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* Comparative clinical significance is unknown.
† This landing page is open to the general public.
‡ Comparative clinical significance not established.
BMI, body mass index; CVD, cardiovascular disease; GLP-1 RA, glucagon-like peptide-1 receptor agonist.

References: 1. Novo Nordisk Canada Inc. Data on file. 2025. **2.** Novo Nordisk Canada Inc. Wegovy® Product Monograph. April 8, 2025. **3.** IQVIA Inc. Xponent Data (MAR2024 to FEB2025). 2025. **4.** Novo Nordisk Canada Inc. Ozempic® Product Monograph. January 29, 2025. **5.** Novo Nordisk Canada Inc. RYBELSUS® Product Monograph. January 22, 2025. **6.** Novo Nordisk Canada Inc. Awiqli® Product Monograph. March 12, 2024.

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Alanna Chambers is a Registered Dietitian, Certified Diabetes Educator, and Certified Pump Trainer based in Kelowna, BC. With extensive experience in various diabetes settings across Canada, she now focuses on technology training and education for both individuals living with diabetes and healthcare professionals. In recent years, Alanna has been honoured to contribute to Diabetes Canada initiatives and guidelines focused on type 1 diabetes care. Her passion for diabetes education led her to launch Type One Journeys Inc., where she is dedicated to expanding educational initiatives in Canada's type 1 diabetes community. Having lived with type 1 diabetes for over 30 years, Alanna understands that effective daily management requires a balance of knowledge, tools, creativity, support, and self-compassion.

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Optimizing the Use of Automated Insulin Delivery (AID) Systems in Routine Clinical Care of People with Type 1 Diabetes

Alanna Chambers, RD, CDE
Ilana Halperin, MD, MSc, FRCPC

Introduction

With the updated Diabetes Canada Clinical Practice Guidelines recognizing automated insulin delivery (AID) as the standard of care for people with type 1 diabetes (PwT1D),[1] clinicians play a vital role in supporting individuals to adopt and optimize use of this technology.

AID systems integrate insulin pump therapy (IPT) and real-time continuous glucose monitors (rtCGM) in conjunction with a control algorithm to automate various aspects of insulin delivery. The recommendation to adopt AID is supported by robust evidence from both randomized-controlled trials and real-world studies across diverse populations, including all ages, previous experience with technology, baseline glycemia, and self-management behaviours.[1] Glycemic benefits include consistent improvements in time in range (TIR) (often by >10%), and reductions in A1C, mean glucose levels, and hypoglycemia.[2-4] Additionally, AID use has shown important improvements in person-reported outcomes, including reduced diabetes distress, reduced fear of hypoglycemia, improved quality of life, and improved sleep.[5]

Although strong evidence supports the glycemic and non glycemic benefits of AID for PwT1D, uptake remains limited. US data from the type 1 diabetes (T1D) exchange showed that only 30% of participants were using AID in 2022, with lower levels of uptake among marginalized populations.[6] Clinical practice and current evidence across various AID systems has revealed that those struggling most with diabetes management often experience the greatest benefit from AID, with greater than 20% TIR improvements for those with baseline A1C levels >8.5%.[7] Even without refined carbohydrate counting or consistent bolus behaviours PwT1D do better with any form of automation compared to basal: bolus injections (BBI) or IPT.[8-10] Therefore, clinicians are encouraged to offer AID to all PwT1D who are willing to use the devices, and to actively support its effective, ongoing use.

As AID becomes integrated into routine care, clinicians must adapt their approach to self-management education and counselling. This includes considering key AID self-management themes **(Table 1)** and applying system-specific strategies to optimize outcomes and experiences

We will follow a series of common clinical scenarios, offering guidance on how to approach and optimize care using the available Canadian AID systems. For all clinical scenarios we suggest beginning assessments by reviewing key AID data **(Table 2)** to guide discussions and collaboratively develop a management plan to achieve the personal goals of the PwT1D.

Optimization Opportunity 1: Build Trust to Minimize Variability

Presentation:

The AID user reports ongoing self-management burden, describing frequent cycles of “chasing highs and lows.” Daily reports reveal a pattern where episodes of hypo- and hyper-glycemia precede one another. Glucose sensor data may show glycemic variability (coefficient of variation >36%), hypoglycemia >4%, and/or frequent preventative treatments for anticipated lows. These patterns may reflect limited trust in the AID system, leading to user-driven interventions that increase variability.)

Clinical Explorations:

· How is hypoglycemia treated (glucose level/trend and carbohydrate source)?
· How frequently do they treat in anticipation of hypoglycemia?
· How do they respond to continuous glucose monitoring (CGM) low and high alerts? What are their alert thresholds?
· Have settings been optimized?

Potential Solutions:

1. **Refine Hypoglycemia Treatment:** Because AID systems reduce or suspend insulin delivery to prevent hypoglycemia, less fast-acting carbohydrate (~5-10 grams) is usually sufficient if mild hypoglycemia does occur, compared with BBI or IPT.[1,11] Treatment should be prompt with fast-acting carbohydrate to avoid unnecessary subsequent treatments and rebound hyperglycemia. Encourage PwT1D to consider their glucose level, trend arrows, insulin-on-board/active insulin, activity levels, and duration of suspension.
2. **Follow the bolus calculator:** Discourage overriding bolus calculations or entering additional "phantom carbs" to influence the aggressiveness of insulin delivery. Over-interference with AID systems can negatively impact outcomes and experiences.[12]
3. **Evaluate CGM alert settings:** Ensure that high and low glucose alerts are set at actionable thresholds. Encourage patience and a "watch and wait" approach, allowing the system time to adjust to out-of-range glucose levels.
4. **Tailor system settings:** Fine-tune the adjustable settings based on the specific AID system **(Table 3)**. Among these, only certain settings—known as "automation levers"—directly influence how aggressively the system

1. Refine hypoglycemia treatment	• Treat mild hypoglycemia with less fast-acting carbohydrate (i.e., 5-10 grams) than with IPT or BBI[1,11] • Be patient and wait at least 15 minutes before re-treating • Consider CBG (finger poke) prior to retreating as sensor glucose values often lag • Consider adapting treatment based on glucose level, trend arrows, insulin-on-board, activity levels, and time spent suspended
2. Optimize bolus timing	• Deliver meal boluses 10-20 minutes before eating • If carbohydrate bolus delayed by > 1 hour, reduce the entered carbohydrates or use system advised corrections
3. Adapt strategies for exercise/ physical activity	• Activate exercise/activity feature 1-2 hours beforehand • Use small amounts of carbohydrates during activity based on sensor glucose trends
4. Teach DKA prevention and prompt treatment	• Be proactive with hyperglycemia. Teach practical points such as: ∘ For sensor accuracy concerns: "If symptoms do not match your sensor reading, check blood glucose with a meter" ∘ For pump/pod site failures: "When in doubt, change it out" • Educate on ketone monitoring with prolonged hyperglycemia, and treatment • Ensure that all AID users have back-up insulin pens and/or syringes and a clear plan for subcutaneous insulin injections
5. Follow system prompts to maximize time in automation	• To maximize outcomes, time spent in automation should be >80% • Maintain "manual mode" settings that are not used by the system in automation

Table 1. Key educational points applicable to all AID systems*; courtesy of Alanna Chambers, RD, CDE, Ilana Halperin, MD, MSc, FRCPC*

Abbreviations: AID: automated insulin delivery; **BBI:** basal:bolus injections; **CBG:** capillary blood glucose; **DKA:** diabetic ketoacidosis; **IPT:** insulin pump therapy

automates insulin delivery. These should be personalized according to the user's goals, comfort with automation, and individual circumstances.

