Closed-Loop Insulin Delivery Systems for People with Type 1 Diabetes*.

Diabetes Canada's scientific and patient experts have provided comments on this draft document, for your consideration. Overall, our expert reviewers were encouraged with the findings and the direction that the report sets for the future. Administration of insulin and monitoring of glucose is essential for individuals with type 1 diabetes to support healthy behaviours, guide therapy, maximize safety, and achieve optimal health and quality of life. We appreciate the role that CADTH can play to ensure people have access to what they need to achieve these outcomes.

Access to the right medications, devices, supplies, and services with appropriate education and support, help people living with diabetes achieve optimal health outcomes. Diabetes is a disease that places many burdens on patients and their families. The mental health burden of diabetes causes stress and anxiety. The high cost of diabetes medicines, supplies, and devices is a financial burden, and patients report inadequate coverage by private and public insurers. Caregivers, especially parents of children with type 1 diabetes, must change their lives to help with diabetes management: not sleeping at night, changing or leaving employment to be present at school when school staff refuse to test blood glucose or deliver insulin. People with diabetes experience stress due to fear of nighttime episodes of hypoglycemia, and/or worrying about the ability to afford diabetes supplies. Diabetes also impacts family & life decisions: some women with type 1 diabetes choose not to have children—some for fear of passing on the genetic predisposition of diabetes and others worry about being able to care for a baby while managing their diabetes. For adults living with diabetes, there is also a professional burden: some people are unable to take employment opportunities, they are often worried about experiencing episodes of hypoglycemia at work (and may subsequently decide to endure long-term periods of hyperglycemia while at work), or they may be forced to choose a job based on benefits plan and not the actual role. Diabetes imparts a physical burden on people of all ages. More planning is required for exercise and physical play, some place limits on their activity to manage their blood glucose. Other health issues and complications due to diabetes increase health-care needs, wounds take longer to heal, infectious illnesses are more severe (e.g., influenza), and healthy sleep patterns are impacted (worry about lows, finances, etc.). Some of these burdens can be attenuated with the right individualized therapy, monitoring, and support. Indeed, people

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living with diabetes should have timely and equitable access to the medications, devices, and supplies that best suit their clinical needs and personal context based on best evidence, including hybrid closed-loop systems (HCLs). It is in this spirit that Diabetes Canada has provided the enclosed considerations regarding this report.

Diabetes Canada is an organization that produces world-renowned, evidence-based clinical practice guidelines and represents health-care providers who practice evidence-based medicine. Our comments are grounded in the perspectives and experiences of people living with diabetes, and the experts who provide health care. The comments reflect the opinions of the staff of Diabetes Canada, our professional network across the country, and patient experts. We would welcome the opportunity to discuss these views with you, to provide better advice to clinicians and policy makers.

Sincerely,

Seema Nagpal, B.Sc.Pharm, M.Sc., Ph.D.
Vice President, Science & Policy
Diabetes Canada

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Diabetes Canada Feedback on the Hybrid Closed-Loop Insulin Delivery Systems for People with Type 1 Diabetes Technology Review - Key Issues

Health Policy Decision-Making. While considering financial constraints and health policy development, patients need to remain at the center of decision-making. This entails acknowledging the patient perspective as a unique knowledge source, and meaningfully engaging patients early and frequently in the policy development process. The conclusions provided in the technology review are largely focused on clinical trial outcomes and cost-effectiveness, while placing little emphasis on other outcomes that are also important to patients. Therefore, while developing health policy recommendations, it is important to be inclusive, move beyond only clinical trial outcomes and cost-effectiveness, and to adopt a patient-centered approach that considers significant patient experiences. This includes a range of structural and psychosocial aspects of diabetes that affect patients' lives, treatment, care, and environment, for example, caregiver support, overall well-being (including mental health and distress), employment, socioeconomic status, education, etc. HTAs need to evolve beyond the current model of assessment to meaningfully acknowledge the value of patient experiences and the societal cost savings when patients have access to the most appropriate technology to manage their condition. While clinical trial data provide an important evidence source about those who will benefit from relevant interventions, there is a need to understand and apply these data to public policy that helps patients beyond the narrow boundaries of research studies. Patient experience and clinical experience can help build that bridge from research to healthy public policy.

The report rightly notes that *"One of the limitations of the clinical review is that there was no evidence on the effectiveness or safety of HCLs based on patient age, sex, race, glycemic control, or other clinical features (e.g., those who were pregnant or planning pregnancy, with a history of severe hypoglycemia, or those with hypoglycemia unawareness)"* (Line 3479). It also acknowledges that some consulted clinicians identified groups such as teenagers and older adults who traditionally experience less consistent glucose management as good candidates for the HCL systems; thus, the report demonstrates the flaw of relying solely on tightly controlled clinical trials to dictate health policy decisions.

