



March 24, 2021

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

**Re: Diabetes Canada Feedback on CADTH HEALTH TECHNOLOGY REVIEW APPROPRIATE USE
RECOMMENDATION - Hybrid Closed-Loop Insulin Delivery Systems for People with Type 1
Diabetes**

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

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 the best possible outcomes.

Access to the right medications, devices, supplies, and services with appropriate education and support, help people living with diabetes attain the most favourable health outcomes.

In our previous submission, we provided suggestions on the draft clinical report and budget impact analysis. However, these concerns did not appear to cause your reviewers or HTERP to pause and meaningfully reflect on the patient experience and how to incorporate it into the HTA. In fact, the draft optimal use recommendations were released prior to the final scientific report, which might have changed due to stakeholder comments. This approach forces us to question the value placed on the feedback from patient and clinical experts across the country and the impact on their care. It is, indeed, very discouraging. CADTH could have guided use of this innovative and effective treatment in a measured and responsible manner. But these recommendations do not guide policy makers who develop healthy public policy with all of the best possible information. It provides a one-sided assessment with little insight into the patients who ought to be at the centre of this public policy. As a result, some people living with diabetes may be deprived of therapies that can improve their experience and their management of diabetes.

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

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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 in the near future.

Sincerely,

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Diabetes Canada



Diabetes Canada Feedback on CADTH HEALTH TECHNOLOGY REVIEW APPROPRIATE USE RECOMMENDATION - Hybrid Closed-Loop Insulin Delivery Systems for People with Type 1 Diabetes

CADTH Rationale, long-term data: *“Insufficient long-term data on clinical and patient important outcomes as compared to standard therapy means it is, at present, not possible to make stronger conclusions of the effectiveness of HCLs. The effectiveness of HCLs, as compared to standard therapy, has been demonstrated using intermediate clinical outcome measures assessed between 2 days and up to 6 months.”*

Diabetes Canada’s Response: The unilateral focus on long-term data while ignoring other indicators that are also important has produced misleading conclusions. An insistence of waiting for long-term randomized controlled trial (RCT) data is inconsistent with the pace of technological innovation in diabetes devices and will continue to drive patients to unregulated devices which may risk their health.

CADTH Rationale, time in range validity: *“The clinical validity of using glucose time-in-range metrics as surrogate outcome measures for risk of developing diabetes-related complications has not yet been established.”*

Diabetes Canada’s Response: There are data demonstrating the importance of a reduction of A1C and that increased time in range (TIR) improves A1C levels. 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, TIR has been shown to correlate with diabetes complications, including progressions of diabetic retinopathy and development of microalbuminuria (1,2). Phase 3 registration trials of new insulins are using TIR as their primary endpoint, after discussion with regulators. Thus, the dismissal of TIR seems out-of-step for a body charged with assessing new technology and innovations. Per our previous correspondence, this perspective appears to be based on a non-peer reviewed report that is not in the public domain.

CADTH Rationale, HCL vs standard therapy: *“Randomized clinical trials have demonstrated small improvements, or no statistically significant differences, regarding the effectiveness of HCLs as compared to standard therapy with respect to quality of life and patient satisfaction assessed between 2 days and up to 6 months. Qualitative evidence suggests that for some, but not all, people living with type 1 diabetes that HCLs can offer some space from the perceived demands of diabetes management, and enable people to become more immersed in, and part of, the flow of life around them.”*

Diabetes Canada’s Response: Management of type 1 diabetes varies highly between individuals, and it is the role of the health-care provider and the patient to determine individualized therapy. Mean clinical trial results may overlook substantial variance in response between individuals. No single treatment will be suitable for all people. Benefits for individuals who would experience the most value would be overlooked in aggregate by an assessment of all people living with type 1 diabetes. A clear example would be individuals with a history of severe hypoglycemia, or those with hypoglycemia unawareness who experience fewer events, or less severe events with this system.



A newly-published Canadian study investigated long-term, real-world patient experiences with HCL technology (3). The authors reported that, “Patients with the most suboptimal glycemic control described the greatest benefits and easiest adaptation process, challenging commonly-held assumptions for patient selection for pump therapy.” These patients faced the greatest barriers in accessing HCL technology—financial and policy, as well as clinicians’ opinions on whether they are suitable candidates for HCL. This emphasizes the need to place best evidence within the context of the individualized requirements of the patient.

Additionally, living with type 1 diabetes can be hard for many people. Patients frequently describe how unrelenting the disease can be and its impact on daily life. A device or system that can help to lessen the burden as well as improve outcomes has value. Assessing new technologies that improve patient experience is a challenge that HTA methodologists and experts are well aware of, and CADTH’s own VP of Medical Devices and Clinical Intervention, Lesley Dunfield, said it well. She asserted that HTAs can play a role in innovation when it comes to patient experience: “What are the differences with a newer technology versus something that’s older, something that is already in practice? Looking at those requirements and helping jurisdictions decide if that is something that is going to enhance patient experience. That’s a lot of what we’re seeing now: what are those technologies that might have the same patient outcomes but if they’re improving patient experience or they’re easier to use for a patient, then that’s certainly something I think we should be looking at a lot closer and doing those assessments to help ensure those technologies do get into the system to help with that patient experience as well as doing the same function as another technology on the market” (4). These remarks suggest that there is a place for new technologies within the diabetes treatment sphere and patient experience should be strongly considered in assessing their value. We encourage HTERP to rise to the challenge posed by this CADTH vision.