5. **Explore other root causes of hypo- and/or hyper-glycemia:** Review bolus settings, mealtime behaviours, strategies for physical activity, and other concerns.

Optimization Opportunity 2: Reduce Postprandial Excursions

Presentation:

A PwD reports routine postprandial "spikes," negatively impacting TIR and causing frustration. Glucose data shows time above range is elevated (time above >10 mmol/L and >13.9 mmol/L are >25% and 5%, respectively). Daytime glycemic variability may be evident in the glucose profile. Alternatively, they may meet overall glycemic goals, but experience postprandial hyperglycemia with specific mealtimes or food choices.

Clinical Explorations:

- Has the insulin-to-carbohydrate ratio been optimized?
- How are meals quantified (carbohydrate counting, carbohydrate estimates, meal-size estimates)?
- Are boluses delivered before, during, or after eating?
- How often are boluses missed (while normalizing occasional missed boluses)?
- Does meal composition or glycemic index of food choices contribute to postprandial hyperglycemia?

Potential Solutions:

1. **Optimize the mealtime dose:** More insulin is likely required if the postprandial peak glucose level is consistently above target and daily reports reveal routine increases to insulin delivery over the postprandial period (e.g., increased basal delivery, reaching basal

Step 1: Glycemic Metrics	• Time in glucose ranges: hypoglycemia, time in range, time above range • Mean glucose • Glycemic variability (coefficient of variability) • Shape of the glucose profile
Step 2: Insulin Delivery and Settings	• Total daily dose (useful for checking settings using certain rules-see Table 3) • Basal: bolus distribution • Units of daily basal delivered vs. programmed basal settings • Bolus delivery data per day: number of user-initiated boluses, carbohydrate entries, overrides, and auto-corrections (varies by system) • Have adjustable settings been optimized? (see Table 3) • Frequency of infusion site or pod changes
Step 3: Automation	• Percent of time in automation • Use of temporary or activity modes (exercise, sleep, different profiles, adjustable targets—vary by system see Table 3)
Step 4: Review Daily Reports	• Hypoglycemia patterns • Overnight patterns: glucose trends, automated insulin adjustments • Daytime patterns: bolus behaviours, pre- and post-meal glucose patterns, responses to automated insulin delivery (basal modulations and auto-corrections if applicable) • Use of temporary or exercise modes/targets • Patterns of automation exits or loss of sensor data

Table 2. Approach to data review with automated insulin delivery*; courtesy of Alanna Chambers, RD, CDE, Ilana Halperin, MD, MSc, FRCPC*

delivery limits, and/or frequent auto-correction boluses).

To address this:

a. **Strengthen the insulin-to-carbohydrate ratio:** Consider reducing the ratio by 10–20% at a time for the affected meal(s).[11]

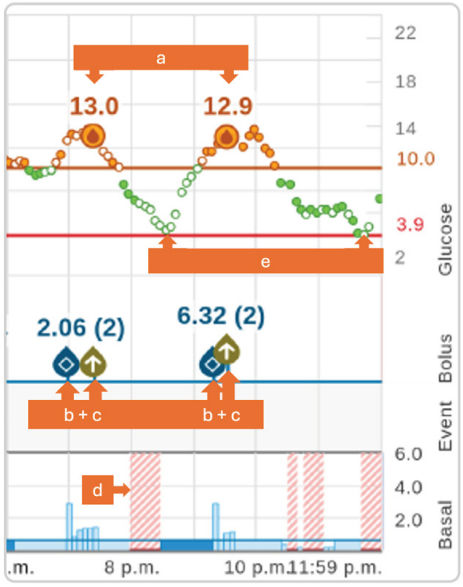
b. **Review the accuracy of carbohydrate estimation or meal entries:** Even simplified approaches to carbohydrate estimation with rounded values (ex: 25 grams, 50 grams, 75 grams) can yield effective results.[9,17] Continuing education on carbohydrate counting approaches or "carbohydrate awareness" may be helpful. For those using meal size entries, re-evaluate the parameters used.

2. **Prioritize meal-dose timing:** Bolus timing may be the issue if postprandial glucose levels are above target but resolve without significant automated increases to insulin delivery. For individuals who bolus after eating, increased sensor daily reports show rising glucose and increased insulin delivery is visible before the user-initiated boluses (**Figure 2**). This can lead to immediate postprandial hyperglycemia followed by late postprandial hypoglycemia if bolus doses are not adjusted to account for insulin delivered by the automation.

Encourage pre-meal bolusing (10-20 minutes before eating):[1,11] Work collaboratively on a specific and realistic action plan to help implement this behaviour. Consider further adjustments based on glucose trends, the glycemic load of the meal, and/or digestion-related concerns (e.g., gastroparesis).

Educate on adjustments for delayed or omitted bolus doses:

- If the bolus is delayed within 30-60 minutes of the meal start, reduce the dose by 50%[11]
- If >1 hour has passed after the meal start, consider system-specific correction strategies:
  - Minimed 780G & Tandem Control-IQ: rely on automatic correction boluses. (Manual correction boluses may be added but are typically not necessary).
  - mylife camAPS FX: rely on automated adjustments for correction. Avoid manual correction boluses (the system does not factor automated insulin into insulin-on-board calculations within the bolus calculator).
  - Omnipod 5: deliver a manual correction bolus to avoid reaching the system's automation delivery limits (the system accounts for increases to basal insulin delivery as insulin-on-board).



The individual responds to subsequent above-range glucose levels (a). The system had already delivered auto-correction boluses (b). Yet the user chose to override recommendations and deliver additional, overlapping correction insulin (c). As glucose dropped, the system responded by suspending insulin delivery (d). However treatment was required for impending hypoglycemia following both overrides (e). Overtreatment of the first impending hypoglycemia leads to the next glucose rise, contributing to significant variability and frustration for the PwD.