Clinical Measurements. The report questions the validity of using time in range measures: *"the clinical validity of using glucose time in range metrics as a surrogate marker for the risk of developing diabetes-related complications is contentious"* [Line 1483-1484]. However, the Advanced Technologies & Treatments for Diabetes (ATTD) Congress recently published a consensus statement to support use of time in range (TIR), time below range (TBR), and time above range (TAR) as clinical targets (1). In fact, time in range has been shown to correlate with diabetes complications, including progressions of diabetic retinopathy and development of microalbuminuria (1,2). As such, the ATTD consensus panel identified time in range as a "metric of glycemic control that provides more actionable information than A1C alone" (1). The report has missed the clinical and real-world significance of the range metrics (TIR, TBR, TAR) to reduce undue

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exposure to severe hypoglycemia. Furthermore, it is important to not focus on the use of TIR solely as a surrogate marker of complications. This neglects its utility as a management tool for both patients and health-care providers, and accumulating evidence in this area cannot be overlooked.

The authors quote an unpublished, not-peer-reviewed analysis by University of Calgary researchers to support the assertion that time in range is an unvalidated outcome. This is not appropriate for a science-based review by a national HTA agency like CADTH. Upon review of that same University of Calgary analysis, we have several concerns about the methods and the interpretation of the data that are significant. We encourage you to remove reference to this analysis until there has been a public release and a peer review of their methods and interpretation.

Long-Term Effects of Using HCL. The report asserts that long-term data are lacking and thus funding decisions cannot be made. There are sufficient data demonstrating a reduction of A1C and that increased time in range improves A1C levels. Glycemic management measured by A1C is a surrogate outcome used in clinical trials that has been a standard metric for decades. While we agree, long-term health outcomes are ideal, in the absence of outcome data, A1C is useful to guide decision-making. In fact, we know that some outcomes track closely with lower A1C based on the DCCT (Diabetes Control & Complications Trial), that reported reduced early stages of microvascular complications (retinopathy, neuropathy, and nephropathy) that were still evident years after the study ended (3). Given that these devices under review are relatively new, having only been approved in Canada within the past 5 years, Diabetes Canada views it as unethical to withhold technological advances from patients to wait for more data on the devices' clinical effectiveness and safety when surrogate data currently exist. It is appropriate to ensure that HTA and policy decisions are reconsidered and updated as more data become available to ensure all patients have access to treatments based on current best evidence.

Inclusion of Devices and Data. The report states it will evaluate *"HCLs in their commercially available (or expected to be commercially available) form"* (Line 495). Non-approved devices that are in late phase clinical trials should be addressed given the likely class-effect of HCL systems. This report is very important to the diabetes community, so making it relevant for the near future and able to address predictable questions in the short term is desirable. The report also states that there is a lack of Canadian data on HCLs. We kindly point you to two recent publications in this arena: the first explores patient experiences with these systems, while the second provides results of a randomized crossover trial of HCLs vs sensor-augmented pump therapy (4,5). These newly published studies highlight the need to continually review and update the literature on the ever-evolving field of HCLs.

Budget Analysis. A budget impact analysis (BIA) is performed to simply describe the impact on the program budget. This approach is too simplistic and does not present the full picture given the absence of a full cost effectiveness within the report The BIA fails to capture the full savings to the health-care system, i.e., cost offsets of reducing complications (both short- and long-term) and reduced health-care utilization, as seen by fewer emergency room visits and hospitalizations. In its own work, through review

of CDR submissions and optimal use reports, CADTH has reviewed and estimated the costs of complications due to diabetes. While it is beyond the scope of our work to provide a specific estimate or a review of these economic analyses, these costs must be considered when evaluating interventions like HCLs, that can prevent or delay the onset of these significant outcomes and health care services. It is misleading to show a budget impact analysis without capturing the potential cost savings associated with improvements in glucose management anywhere in the report. It implies that the budget impact is the net cost of the program, which it is not.

Diabetes Canada acknowledges that provincial/territorial governments have finite resources and that the cost benefits gained from improved management of chronic diseases like diabetes take years to be fully realized. However, this is a bias that should not be placed against people living with chronic disease by implementing a time horizon of only 3 years in the analysis. A cost analysis should at least describe the longer-term benefits of A1C reduction on outcomes, based on DCCT trial data, as a sensitivity analysis.

Use of devices like HCLs reduces the disease burden for people with diabetes and improves their mental health in the form of reduced stress/anxiety, improved sleep patterns and health-related quality of life. According to the Mental Health Commission of Canada, the cost per case of the population that comprises mental illness other than cognitive impairment, *"includes physician and hospital care, medication, community and social services, and income support"* (6). The cost for all mental illness (including cognitive impairment) has been estimated at $42.3 billion (6). The cost savings to health-care systems through improved mental health and the productivity of people with diabetes and their caregivers should have been measured in this analysis. If not part of the primary analysis, it should certainly be part of the narrative on the benefits not quantified.