CADTH Rationale, short-term benefits of HCL: *“The demonstrated short term benefits of HCLs on clinical outcomes, as compared to standard therapy, do not appear to occur at the cost of safety considerations including hypoglycemic events, hyperglycemic events, diabetic ketoacidosis events, ketosis events, or other adverse events.”*

Diabetes Canada’s Response: The reviewers seem to require evidence of superiority, which is difficult to achieve ethically in clinical trials of glucose management for type 1 diabetes. It would seem unlikely that HCL interventions would have been inferior, so a more permissive recommendation for selected individuals is justifiable.

CADTH Consideration, real-world evidence: *“Real world evidence – defined as clinical evidence regarding the benefits and use of a health technology derived from routinely collected health care data – has the potential to reduce the uncertainty in the long-term clinical effectiveness, safety, utilization, and health system impact of HCLs, as compared to other insulin delivery methods. HTERP considers, however, that real*



world evidence not be considered until evidence generated through randomized controlled trials demonstrates long term clinical effectiveness and safety with high certainty.”

Diabetes Canada’s Response: 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 trials. Patient experience and clinical experience can help build that bridge from research to healthy public policy. It is summarily unfair to patients to deny new and emerging technologies that have data—but not unequivocal data—for patient-centered policy. In fact, validated surrogate data—as identified in Diabetes Canada’s response to the HCL HTA—should be used when long-term data are not available in order to provide timely recommendations (5).

CADTH CEO Suzanne McGurn, a leader and visionary in the HTA environment, stated publicly last year that RCTs can’t be the only source of evidence:

“High-quality evidence is not always available. For many drugs, health technologies and health interventions, definitive answers are not always available when the decision needs to be made. Sometimes, decisions need to be made in the absence of high-quality evidence. Some health emergencies, such as the pandemic we’re currently experiencing, highlight the requirement for an immediate response and cannot wait for high-quality evidence to become available. Even in the absence of gold standard evidence, like randomized clinical control trials, there was always evidence that can be used to inform decisions. CADTH and other HTA organizations are in the business of reviewing the best-available evidence. We are not in the business of only reviewing high-quality evidence. We will search for and find the best-available evidence, appraise its quality, and provide it to decision-makers in a timely fashion and easy-to-use format” (6).

Diabetes Canada interprets this statement to mean that CADTH’s vision is supportive of applying best-available evidence in a timely manner to improve patient outcomes.

Health Technology Assessment International (HTAi), the global scientific society for HTAs and to which CADTH belongs as an active member, also recommends that patients’ experiences be included in the HTA process: “Patients have unique knowledge, perspectives and experiences that can contribute to essential evidence for HTAs, and therefore ‘relevance’” (7). This includes looking beyond RCT data to real-world evidence and includes the patient’s lived experience as a source of data. Real-world evidence has been incorporated into other aspects of Canadian health care, most recently with the rollout of COVID-19 vaccines when the National Advisory Committee on Immunization (NACI) implemented policy change to extend the timing of second doses (8). This move recognized that it was unethical and unsafe to wait for more clinical evidence and placed equal weight on data obtained outside the rigorous and lengthy RCT process.

Diabetes Canada supports making evidence-based decisions and making health-care decisions based on all information. These goals are complimentary and are consistent with the vision of CADTH. We



encourage the reviewers and HTERP to rise to the challenge and support patient-centered public policy.

CADTH Considerations, cost-effectiveness & budget analysis: *“HTERP suggests that a cost-effectiveness analysis is required to make a recommendation about the place in care of HCLs for people with type 1 diabetes. A cost-effectiveness analysis was not possible due to insufficient long term clinical outcome data for HCLs as compared to currently reimbursed technologies, and insufficient understanding of the relationship between glucose time-in-range metrics and the risk of developing diabetes-related complications.*

The budget impact analysis estimated the financial impact of reimbursing HCL for the care of people with type 1 diabetes as compared with currently reimbursed technologies over a 3 year time horizon. The budget impact is expected to increase by \$823 million from a pan-Canadian perspective. Given the uncertainty in long term clinical and patient important outcomes, HTERP discussed the uncertainties associated with the opportunity cost of recommending a stronger role for HCLs in the care for people with type 1 diabetes in relation to other health care needs of Canadians.”

Diabetes Canada’s Response: The budget impact analysis is limited, as was outlined in the January 2021 HTA response (5). At a high level, the analysis conducted by CADTH 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. We contest the assumptions in the analysis regarding device adoption and initial cost layout. It is not clear if the feedback on the budget impact analysis was considered by the reviewers or the committee.