Recommendations to prevent variability for this case:

- encourage user to follow system recommendations and be patient with insulin action
- if hyperglycemia is not adequately corrected with auto-correction boluses, consider strengthening the correction factor and assess other settings
- treat hypoglycemia with ~5-10 grams of carbohydrate to prevent rebound hyperglycemia

Figure 1. Glycemic variability due to over-interference with the system: Tandem Control-IQ daily snap-shot; *courtesy of Alanna Chambers, RD, CDE, Ilana Halperin, MD, MSc, FRCPC*

	Minimed 780G	mylife CamAPS FX	Omnipod 5	Tandem Control-IQ
Adjustable Settings Important for overall insulin delivery and glycemic management optimization	✓ Insulin-to-carbohydrate ratio ✓ Insulin action time ✓ Target	✓ Insulin-to-carbohydrate ratio ✓ Correction Factor ✓ Insulin action time ✓ Target	✓ Insulin-to-carbohydrate ratio ✓ Correction factor ✓ Insulin action time ✓ Target	✓ Insulin-to-carbohydrate ratio ✓ Basal rates ✓ Correction factor
"Automation Levers" Adjustable settings that influence the strength of automation	✓ **Insulin action time:** 2-8 hours ✓ **Target:** 5.5, 6.1, or 6.7 mmol/L	✓ **Target:** value within 4.4-11.0 mmol/L (adjustable by time of day	✓ **Target:** 6.1, 6.7, 7.2, 7.8, or 8.3 mmol/L (adjustable by time of day)	✓ **Basal rates** ✓ **Correction Factor: adjustable by time of day**
Specific Settings Considerations	For optimal glycemic outcomes consider[13] • IAT: 2 hours • Target: 5.5 mmol/L • Bolus increment of 0.025 If frequent hypoglycemia consider loosening Carbohydrate ratios to ensure basal: bolus ratio is closer to 50/50. If hypoglycemia persists, raise target and increase IAT	Adjust target within 5.8-7.0 mmol/L for most individuals[14] considering hypoglycemia risk and personal goals Consider adjusting target by time of day to meet specific needs	For optimal glycemic outcomes consider target of 6.1 mmol/L[15] An accurate total daily insulin dose influences accuracy of the system calculated "adaptive basal" rate.[15] Bolus settings should be refined to ensure adequate bolus delivery	Strengthen the correction factor for more aggressive insulin delivery, especially for those who routinely omit boluses. Consider using a '90 rule' (90/TDD) or stronger for calculations[16] Compare delivered vs. programmed basal rates: • to increase TIR: ensure the programmed rate is higher than delivered • to reduce hypoglycemia: ensure the programmed basal rate is set lower than delivered Consider setting alternate profiles with weaker and/or stronger settings.

Table 3. Adjustable settings and considerations for AID systems currently available in Canada*; courtesy of Alanna Chambers, RD, CDE, Ilana Halperin, MD, MSc, FRCPC*

Abbreviations: IAT: insulin action time; **TDD:** total daily dose; **TIR:** time in range

3. **Refine Meal Composition:** Encourage balanced meals and lower glycemic index options to minimize postprandial variability. Discussions around food choices should remain nonjudgmental, respect individual dietary preferences, and consider food security challenges. When high–glycemic index foods are chosen, insulin dose timing may require further refinement.
4. **Incorporate Postprandial Activity:** For level 1 hyperglycemia (10.0–13.9 mmol/L) 10–30 minutes of moderate-intensity physical activity in the postprandial time period effectively lowers glucose levels without causing hypoglycemia.[19] This strategy can reduce time spent in hyperglycemia and minimize reliance on additional corrective insulin. Prolonged exercise will likely require further management strategies.

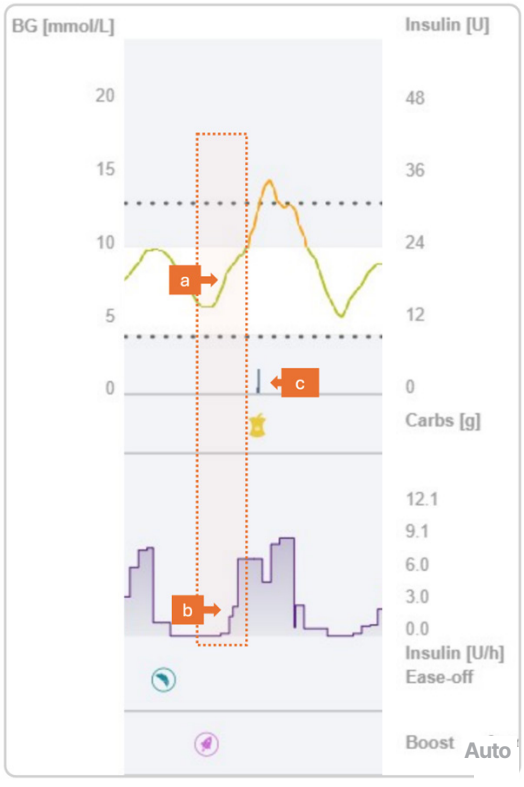
Optimization Opportunity 3: Reframe Exercise Management Strategies

Presentation:

A PwD may feel confident with day-to day management, but encounter challenges adapting hypoglycemia prevention strategies for physical activity and exercise (**Figure 3**). Pre-AID behaviours such as "carbohydrate loading" or "running high" can lead to hypoglycemia due to increased automated insulin delivery. Some individuals may choose to disable automation for exercise, while for others, the fear of hypoglycemia may be a barrier to exercise altogether.

Clinical Explorations:

- What are the individual's typical physical activity patterns (type, timing, planning, duration)?
- What is their current strategy for glycemic management during activity?
- What are their glucose patterns before, during, and after physical activity?



Notice the rising sensor glucose (a) and corresponding automated increase to insulin delivery (b), *before* the carbohydrates and meal bolus are entered (c). This indicates that the meal dose was delivered after eating. In this situation the user reduced the bolus by ~50%, and prevented hypoglycemia.

Figure 2. Identifying delayed meal bolus entries: CamAPS FX daily report snap-shot; *courtesy of Alanna Chambers, RD, CDE, Ilana Halperin, MD, MSc, FRCPC*

Potential Strategies:

1. **Use system-specific exercise modes or targets:** Activate 1–2 hours before activity to allow time for the effects of reduced insulin delivery **(Table 4**).
2. **Encourage in-range exercise**: Avoid excessive carbohydrate intake prior to exercise which results in hyperglycemia and increased insulin delivery. When needed, use small amounts of supplementary fast-acting carbohydrate immediately before and/or during exercise, based on real-time glucose trends.[18] If feasible, exercising in a fasted state with minimal insulin-on-board may help reduce the risk of hypoglycemia and minimize supplementary carbohydrate needs.[18]
3. **Reduce pre-exercise meal bolus:** If planned exercise is scheduled within 2 hours of a meal, reduce the mealtime insulin dose by 25–33%, with the exercise mode/target already activated.[19] Carefully balance dose reduction decisions with the risk of hyperglycemia and subsequent increases to insulin delivery.
4. **Provide individualized guidance:** Tailor strategies to the specific AID system being used and individual glucose responses. Refer to specific guidance in the recent position statement: "The use of AID around physical activity and exercise in type 1 diabetes: a position statement of the European Association for the Study of Diabetes (EASD) and the International Society for Pediatric and Adolescent Diabetes (ISPAD)"[19]
5. **Reinforce and revisit strategies:** Provide ongoing support to continue building and maintaining confidence. Reinforce the importance of routine physical activity for glycemic, mental, and additional health benefits.

Optimization Opportunity 4: Pursuing Tighter Glycemic Management

Presentation:

A PwT1D who meets guideline-based targets may aim for even tighter glucose management. This decision may reflect specific needs, such as preparing for pregnancy, or a personal desire to optimize outcomes. Their autonomy should be respected while balancing potential risks such as hypoglycemia, psychosocial burden, and impact on lifestyle flexibility. When appropriate and achievable, targeted strategies can help support these efforts.