It is understood that the BIA is a limited estimate from the perspective of the public payer. If it were a patient-centred cost analysis, it would also value those additional costs and benefits (human and financial) to the patient. For example, short-term complications like episodes of hypoglycemia that may or may not require medical intervention still produce a drain on a person's well-being, as it can take one to two hours for the physiological effects to dissipate. Diabetes Canada suggests that, if not part of the primary public payer budget impact analysis, the patient-centred factors should nevertheless be considerations in a sensitivity analysis. If that is not possible, i.e., those factors are not considered, this information should be explicitly and transparently stated.

The budget assumptions do not take factor in the number of people who currently pay out of pocket for these devices—so they do not require new transmitters, receivers, etc., right away—or those whose private insurance currently covers a portion of the devices. While the public payer is not bearing the financial burden of these devices, they are still enjoying the benefits through short- and long-term cost savings to the health-care system.

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We disagree with the assumptions regarding device uptake: e.g., assuming 90% of people with type 1 diabetes will access HCLs in the short term is likely a gross over-estimate, given people have many individual reasons to prefer alternative methods of treatment and monitoring. Some do not like to use technology, some do not like wearing devices, some are accustomed to their current therapies and are not interested in training on new systems. For example, users of flash glucose monitors who are committed to intermittently scanned glucose monitoring cannot use HCL, which requires real-time data in the form of a continuous glucose monitor (CGM) and would thus not adopt the HCL system. Our informal estimates are that, even with public payer coverage, device uptake does not historically increase exponentially to 90%. Insulin pump usage, for example, is in the 30-40% range. However, you may be able to verify actual insulin pump and CGM usage with provincial plan administrators.

Patient Experiences. Type 1 diabetes is one of the most complex chronic diseases in terms of self-management. Diabetes impacts every aspect of people's day-to-day life: financial, physical, emotional, social, and professional. It is a condition that requires constant monitoring, 24 hours a day, seven days a week, making patients and/or their caregivers feel like they have another full-time job. Diabetes management is time-consuming, taking an average of 14 to 20 hours per week to manage, and there is never a chance for a break from diabetes. The variable nature of diabetes means that management success changes day to day.

Frequent or severe hypoglycemia can negatively impact one's quality of life and bring about fear of future hypoglycemia. This fear can result in some people, unconsciously or intentionally, allowing their glucose level to be higher than their target range, to avoid going below target range and experiencing an episode of hypoglycemia. This puts people at increased risk of future complications due to elevated glucose levels. Many people with diabetes develop an inability to feel symptoms of hypoglycemia over time (known as hypoglycemia unawareness). This can prevent people from taking action to treat hypoglycemia, particularly when they are sleeping, which increases the risk of severe hypoglycemia, potentially resulting in coma or death. Using an HCL that will suspend insulin delivery when a person's glucose levels are dropping can prevent these types of episodes.

The report accurately identifies that using HCLs resulted in *"improved sleep due to reduced fears of hypoglycemia overnight, the ability to engage in physical activity more easily and safely, improved performance at work, less anxiety around food and eating out, reduced stress for family members, relief knowing the system is able to correct human error, reassurance and improved control, a greater sense of safety and peacefulness, decreased stress with allowing the technology to "take over", and, overall, a reduced burden for type 1 diabetes management."*

The report also acknowledged that some study participants experience a decrease in time in range when they stopped using the devices: *"Some study participants who transitioned from an HCL system back to other modalities noted frustration because even with their best efforts, they were unable to attain the glycemic control that was possible through the HCL system. This transition was difficult for parents of people*

with type 1 diabetes as they noted a decrease in quality of life, as they experienced the return of family conflict, worry, strain, and sleepless nights that had characterized their day to day lives prior to using the HCL system. These consequences of HCL use highlight the need for individuals using HCL systems to be prepared for shifts to less technical modalities should their access to HCL systems be limited (e.g. by loss of insurance coverage or technical malfunction)." In fact, this statement highlights the positive aspects of using HCLs, both for glycemic management as well as the improvement of the patient experience.

However, the report stops short of identifying how these life-changing improvements will result in improvements in family life, work productivity, social interactions, etc. This must be acknowledged in the limitations of the impact analysis. We look forward to how the authors can integrate these experiences into the development of policy recommendations.

Language has a profound impact on health behaviours and health-care experiences. Last year, Diabetes Canada released a consensus statement on the importance of language to facilitate positive and affirming attitudes towards diabetes (7). National agencies like CADTH have a role to play to reduce the impact of stigma and discrimination against people living with diabetes through better use of language. This document requires a thorough review to modify the language and all future documentation related to people with diabetes. For example, instead of referring to "glycemic control," we ask that you use the term "glucose management." Please refer to the line-by-line comments for further examples of potentially stigmatizing wording and suggested changes.