With regards to cost effectiveness, CADTH’s own vision, “Canada has a world-class system for assessing and managing health technologies to achieve better outcomes and value for Canadians,” highlights both *outcomes* and *value* (9). Canada should look to the examples of New Zealand and Belgium, countries that have changed their HTA funding processes to “place emphasis on quality of life rather than cost-effectiveness across all diseases” (7). This statement implies that an analysis of the opportunity cost of a system like HCL in relation to all diseases (and their related health-care needs) experienced by Canadians misses the larger issue of quality of life. HTAi defines the role of HTA agencies thusly: “HTA agencies have an important role in the evaluation and approval of new technologies. They determine their value within a health system so to promote equitable, quality care with available healthcare resources” (7). Equitable care in a health system with finite resources does not mean equal; rather, it refers to equity and fairness. The disease burden of type 1 diabetes is high, in part because the bulk (>90%) of the care is self-management. As such, an equitable distribution of health care resources should lean towards individuals who bear the greatest burden of their disease management. Diabetes Canada believes that equitable distribution of funding for medical devices includes a greater share of coverage for new technologies that will lessen the disease burden—and consequently improve quality of life as well as health outcomes—for people living with type 1



diabetes and their caregivers.

CADTH’s HTA Review Process. Is there a role for health technology assessment to provide recommendations based on all types of evidence? While the HTA process as it is currently defined was followed, we would argue that this very process is in need of an update. An insistence of waiting for long-term RCT data is inconsistent with the pace of technological innovation in diabetes devices and will continue to drive patients to unregulated devices, which may risk their health. It is also in direct contradiction to HTAi’s call to action for greater patient involvement: “The accelerating pace of medical innovation creates a need to improve the depth and breadth of patient involvement in the HTA process” (7). Indeed, this international body is looking to “comprehensive, robust practices for [patient] involvement” (7).

Patient Group Input. These Optimal Use recommendations do not address the comprehensive responses to CADTH’s HTA on Hybrid Closed-Loop (HCL) Systems for People with Type 1 Diabetes. While the methods section in the recommendations document indicates that the Health Technology Expert Review Panel (HTERP) “considered stakeholder feedback,” there is no indication of this in the report. Diabetes Canada and other key stakeholders—including, but not limited to, JDRF Canada, Type 1 Together, and CNIB—all provided relevant and timely input to the HTA. Health Technology Assessment International (HTAi) has recommended that patients or their advocates be more involved in the HTA process, stating that the decisions of HTA agencies “can have profound impact on the length and quality of patients’ lives” (7).

As recently as August 2020, CADTH’s own Patient and Community Advisory Committee (PCAC) heard from CADTH about their processes. PCAC members were surprised to learn that “stakeholders who contribute feedback do not hear back from CADTH to know they’ve been acknowledged and/or what becomes of their advice and asked CADTH staff to look into alternative options. Members were also interested in hearing what ‘ah-ha’ moments were inspired by patient insights during assessments. It was shared that patient experience is important and can influence reviews by identifying new angles to consider, identifying any mismatch between what we heard was important to patient groups and what was measured in trials, in defining drug recommendation conditions for reimbursement and in creating patient-focused resources” (10). Patient groups echo these concerns and appeal to CADTH, their HTA division, and HTERP to do better. Diabetes Canada urges CADTH to heed HTAi’s call to action to work more closely with patients, their caregivers, and other stakeholders to increase **meaningful** patient involvement in all stages of the process (7). By calling for feedback from patient organizations and not appearing to consider or incorporate this feedback into the process, CADTH and HTERP are stripping hope from patients and their advocates. HTAi’s call to action for HTA stakeholders recommends more—not less—interaction with patient groups: “We propose a ‘Call to action’ for HTA stakeholders to undertake serious dialogue with patient advocates aimed at creating shared goals” (7). Indeed, this current process works to discourage groups from even trying to engage in policy that impacts them so significantly.



Working Together for a Common Goal. The COVID-19 pandemic has changed the way health care is delivered and accelerated the adoption of virtual care. All the pan-Canadian organizations involved in health-care funding decisions have identified virtual care as a priority (4). Diabetes devices such as HCLs and the components that make up the hybrid closed-loop system—insulin pumps and continuous glucose monitors—are well-suited to deliver quality virtual care (11,12). In fact, a recent publication presents successful HCL virtual training during pandemic lockdown restrictions (12).

We encourage CADTH to reconsider the recommendations as they have potential to deny patients access to an intervention that can meaningfully change their life. To proceed without pause, overlooking the perspectives of patient groups, contrasts with CADTH’s own vision. We also encourage you to critically examine your current HTA review methods and processes, with a view to modifying them to truly consider the needs of both patients and health-care decision makers. We respectfully ask HTERP to rise to the challenge and “take up this call to work together for visionary and transformative elevation of the voice of patients in HTA” (7).

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