Clinical Explorations:

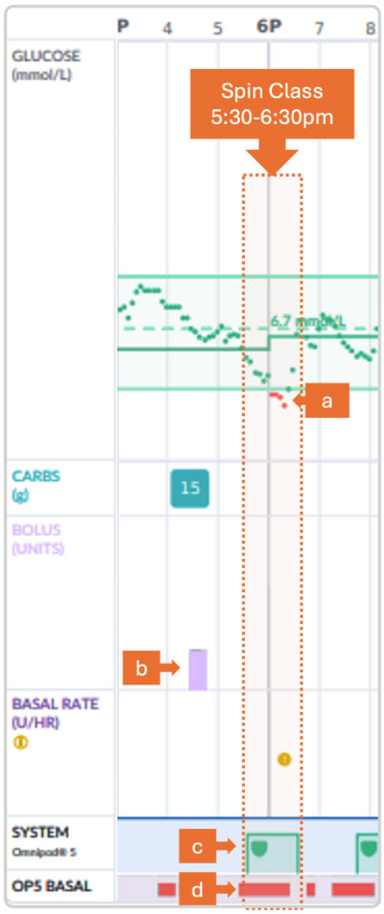
- What are their goals and expectations of AID?
- What is motivating tighter glycemic management?
- What are their risks of hypoglycemia and hypoglycemia unawareness?
- Were these goals achievable before using AID, and what strategies were used (e.g., adjunctive therapy, dietary strategies, exercise strategies, insulin dose timing)?

Potential Strategies:

1. **Strengthen system-specific settings:** Gradually strengthen system-specific adjustable settings **(Table 2)** to improve TIR and mean glucose levels. Monitor closely for increases in hypoglycemia (ensure time below range remains <4%). If hypoglycemia increases, discontinue adjustments and revert to previous settings.
2. **Refine bolus behaviours and meal-dose bolus timing:** Review meal-dose strategies and consider further optimization of meal-dose timing based on glucose patterns, trends, and meal composition.

	Minimed 780G	mylife CamAPS FX	Omnipod 5	Tandem Control-IQ
Flexible Modes for Exercise/ Activity	✓ Temp Target	✓ Ease Off Additional option: customize glucose target	✓ Activity Feature	✓ Exercise Activity Additional option: create alternate personal profile with less aggressive basal rate, correction factor, and carbohydrate ratio

Table 4. System-Specific Features for Exercise and Activity; *courtesy of Alanna Chambers, RD, CDE, Ilana Halperin, MD, MSc, FRCPC*



Contributing factors to this hypoglycemia episode (a) during a "spin class" were:

- 100% bolus delivery (b) for a carbohydrate snack ~1 hour before exercise started
- activated OP5 "Activity" feature at start of exercise (c)

The resulting insulin delivery suspension (d) was not sufficient to prevent hypoglycemia.

Recommendations to improve effectiveness of exercise management:

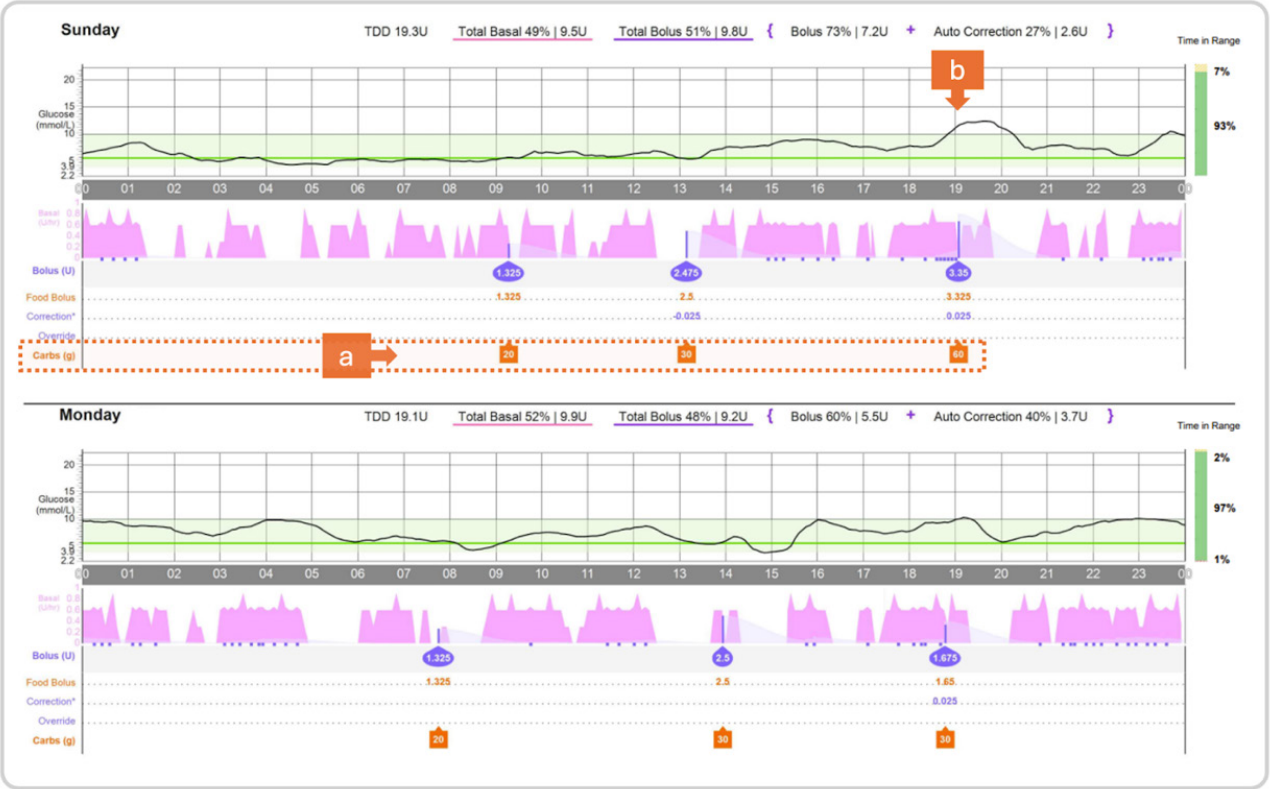
- if possible/desirable, avoid carbohydrate intake 1-3 hours before exercise to minimize insulin-on-board, or reduce bolus if carbohydrate is consumed
- monitor glucose and consume small amounts of fast-acting carbohydrate as needed throughout the exercise session
- activate the "Activity" feature 1-2 hours before the start of exercise to pro-actively reduce insulin delivery

Figure 3. Hypoglycemia with exercise: Omnipod 5 daily snap-shot; *courtesy of Alanna Chambers, RD, CDE, Ilana Halperin, MD, MSc, FRCPC*

3. **Utilize exercise strategically:** Explore using exercise to minimize postprandial excursions and to correct for rising or above range glucose levels.[20,21] Routine structured physical activity has been shown to improve TIR, but it may also increase time below range.[20,22] Apply hypoglycemia prevention strategies as discussed in the previous section.
4. **Consider adjunctive therapy:** Adjunctive agents (metformin, GLP-1 receptor agonists, or SGLT2 inhibitors) may be considered in adults with T1D to support individualized treatment goals (**Figure 4**).[1] Emerging evidence suggests that semaglutide may improve TIR and promote weight loss in PwT1D and obesity using AID.[23] Use shared decision-making and risk mitigation strategies to guide strategies for safety, efficacy, and tolerability.