Another example of phrasing that is not patient-centered appears on Line 136: *"Hypoglycemia as a result of insulin therapy is the major limiting factor and obstacle in the management of type 1 diabetes."* While hypoglycemia is an obstacle, there are many other components of disease management that people living with type 1 diabetes have identified: Diabetes requires considerable self-management and is not simply glycemic management. It includes eating well, engaging in regular physical activity, maintaining a healthy body weight, taking medications (oral and/or injectable) as prescribed, monitoring blood glucose, managing stress, and adapting various aspects of your life (work, relationships, routines). The mental health burden of diabetes causes stress and anxiety. The high cost of diabetes medicines, supplies, and devices is a financial burden. Caregivers, especially mothers of children with type 1 diabetes, have to change their lives to help with diabetes management: not sleeping at night, employment changes to support children at school when school staff refuse to test a child's glucose level or deliver life-sustaining insulin. Concern about long-term complications related to high glucose levels and the risk of developing irreversible damage to blood vessels and nerves, resulting in blindness, heart disease, kidney problems, and lower limb amputations also weigh on the minds of patients and their caregivers. We request that you adjust the wording of this statement to reflect this, by highlighting hypoglycemia as a major limiting factor not *the* major limiting factor. For example: *"Hypoglycemia as a result of insulin therapy is a major limiting factor and obstacle in* safely achieving within-range glycemia *in the management of type 1 diabetes."*

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The Value of Patient Evidence. The objective of this CADTH health technology assessment is to *"address the decision problem through an assessment of the clinical effectiveness and safety of HCLs, a budget impact analysis to address affordability considerations, a qualitative analysis of the perspectives and experiences of users and clinicians, and a review of ethical issues."* Some known patient experiences on the benefits of using HCL systems include: less pain, effective prevention of hyperglycemia and hypoglycemia, increased feeling of safety for both the person living with diabetes and their loved ones, the ability to share data with loved ones, caregivers, and health-care providers, and less cumbersome testing. However, throughout the technology review, there is minimal integration of the patient experience. New, innovative methods that allow the incorporation of qualitative patient evidence and the lived experience is an essential step for CADTH to take to value all evidence including clinical, economic, and patient evidence.

Ethics Review. The ethics review stigmatizes people with diabetes as being unskilled and prone to bad habits: *"The potentially negative consequences of this decreased involvement in day-to-day management include that users may become less skilled at basic diabetes management and may develop "bad habits" – lifestyle choices which are not optimal for good diabetes-related health."* As one of our patient expert reviewers noted, "This de-skilling concept precluding people from using HCL is like suggesting people without limbs should be denied prosthetics so that they don't forget how to hop on one foot."

It is also erroneous to describe the potential harms of individuals' data being monitored by others as the HCL user chooses who can monitor their data, as an optional feature: *"There may be a grey zone in the case of teenagers, who may be monitored by their parents, or may not have a full say in whether/how their data is shared, but are developing the capacity to be more centrally involved in these issues."* While teenagers with type 1 diabetes may not want their parents to have access to their data, these children are minors, and their parents are still responsible for their health and related health-care decisions.

Self-management is a key component of diabetes management overall and education is required for all aspects of disease management, whether it involves teaching a patient how to use a lancet for finger-prick testing or programming an HCL. While the report highlights the ongoing role of the health-care team in HCL training, we would argue that categorizing care providers as "machine operators or technicians" is erroneous at best. Much of the device troubleshooting happens directly with the device companies, not the health-care team, so we disagree that *"more time in a clinic visit will be taken up by trouble-shooting and technical matters, taking away from discussions about other aspects of diabetes care"* (Line 3016). In fact, we would like to draw your attention to a recent publication that presents successful HCL virtual training during pandemic lockdown restrictions (8). This type of approach saves both time and money and is a model that could be adopted for patient education even after the pandemic is over.

Presentation of Data. We are concerned about some inaccurate or misleading data that appears in the report. The presentation of data in the tables is confusing and the directional arrows in the summary tables appear misleading. We respectfully request that CADTH consider changing directional arrows in

the summary tables to a clearer indicator, e.g., + to reflect beneficial effects and – to indicate negative effects.

The diabetes rates in Canada are incorrect in Lines 1675-1677, *"The introduction of this report notes that 7.8% of Canadians 12 years and older are living with type 1 diabetes based on a 2019 figure."* The data referenced by this statistic refers to Canadians that live with type 1 OR type 2 diabetes (9). We noted another incorrect data point on Line 1682, *"New individuals were added into the analysis in subsequent years through jurisdiction-specific population growth rates and by using an incident estimate of 0.0531%"*. In fact, the incident rate is 0.531% (from the source data: "In 2013–2014, close to 200,000 Canadians were newly diagnosed with diabetes (5.9 per 1,000 population)." Would you please release the formulae in your model that you used to calculate the incidence, prevalence, and growth rates per year?

Below please find specific issues and the related lines in the report. The layout of this section begins with the relevant line(s) in the CADTH report, the specific wording from the report (in quotation marks), underlined text to highlight a specific passage where relevant, and bullet(s) to elucidate Diabetes Canada's feedback on these sections.

[Line 136] "Hypoglycemia as a result of insulin therapy is the major limiting factor and obstacle in the management of type 1 diabetes."

- We believe this statement needs to be reworded and suggest, "Hypoglycemia as a result of insulin therapy is a major limiting factor and obstacle in safely achieving within-range glycemia in the management of type 1 diabetes."

[Line 142] "This fear is associated with reduced self-care and poor blood glucose control and may make people with type 1 diabetes"

- Suggested change: glucose levels that are not within target range

[Line 150] "cells and is read on-demand using a handheld reader)"

- Suggested addition: or a smartphone

[Line 180] "adolescents to prevent negative outcomes as they transition to adult care."

- Suggested addition: attempt to prevent / reduce the risk

[Line 189] "insulin if blood glucose levels have reached or are approaching a predefined low glucose threshold."

- Suggested change: are predicted to reach in the future

[Line 190] "systems because the user must still manually account for insulin needs before or after eating."

- Suggested change: manually input carbohydrates when eating and manually confirm the amount of any insulin bolus.

[Line 196] Hybrid closed-loop insulin delivery systems promise to provide people with type 1 diabetes and their caregivers a degree of distance from the ongoing needs created when living with diabetes.

- This statement minimizes the impact (and benefit) of HCLs for people with diabetes and their caregivers.

[Line 220] some people with type 1 diabetes in Ontario

- A very small proportion of people with type 1 diabetes are covered by the Ontario CGM guidelines: please be specific about this fact. Please clarify what proportion of the T1 diabetes population also qualifies for ODSP.

[Line 223] Based on customer feedback, the purpose of a CADTH review of this topic is to inform decisions regarding if HCLs have a place in management of type 1 diabetes.

- The focus of this HTA also needs to include the users of the devices.

[Line 921]

- The references for device coverage should be corrected:

2. Diabetes Canada. Type 1 symptoms. 2020: https://www.diabetes.ca/en-CA/about-diabetes/type-1/symptoms. Accessed 2020 Nov 23. [repeat of ref #1]

5. Punthakee Z, Goldenberg R, Katz P. Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada: Definition, classification and diagnosis of diabetes, prediabetes and metabolic syndrome. Can J Diabetes. 2018;42(Suppl 1):S10-S15.

- should be:

2. Diabetes Canada. Coverage of advanced glucose monitoring devices. 2020: https://www.diabetes.ca/DiabetesCanadaWebsite/media/Advocacy-and-Policy/Advocacy%20Reports/Advanced_Glucose_Monitoring_EN_OCT-2020.pdf. Accessed 2020 Nov 11.

5. Diabetes Canada. Coverage of insulin pumps across Canada. 2020: https://www.diabetes.ca/DiabetesCanadaWebsite/media/Advocacy-and-Policy/Advocacy%20Reports/Insulin-Pumps-Comparison-EN.pdf. Accessed 2020 Nov 11.

[Line 974] Table 4 High-Level Summary of Glucose Time-in-Range Findings by Comparison in the Included Primary Clinical Studies

- The arrows are misleading. Consider using a + to indicate beneficial changes and – to indicate negative changes.

[Line 1083] Table 8 High-Level Summary of Findings Related to A1C by Comparison in the Included Primary Clinical Studies

- Again, the arrows are misleading. Consider using a + to indicate beneficial changes and – to indicate negative changes.

[Line 1215] Table 17 High-Level Summary of Findings Related to Additional Clinical Outcomes by Comparison in the Included Primary Clinical Studies

- Arrows are misleading. Consider using a + to indicate beneficial changes and – to indicate negative changes.

[Lines 1507-1511] "improved mean glucose concentrations and glycemic variability compared to open-loop SAP therapy (with or without PLGS) or MDII or insulin pump therapy informed by self-monitoring of blood glucose across most studies; however, the clinical benefit of these statistically significant improvements is unclear. There was no consistent benefit of HCL therapy with respect to patient satisfaction, body weight, and total daily insulin amount."

- This is an erroneous statement. A reduction of mean blood glucose cannot be considered as of unclear benefit. Minimally, the potential benefit is quite significant

[Lines 1532-1534] "None of the included primary studies were conducted in Canada, and any differences between the Canadian health system and the health systems of the countries where the studies were conducted (i.e., the United States, France, Italy, and Australia) may require consideration."

- A recently released Canadian study provides relevant data to consider for this HTA

[Lines 1675-1677] "The introduction of this report notes that 7.8% of Canadians 12 years and older are living with type 1 diabetes based on a 2019 figure.

- This statement is erroneous. The reference lists 7.8% of Canadians as having type 1 OR type 2 diabetes. https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310009607

[Line 1682] "New individuals were added into the analysis in subsequent years through jurisdiction-specific population growth rates and by using an incident estimate of 0.0531%"

- In fact, the incident rate is 0.531% (from the source data: "In 2013–2014, close to 200,000 Canadians were newly diagnosed with diabetes (5.9 per 1,000 population)."