Proactive Safety Considerations:

While AID offers many benefits, PwT1D should be regularly counselled on troubleshooting technology-related issues, including failures of infusion sets or pods and glucose sensors. Clinicians should review manual pump settings annually to ensure they meet current insulin needs. Provide written instructions on managing hyperglycemia, temporarily transitioning to BBI therapy, increasing the insulin dose during ketosis, and using confirmatory blood glucose monitoring (e.g., before repeat hypoglycemia treatment or large correction doses). Provide PwT1D with updated prescriptions for long-acting insulin, ketone testing supplies, intranasal glucagon, and blood glucose test strips.



This individual began using semaglutide 6 months ago while already using 780G. She has experienced significant improvements to time in range, less postprandial variability, and a reduction to total daily insulin requirements. She effectively estimates carbohydrates by 10-gram increments (a) and aims to bolus 20 minutes before most meals. She prioritizes low glycemic index and lower carb food choices. Even with a 60-gram carbohydrate meal delivered after eating (b), time above range is minimal and short-lived.

Figure 4. Aiming for tighter management with adjunctive therapy and self-management strategies: Minimed 780G daily snap-shot*; courtesy of Alanna Chambers, RD, CDE, Ilana Halperin, MD, MSc, FRCPC*

Conclusion:

AID is now considered the standard of care for individuals with T1D and should be offered to all eligible individuals. Clinicians play a key role in supporting its adoption, optimization, and sustained use. This paper provides a structured approach to common clinical scenarios across various AID systems, emphasizing the importance of building on foundational knowledge. By applying evolving best practices, tailoring strategies, and maintaining a person-centred approach, healthcare professionals can improve meaningful outcomes. Ongoing education and proactive support are essential to maximizing AID's benefits for all patients willing to use this technology.

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Financial Disclosures

A.C : Dexcom, Insulet, Medtronic, Tandem.
I.H.: Abbott, Dexcom, Insulet, Medtronic, Novo Nordisk, Sanofi, Tandem, Ypsomed

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Reference: Current Mounjaro Product Monograph. Eli Lilly Canada Inc.

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Youth-Onset Type 2 Diabetes: A Review

M. Constantine Samaan, MD

Introduction

Type 2 diabetes (T2D) was once considered a disease of adults. However, the obesity pandemic has helped its transition to the pediatric population. While type 1 diabetes remains the most common type of pediatric diabetes in Canada, the incidence of youth-onset T2D has increased by 60% in recent years.[1] Canada has one of the highest prevalences of youth-onset T2D in the world,[2] with approximately 50% of new cases annually occurring in Indigenous children,[1] with the remaining 50% of cases occurring in other ethnic groups, including Caucasians.

As a relatively new disease in youth, there is a lack of natural history data for youth-onset T2D to predict long-term outcomes. However, its aggressive nature in youth suggests that these patients will likely have a significant burden of disease related to cardiometabolic risk, comorbidities, and complications.

In this paper, we highlight current knowledge on the pathophysiology of youth-onset T2D, diagnostic criteria, the impact of obesity on diabetes risk, comorbidities and complications, and current treatments.

Pathophysiology of Youth-onset T2D

While the exact pathophysiology of youth-onset T2D is incompletely understood, genetic, epigenetic, and environmental factors all drive its genesis. A strong genetic component exists, often reflected in a significant family history of diabetes, with some families affected by both type 1 and type 2 diabetes. Youth-onset T2D is more common in females than males, and certain ethnic/racial groups are at higher risk of developing T2D than others (see below).

Fetal exposure to an adverse in-utero environment drives the fetal epigenetic programming for ex-utero cardiometabolic risk. Research in Pima Indians, who have the highest rates of T2D in the world, show that in-utero exposure to normoglycemia versus hyperglycemia was associated with an increased risk of developing T2D in the latter group.[3,4] Additionally, fetal exposure to maternal obesity and being born small- or large-for-gestational-age also increases the risk of T2D.[4,5]

The impact of environmental factors, including endocrine disrupting chemicals, in epigenetic programming of risk in youth-onset T2D remains unclear.

Obesity as a Risk Factor for Youth-onset T2D

Obesity is a major driver of youth-onset T2D. The increased body mass and adiposity, especially during puberty, lead to insulin resistance through mechanisms involving glucotoxicity, lipotoxicity, and inflammation, all of which impact insulin action. The insulin resistance in youth with T2D is higher than that seen in adults with comparable body mass index (BMI) levels and is independent of race/ethnicity and sex.[6]

Skeletal muscle insulin resistance is an early and important event in obesity, as skeletal muscle accounts for up to 75% of post-prandial glucose update. Hepatic insulin resistance leads to increased hepatic glucose output. In addition, adipose tissue expansion is associated with inflammation and increased lipolysis that leads to insulin resistance.

In youth with T2D, insulin resistance is coupled with a heightened islet responsiveness to glucose, and elevated insulin and C-peptide levels at diagnosis in many cases. However,

Treatment	Intervention	HbA1c Reduction	Impact on Weight	Effect On Lipids/ Blood Pressure
Lifestyle	Behavioural and psychological approaches, dietary advice, physical activity, sleep hygiene	0.5–1%	↓ modestly (if adherent)	↓ TG, ↑ HDL-C
Biguanide	Metformin	0.8–1%	↓ mild or neutral	↓ TC, LDL-C, TG; ↑ HDL-C
GLP-1 receptor agonists	Liraglutide, Exenatide, Dulaglutide, Semaglutide	0.6–1.5%	↓ or neutral	↓ TG
SGLT-2 inhibitors	Empagliflozin, Dapagliflozin	0.7–1%	↓ modestly or neutral	↓ BP
DPP-4 inhibitors	Sitagliptin, Saxagliptin, Linagliptin, Alogliptin	0.2–0.4%	Neutral	Neutral
Thiazolidine diones	Pioglitazone, Rosiglitazone	0.5–1%	↑ weight	↓ TG, ↑ HDL-C, neutral LDL
α-Glucosidase inhibitors	Acarbose	0.50%	Neutral	Neutral
Sulfonylureas	Glimepiride, Gliclazide	1%	↑ weight	Neutral
Insulin	Basal ± bolus insulin	>2%	↑ weight	Neutral
Metabolic/ Bariatric surgery	Sleeve gastrectomy, Roux-en-Y	Normalization in most cases	↓ ↓ weight	↓ LDL-C, TG, ↑ HDL-C

Table 1. Treatment modalities and their impact on glycemic control and cardiometabolic health outcomes in youth-onset type 2 diabetes; *courtesy of M. Constantine Samaan, MD*

Abbreviations: BP: blood pressure; **DPP-4:** dipeptidyl peptidase-4; **GLP-1:** glucagon-like peptide 1; **HDL-C:** high-density lipoprotein cholesterol; **LDL-C:** low-density lipoprotein cholesterol; **SGLT-2:** sodium-glucose cotransporter-2; **TG:** triglycerides

these patients lose 20-35% of insulin production capacity annually, and many require insulin in late adolescence or early adulthood. This aggressive decline in islet function is not mitigated by insulin or metformin.[7]

While obesity is a major risk factor for youth-onset T2D, it is not a universal phenotype. Approximately one in eight patients do not have obesity.[8] For example, some Japanese children have normal body mass levels yet have a clear phenotype of T2D. These cases may have defects in insulin production or abnormalities with metabolic organ insulin response or signalling that contribute to T2D occurrence. What is classified as T2D in youth today likely encompasses several subtypes that are driven by different pathophysiologic mechanisms, which require further elucidation.