[Line 1706] Table 23 Current Public Funding Status for Diabetes Supplies, to inform Reference Scenario

- Please clarify what proportion of the T1 population also qualifies for ODSP (Ontario)
- PEI's insulin pump program and test strip coverage have changed (effective January 1, 2021), and this is not reflected on page 60. The IPP is now covering ages 25 and under, and annual coverage of strips is $1,440 annually ($120 per month)

[Line 1737] "Of note, CGMs is not expected to fully substitute SMBGs, as a degree of SMBG testing is required with CGM use for calibration purposes."

- While a Medtronic CGM requires up to 3 SMBG strips per day, this is not the case with a Dexcom CGM. On average, our patient experience reviewers utilizing HCL with Dexcom reported 1 strip per month for calibration. This should be corrected for the analysis.

[Lines 1740-1741] "In a scenario analysis, CADTH explored the budget impact of an alternative funding policy in which both CGM and up to four test strips daily per HCL user would be reimbursed publicly."

- On average, our patient experience reviewers utilizing HCL with Dexcom reported one strip per month for calibration. Our patient experience reviewers utilizing HCL with Medtronic reported three strips per day for calibration. In both cases, the assumption of four strips per day is not true to the lived experience.

[Lines 1791-1794] "it was further assumed that, amongst those using advanced glucose monitors, 20% would be using a Flash glucose monitoring (GM) system and 80% would be using a CGM. In Ontario, it was assumed that 50% of those eligible for CGM (i.e., Ontario Disability Support Program (ODSP) clients) and Flash GM (i.e. Ontario Drug Benefit clients) would be using these respective technologies".

- Please describe the basis for this assumption. Also, Flash GM systems do not integrate with any current HCL, so it is unclear what this is part of the scenario.

[Lines 1795-1799] "As there are no anticipated changes in the reimbursement policies for insulin pumps and CGMs during the model's time horizon (i.e.,3 years), it was assumed that market shares in the reference scenario would remain unchanged over all three years modelled (i.e., Years 1, 2 and 3) for jurisdictions apart from Yukon."

- This is a false assumption, as Saskatchewan is preparing reimbursement policy for CGMs, and PEI just updated insulin pump coverage to include all residents 25 years of age and under.

[Line 1890] Table 23: Current Public Funding Status for Diabetes Supplies, to inform Reference Scenario

- CGM costs are incorrect, the average annual cost is $3,814 (not $4,783 as listed). This discrepancy will impact all the costing in the budget impact analysis

Dexcom G6 CGM Annual Cost (subscription = $299/month)	$3,588.00
Medtronic Enlite CGM Annual Cost	$3,525.60
Medtronic Guardian CGM Annual Cost	$4,328.35
Average Annual CGM Cost	**$3,813.98**

[Line 1900] Table 31 Key Assumptions

- a 3-year horizon is inappropriate to assess the impact of longer-term consequences that occur with a reduction in A1C demonstrated by RCTs. A longer time horizon should also be incorporated to inform policy makers of the broader impact on government budgets and patient/caregiver budgets.
- It is not apparent that the costs related to hypoglycemia are incorporated. This should be assessed both from the public payer perspective as well as the patient perspective (human and financial outcomes).

[Lines 2014-2015] "CADTH found that, under this scenario, the expected three-year budget impact of reimbursing 2014 CGM would be $1,516,215,450."

- Please correct cost values for CGM and account for the number of people who already pay out-of-pocket for these devices (so do not require new transmitters, receivers, etc., right away) or whose private insurance covers a portion.

[Lines 2018-2022] "CADTH notes that there are a number of limitations with the analysis. Differences in public funding for devices to manage diabetes 2018 across jurisdictions added complexity and uncertainty to the analysis. Despite being unable to incorporate jurisdictional-specific 2019 coverage of MDI supplies, a scenario analysis demonstrated that results of the BIA were not sensitive to varying MDI costs. Additionally, while current use of insulin pumps amongst those eligible was uncertain, results of a scenario analysis demonstrated that results were robust even if higher rates of insulin pump use are assumed. Results were generally robust to changes in key parameters."

- The cost to healthcare systems beyond 3 years were not included in this analysis. Further, many cost impacts important to patients were not measured in this budget impact analysis. These should be considered in a sensitivity analysis or at least be explicitly stated that these patient cost impacts are acknowledged but not presented,

[Line 2098] Perspectives & Experiences

- A recent Canadian study on experiences with HCLs will add to the results.

[Line 2242] "HCLs can help create space from the technical work associated with type 1 diabetes self-management and thus enable people living with the condition to feel a bit more immersed in, and part of, the flow of life around them"

- This statement is condescending and minimizing. HCLs can reduce the cognitive load and improve life for people who use them. They do not just "create space from the technical work".

[Line 2252] "The hope and promise of HCLs was that they could help provide that distance from diabetes and open some space to live differently."

- Live *better*, not differently. Use of the word 'differently' implies living with diabetes is their choice and can be seen as stigmatizing towards people with diabetes.

[Line 2414] "You need to be doing the calibrations at the right time"

- The statement is misleading, as calibrations are only required with Medtronic CGMs, not Dexcom CGMs.

[Lines 2542-2544] "With increased access to their patient's data, clinicians believed they could both see a more complete picture of their patient's out-of-office experience and reduce their own workload given their ability to track how well HCL manages the day-to-day changes to things like basal insulin delivery."

- Less need for health-care providers work/input into patient care & support, translates to cost savings for the health care system.

[Line 2516] "Or there may be an increased need for staff that can help with any glitches or technical needs associated with the new devices systems. If you're not actually having a health problem, but rather a problem with the device is seemingly not functioning properly you'll contact the device professional rather than your specialist"

- This is erroneous as technical support occurs with the device company, not the health-care team

[Line 2532] "This is important as it signals a shift away from non-HCL ideals of good self-management"

- Problematic wording that stigmatizes the patient as practicing "good" self management.

[Line 2735] "The Review also notes that while HCL does appear to offer comparative clinical benefit, it is not clear that this immediate benefit would translate into improved outcomes over the longer terms (e.g., reduced incidence of complications of type 1 diabetes). The conclusions about the clinical benefit presented by HCL compared to open-loop are fairly guarded, suggesting that the potential for benefit of HCL over open-loop technologies is marginal"

- Our patient experience reviewers strongly disagree with this assessment, stating that their experience is counter to this summary. Their satisfaction improved, as did their clinical outcomes.
- Further, one of our expert reviewers stated that "long-term benefits are likely based on short-term results."

[Line 2744] "In many studies on HCL participants reported an improvement in their quality of life as a result of using the HCL system 2,12-14. Participants using the HCL noted more specific benefits including improved sleep due to reduced fears of hypoglycemia overnight 2,6,11-13,15-18, the ability to engage in physical activity more easily and safely 2, improved performance at work 13,19, less anxiety around food and eating out 14,20,21, reduced stress for family members 11,22, relief knowing the system is able to correct human error 14,20, reassurance and improved control 6,15,16, a greater sense of safety and

peacefulness 6,12,13,21, decreased stress with allowing the technology to "take over" 2,11-13,16,20,22, and, overall, a reduced burden for type 1 diabetes management"

- CADTH should make an attempt to integrate these benefits into the report. Currently it is an acknowledgement but how this integrates into the science and the impact of these benefits is unclear.

[Line 2856] "best efforts, they were unable to attain the glycemic control that was possible through the HCL system. This transition was difficult"

- Demonstrates the benefits of HCL, that glucose management worsened when users switched to older modalities

[Lines 2907-2917] remote monitoring of HCL data and its impact on privacy

- This feature is optional, and the device user can remove access at any time

[Lines 2950-2953] "Persons living with type 1 diabetes who have particular clinical needs, traits, attitudes, and social environments may find more benefit with an HCL system than others 2. It has been challenging to determine specifically what these optimal factors for HCL use may be. Furthermore, these factors can evolve over time with an individual patient so drawing a static conclusion about whether a particular patient is suited to an HCL system can be difficult"

- This is true and emphasizes the need for policy to guide decision making, but that individual clinical decisions must be made by health care providers and patients together.

[Line 3085] "For example, someone may not show good adherence to their current diabetes therapy because aspects of these therapies are too burdensome. The less burdensome nature of a HCL system may actually improve their adherence, enabling them to benefit."

- A person with an A1C above 10, is not eligible for pump coverage in Ontario, but many people may be able to reduce their A1C with an HCL. Also please note the terms such as "adherent and nonadherent" are problematic. Labelling people with diabetes this way suggests that they are uncooperative and do not recognize the effort they are putting in to manage their diabetes. These terms deny patients a sense of agency and discount the ways in which they might be balancing the risks and benefits of different behaviours and choices. For example, someone may choose to let their blood glucose levels run higher than the clinically recommended range to better avoid hypoglycemia. These terms also do not acknowledge the impact of social determinants of health. For example, people with higher incomes are more easily able to buy food to follow a particular eating plan. Please avoid use of the term.

[Line 3152] "Concerns about confidentiality and the potential for harm to users by hacking has been widely identified in the HCL literature. HCL presents the possibility of accidental violations of confidentiality (through hacking) and intentional releases of health information (which may or may not be breaches of confidentiality)."

- No references are provided for this statement, and we would believe that it is mitigated by newer versions of HCLs.

[Lines 3165-3171] "Choosing not to cover diabetes technologies, like HCL within public programs could reinforce inequities in access to diabetes management supplies. Though, if technologies like HCL continue to primarily benefit people with diabetes who already have good management and access to care, the

converse argument could be made that using funds that might be used for public funding for HCL to expand the public coverage of more basic diabetes management supplies could result in a more equitable investment in public funds. If public funds are allocated to cover HCL devices, it is important that any program criteria set to determine who may be eligible to have access to the device is evidence based and does not exacerbate current healthcare inequities."