Diagnosis of Youth-onset T2D

The diagnosis of T2D in youth uses the same biochemical diagnostic criteria as adults, with HbA1c of ≥6.5%, fasting glucose of ≥7.0 mmol/L, and a random or a 2-hour glucose of ≥11.1 mmol/L post Oral Glucose Tolerance Test using 1.75 g/kg of glucose up to a maximum of 75 g are all diagnostic.[9] Many patients are asymptomatic at diagnosis; in these cases, confirmation requires two of the above tests or repeat testing on a different day. Negative pancreatic antibody levels support the diagnosis of T2D, in addition to clinical features such as overweight status, signs of insulin resistance, existing comorbidities, and a positive family history of T2D.[10,11]

Targeted versus universal screening for T2D in youth is currently recommended due to considerations such as cost effectiveness, feasibility, and clinical impact. T2D screening is advised for youth who have an age- and sex-based BMI ≥85TH percentile and who are older than 10 years of age or are in puberty with one or more additional risk factors.

The risk factors include: a family history of T2D in first- or second-degree relatives, maternal history of diabetes (including gestational diabetes), high-risk ethnic backgrounds such as Indigenous, Pacific Islander, Black, Hispanic, Latin American, South Asian, and Middle Eastern, along with other groups that include being born small- or large-for-gestational-age, having clinical signs of insulin resistance, (e.g., acanthosis nigricans), metabolic dysfunction associated steatotic liver disease (MASLD), hypertension, dyslipidemia, polycystic ovary syndrome (PCOS), and youth on atypical antipsychotics that are associated with weight gain.[12]

Children younger than 10 years from Indigenous or other risk groups may need screening if their age- and sex-based BMI ≥85TH percentile or if they develop cardiometabolic risk factors.

Comorbidities and Complications

Youth-onset T2D is an aggressive disease, often accompanied by multiple, and at times simultaneous, comorbidities early in the course of the illness. At diagnosis, patients may present with obesity, MASLD, dyslipidemia, hypertension, obstructive sleep apnea, and PCOS. The progression of complications is more rapid in youth compared to adults.

Hypertension and proteinuria are present in approximately 1:4 and 1:5 pediatric T2D cases, respectively.[13] PCOS occurs in approximately 1:4 female patients[14], while MASLD occurs in 1:3 patients increasing to 1:2 patients when multiple diagnostic modalities are implemented. The Middle East reports the highest prevalence of MASLD.[15]

Retinopathy can appear early in 1:14 patients, and its risk escalates rapidly such that within five years of diagnosis, 1:4 have some degree of retinopathy.[16]

Treatment Options for Youth-onset T2D

In the early years after T2D was first recognized as a pediatric disease, treatment strategies focused on lifestyle interventions, such as eliminating sugar sweetened beverages and adding basal insulin to achieve adequate glycemic control. As evidence emerged regarding the aggressive nature of youth-onset T2D, the focus shifted toward a combination of lifestyle intervention plus pharmacotherapy targeting both T2D and its associated comorbidities and complications. The treatment goal is to maintain HbA1c below 6.5%. Treatment is guided by need, patient preferences, regulatory approval, drug mechanism of action, method of administration, adherence considerations, and availability of therapies.[12]

Table 1 summarizes current and potential treatments for youth with T2D.[12] Lifestyle intervention is foundational for all patients. The recommendations should be tailored to individual families and delivered through culturally sensitive

approaches. Lifestyle intervention remains an important cornerstone for treating T2D comorbidities including MASLD, dyslipidemia, and hypertension, in addition to improving insulin sensitivity.[12]

For patients with an HbA1c <8.5% at diagnosis, metformin is the first line pharmacotherapy for patients alongside lifestyle intervention.[17-19] In the TODAY study, the combination of metformin and rosiglitazone was more effective in preventing treatment failure, defined as an HbA1c of ≥8% 6 months after starting treatment, compared to metformin alone or metformin plus lifestyle intervention. However, an analysis of adult studies of rosiglitazone demonstrated a potential risk of adverse cardiovascular outcomes, which limited its use in children.[19]

For patients with an HbA1c ≥8.5% at diagnosis, insulin therapy is warranted in combination with metformin. Basal insulin therapy starts with 0.25-0.5 units/kg/day, and higher doses may be needed based on response. Rapid-acting insulin is added if hyperglycemia persists. If the patient presents with diabetic ketoacidosis (DKA), insulin therapy is initiated immediately, and metformin is introduced after resolution of DKA and stabilization of the glucose levels.[12]

Maintenance therapy is designed to achieve and sustain an HbA1c target of <6.5%. If this goal is not met, treatment may include glucagon-like peptide -1 receptor agonist (GLP-1RA) or sodium-glucose cotransporter-2 (SGLT-2) inhibitors, while dipeptidyl peptidase-4 (DPP-4) inhibitors appear to offer limited benefit.[20-26]

Bariatric surgery has been used to treat youth-onset T2D. While not widely used, it can result in reduced body mass and improved glycemic control, and, in some cases, diabetes remission. This surgery should be performed only in centres with specialized expertise.[12]

In summary, youth-onset T2D is rising in prevalence and represents more aggressive disease than adult-onset T2D or pediatric type 1 diabetes, with several comorbidities and a faster progression of complications compared to adults. Lifestyle intervention is a cornerstone of treatment as it can improve insulin sensitivity and help manage T2D-related comorbidities. While several pharmacotherapies can lower HbA1c, not all treatments impact weight or cardiometabolic risk factors such as blood pressure or lipid levels and some are not easily accessible. It is critical to assess these patients for the presence of comorbidities and complications, alongside ongoing research to clarify long-term outcomes and to define therapeutic entry points for managing diabetes and its associated comorbidities and complications.

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Running a Trans-Welcoming Clinical Practice

Irena Druce, MD, FRCPC, MSc

Introduction

A wide range of terms are used to describe gender-diverse people, including transgender, gender-fluid, gender-queer, non-binary, and two-spirit, reflecting the diversity of the community itself. Transgender and gender-diverse patients (TGDP) may experience gender dysphoria—the distress that arises when their gender identity does not align with the sex assigned at birth. TGDP are estimated to represent between 0.1% and 2% of the global population; in Canada, the 2019 census reported a prevalence of 0.35%.[1]

Access to gender-affirming care is strongly linked to improved health outcomes. One study found that suicidal ideation decreased from 67% prior to transition to just 3% afterward.[2] Yet, despite the clear benefits, TGDP continue to face major barriers to care.[3] According to the Trans PULSE survey, as of 2019, only 35% of respondents had completed their medical transition. Even in general healthcare, access remains inequitable: while 81% of respondents reported having a primary care provider (PCP), only 52% felt comfortable discussing trans-related health issues with their PCP, and over 40% reported having an unmet healthcare need.[1] These disparities reflect the ongoing impact of transphobia and prior trauma within healthcare systems, and as a result, TGDP face disproportionate health burdens compared to the general population, including lower rates of cancer screening, higher rates of mental health disorders, and sexually transmitted infections **(Figure 1)**.

Addressing these inequities requires urgent action to expand access to gender-affirming hormone therapy, surgery, and mental health care. Equally important, healthcare systems must adopt inclusive policies and practices that improve access to all forms of care for TGDP. This article outlines practical measures that any healthcare practice can implement to create a more welcoming and affirming environment.

Trauma-Informed Care

Trauma-informed care (TIC) provides a useful framework for creating safer and more inclusive clinic environments. Trauma refers to the emotional response to a disturbing or threatening event, and its effects can be long-lasting, influencing health, well-being, and a person's ability to engage with care. For TGDP, trauma

is often compounded by experiences of stigma, discrimination, and mistreatment in healthcare. One striking example is conversion therapy, which was only banned in Canada in 2022; data from the Trans PULSE project indicate that 11% of respondents had been subjected to it, with rates rising to 30% among those aged 50 and older.[4]

TIC is not defined as a specific set of treatments, but rather an approach that encourages providers to view patients through the lens of their lived experiences and potential trauma, and to adapt care accordingly.[5] This perspective reduces the risk of retraumatization and fosters a more trusting therapeutic relationship. Importantly, the principles of TIC benefit all patients, not only TGDP, by promoting respect, transparency, and patient autonomy across the healthcare system.

The remainder of this article outlines practical steps for integrating TIC into everyday clinical practice, from the design of clinic spaces to policies, communication, and treatment decisions. These measures can be adopted at every level of healthcare and contribute to creating safer, more welcoming environments for all patients.

Practical Approach

Create Safe and Affirming Environments

Physical markers, such as rainbow flags or signs indicating the clinic's inclusiveness policy, can be displayed in waiting areas and other public spaces. One example is the *Positive Space* poster available through Rainbow Health Ontario **(Figure 3)**, which signals a commitment to

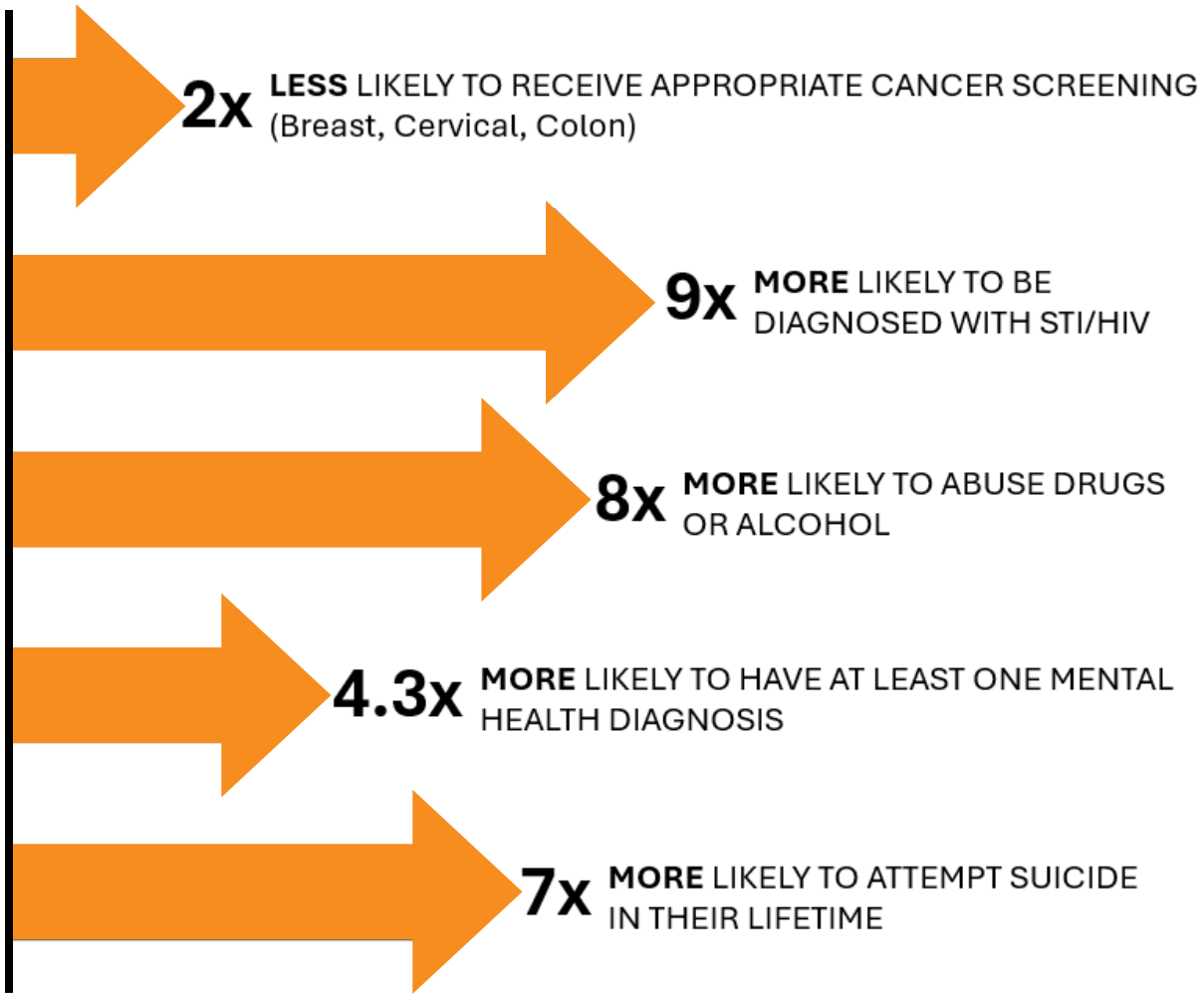

Figure 1. Approximate fold increase of various health outcomes experienced by patients identifying as transgender or non-binary compared to the general population*; courtesy of Irena Druce, MD, FRCPC, MSc*

welcoming all community members and providing a space free of discrimination and harassment based on gender or sexual identity.[6]

Bathrooms should ideally be gender-neutral and single-use. This approach not only provides physical privacy and safety but also reduces the risk of unintended outing or misgendering of transgender individuals. In addition, gender-neutral facilities affirm that people of all genders belong in the clinic space, helping create an environment where patients can access care without fear of judgment or harm.[7]

Intake Forms

Intake forms should provide options for patients to indicate their gender identity, pronouns, and preferred name. Consent should be sought before including certain measures, such as weight or body mass index, which can be stigmatizing. Many patients, particularly those affected by the intersection of transphobia, fatphobia, and racism, have experienced harm in this area.[7]

Language and Communication

Patient-preferred names and pronouns should be clearly documented in their medical record and used consistently. Gendered honorifics should be avoided. When mistakes occur, such as deadnaming or misgendering, providers should offer a brief apology and correct themselves without dwelling on the error.

Providers and staff should also make a habit of introducing themselves and sharing their pronouns to help normalize the practice. This reinforces that respecting pronouns is a standard courtesy extended to all people, not just those who are transgender, and helps to foster a clinic culture where every patient feels acknowledged and respected.