[Lines 3173-3176] "The lack of clear evidentiary connection between immediate clinical benefits (e.g. A1C levels, and glucose time in range) and longer-term outcomes (diabetes related complications, hospital admissions, etc.) makes it difficult to conclude whether funding the HCL system aligns with overall duties to promote clinical benefit at a population level. Further research into the longer-term effects of these types of technologies is necessary.

- The purpose of the HTA is to ask if HCLs have an impact on A1C & TIR, we must conclude (based on previous evidence) they will, in time, result in reductions in specific complications.

[Lines 3485-3491] "While the evidence from this report does not address the appropriateness of these criteria for insulin pump programs, clinicians that were consulted disagreed about whether these criteria should be translated to HCLs if they were to become publicly funded. Some argued that people who are managing their diabetes well should be considered candidates for HCL, whereas others think the device should be available to those who need to improve their management. In particular, some felt that broad populations like teenagers or older adults who were not currently managing well could potentially see the most benefit. These claims were backed by clinical experience of some clinicians who had been able to place their patients with poorer management on HCLs through private insurance."

- This statement highlights the importance of understanding that those who may benefit from new technologies such as HCL may include those subpopulations who have not been explicitly named in the RCTs (e.g., people living with vision loss and diabetes) but should not be excluded from access to these life-changing technologies.

[Line 3541] CADTH's BIA estimated an average annual pan-Canadian cost of $4,783 per patient for CGM.

- This number based on assumptions that we do not consider valid (see previous commentary on Budget Impact Analysis).

[Line 3681] "This review touches on "looping" and do-it-yourself HCLs, which some people living with type 1 diabetes have chosen to use despite a lack of regulatory approval."

- This phrase is judgemental. According to the Loop Facebook page, there are 24,000 loopers worldwide despite the numerous technical obstacles to start looping. This is a testament to how determined the T1D community is to reap the benefits of looping. One of our expert reviewers stated, "I have lived with T1 DM for 57 years and started using an insulin pump in 2002. I'm a pharmacist by profession as well as a CDE, Certified Pump Trainer and Certified CGM Trainer. Due to gastroparesis, my absorption is not consistent, and I had trouble achieving an A1c of 7.0 or less. I started to loop June 2019 and within 2 months my glycemic control had improved tremendously with my A1c going from 7.4 to 6.5."

References

1. Battelino T, Danne T, Bergenstal RM, Amiel SA, Beck R, Biester T, et al. Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range. Diabetes Care. 2019 Aug 1;42(8):1593–603.

2. Vigersky RA, McMahon C. The Relationship of Hemoglobin A1C to Time-in-Range in Patients with Diabetes. Diabetes Technology & Therapeutics. 2018 Dec 21;21(2):81–5.

3. Nathan DM, Group for the DR. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study at 30 Years: Overview. Diabetes Care. 2014 Jan 1;37(1):9–16.

4. Taleb N, Quintal A, Rakheja R, Messier V, Legault L, Racine E, et al. Perceptions and expectations of adults with type 1 diabetes for the use of artificial pancreas systems with and without glucagon addition: Results of an online survey. Nutrition, Metabolism and Cardiovascular Diseases [Internet]. 2020 Oct 16 [cited 2021 Jan 5];0(0). Available from: https://www.nmcd-journal.com/article/S0939-4753(20)30445-2/abstract

5. Haidar A, Legault L, Raffray M, Gouchie-Provencher N, Jacobs PG, El-Fathi A, et al. Comparison Between Closed-Loop Insulin Delivery System (the Artificial Pancreas) and Sensor-Augmented Pump Therapy: A Randomized-Controlled Crossover Trial. Diabetes Technology & Therapeutics [Internet]. 2020 Oct 13 [cited 2021 Jan 5]; Available from: https://www.liebertpub.com/doi/10.1089/dia.2020.0365

6. Investing in Mental Health [Internet]. Ottawa, ON: Mental Health Commission of Canada; 2016 [cited 2021 Jan 9]. Available from: https://www.mentalhealthcommission.ca/sites/default/files/2016-06/Investing_in_Mental_Health_FINAL_Version_ENG.pdf

7. Banasiak K, Cleary D, Bajurny V, Barbieri P, Nagpal S, Sorensen M, et al. Language Matters – A Diabetes Canada Consensus Statement. Canadian Journal of Diabetes. 2020 Jul;44(5):370–3.

8. Gomez AM, Henao D, Parra D, Kerguelen A, Pinilla MV, Muñoz OM, et al. Virtual training on the hybrid close loop system in people with type 1 diabetes (T1D) during the COVID-19 pandemic. Diabetes & Metabolic Syndrome: Clinical Research & Reviews [Internet]. 2021 [cited 2021 Jan 11]; Available from: https://reader.elsevier.com/reader/sd/pii/S1871402120305361?token=C3D2BB5E4B5B8441C9B7F16F6859815617E5A687D67EF4B2ED5CB67E202A4AA341824FAF3A7CA96A23222403BF4C07B2

9. Government of Canada SC. Diabetes, by age group [Internet]. 2017 [cited 2021 Jan 7]. Available from: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310009607

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