Equally important is to avoid making assumptions. Gender identity, expression, anatomy, and sexual orientation exist in countless combinations, and no single trait predicts the others. Staff should mirror the language patients use for their identities, partners, and bodies rather than inferring or imposing terms.[5]

Staff Training

TIC training is essential for creating safe and supportive environments. It equips staff to recognize the impact of trauma, respond empathetically, and avoid retraumatization. Such training fosters a culture of care that benefits patients and staff alike, by reducing burnout and improving relationships. Programs are available through organizations such as Rainbow Health Ontario and the World Professional Association for Transgender Health Global Education Initiative (WPATH GEI).

Safety	Throughout the organization, staff and the people they serve feel physically and psychologically safe.
Trustworthiness and Transparency	Organizational operations and decisions are conducted with transparency and goal of building and maintaining trust among staff, clients and family members of those receiving services.
Peer Support	Integral to the organization and service delivery approach and are understood as a key vehicle for building trust, establishing safety, and empowerment.
Collaboration and Mutuality	Recognition that healing happens in relationships and is the meaningful sharing of power and decision making.
Empowerment, Voice and Choice	Organization aims to strengthen the staff, client and family members' experience of choice and recognizes that every person's experience is unique and requires an individualized approach.
Cultural, Historical and Gender Issues	Organization moves past cultural stereotypes and biases, offers culturally response services, leverages the healing value of traditional cultural connections, and recognizes and addresses historical trauma.

Figure 2. Principles of trauma-informed care; *courtesy of Irena Druce, MD, FRCPC, MSc*

Figure 3. Positive Space Poster - www.rainbowhealthontario.ca/wp-content/uploads/woocommerce_uploads/2014/09/Poster_English-ovyxku.pdf; *courtesy of Irena Druce, MD, FRCPC, MSc*

Trauma-Informed Assessments

Clinical assessments, including both history-taking and physical examinations, should be conducted with an awareness of prior trauma and a commitment to ensuring patients retain as much choice and control as possible throughout the process. A trauma-informed approach recognizes that even routine questions or procedures may be triggering for patients who have experienced stigma or mistreatment in healthcare settings.

Sensitive information, such as sexual or social history, should be requested with a clear explanation of why it is relevant. This approach builds trust and signals respect for boundaries. The same principle applies to physical examinations. Sensitive aspects of the exam should be described in advance, with the purpose and necessity explained clearly, and explicit consent should be obtained before proceeding. Whenever possible, patients should be offered choices—such as whether an examination occurs during the current visit or can be deferred, or whether a chaperone is present.[7] The routine and proactive offer of a chaperone of the patient's choosing should be standard practice for all patients, including TGDP and cisgender individuals, as this reinforces equity and consistency in care.

Transparency and Open Communication

Clear communication about clinic practices, care options, and decision-making processes is key to building trust. For example, fee schedules and no-show policies should be explained upfront and applied with sensitivity, recognizing that TGDP are disproportionately represented among lower socioeconomic groups. Framing policies in a way that balances accountability with compassion—such as offering grace periods, flexible rescheduling options, or sliding-scale fees—can help reduce barriers to ongoing care.

Communication policies should also be explicit: patients should know how to contact their provider, what response times to expect, and the appropriate use of different communication channels. Documentation should be open and collaborative, with patients generally having access to their records. Diagnostic codes, such as "Gender Dysphoria," should only be used after discussion and with patient consent, to avoid unintended stigma or outing.

Patient Choice and Control

Respecting patient autonomy is a cornerstone of ethical care. A trauma-informed and patient-centred approach requires full adherence to the principles of informed consent. Patients should be active participants in treatment decisions, with clear explanations of risks, benefits, and alternatives. Informed consent must be thorough and meaningful, giving patients the opportunity to ask questions and voice preferences.[5]

At the same time, it is important to recognize that patient choice operates within the boundaries of what is medically safe and feasible. Providers must balance respect for autonomy with their duty to avoid harm and uphold standards of care. Clear communication about these boundaries—including why certain treatments may not be advisable or possible—is essential to preserving trust while ensuring safety.

Collaboration

Collaboration extends patient autonomy from the clinical encounter to the broader healthcare system. At the individual level, this means engaging patients in shared decision-making and recognizing them as experts in their own experiences. At the organizational level, it involves seeking patient feedback on policies, communication practices, and clinic design.

Practical strategies include establishing patient advisory groups or involving patient partners in quality improvement initiatives. Such collaboration is particularly valuable when developing policies for TGDP, yet the resulting improvements—greater safety, responsiveness, and inclusivity—benefit all patients.

Conclusion

Creating a transgender-welcoming practice does not require large-scale structural change; rather, it relies on consistent implementation of simple, intentional steps that align with the principles of TIC. Measures such as displaying inclusive signage, providing gender-neutral bathrooms, implementing respectful intake processes, maintaining transparent policies, and fostering collaborative communication all serve to affirm patient dignity and autonomy. These practices not only make clinics safer and more accessible for TGDP, but also foster a culture of respect that benefits every patient who walks through the door. By committing to these

approaches, healthcare providers can move toward systems that are more inclusive, equitable, and responsive, ensuring that all patients feel both welcomed and cared for.

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Novel Treatment Options For Menopausal Symptoms

Nathalie Gamache, MD, BSc, MSc

Introduction

The world of menopause is undergoing a renaissance. In recent years, medical experts have taken to social media, igniting a long overdue surge of information on the subject that helps debunk the fear of menopausal hormone therapy (MHT), which stems from the 2002 Women's Health Initiative (WHI) study.[1] The devastating consequences on health and wellness were profound: an entire generation of women was suddenly deprived of symptom relief and quality of life (QOL) due to the marked decline in hormone prescriptions in North America. These effects continue to echo today. The near extinction of medical education on mature women's health and wellness in our academic institutions since 2002 has left healthcare professionals ill-equipped to guide the next generation of menopausal women who seek contemporary medical advice and refuse to "live their mothers' menopause." The creation of the Menopause Foundation of Canada in 2022, recent sold-out menopause conferences, and renewed interest from pharmaceutical companies is convincing evidence that menopause is finally receiving the recognition and attention it deserves.

Recent Guidelines

Since the publication of the WHI study, guidelines have undergone regular updates to incorporate evolving evidence on safety and benefits. The latest version, published in 2022 by the North American Menopause Society (NAMS), is summarized in **(Table 1)**.

Contraindications to MHT

There is still considerable misunderstanding regarding contraindications to MHT. Symptomatic women who are generally healthy and within 10 years of menopause onset or below age 60 are ideal candidates. Women within this 'window of opportunity' who smoke, or have mild, well-controlled medical conditions not listed below who are negatively affected by menopausal symptoms should be offered MHT. Enhancing wellness and QOL may optimize their ability to

modify lifestyle factors to benefit health and reduce risks associated with chronic illnesses.

Hormone Therapy for Systemic Symptoms

Prior to the publication of the WHI study, most MHT prescriptions in North America consisted of conjugated equine estrogen (CEE) with medroxyprogesterone acetate (MPA) for those requiring endometrial protection. Findings from the WHI study suggested potential increased health risks associated with CEE and MPA,[1] which resulted in a marked reduction in prescribing habits in North America.[4] Over time, as concerns slowly subsided, innovative MHT formulations deemed safer were introduced and adopted.

Transdermal estrogen preparations, available as patches in Canada since the late 1970s, and as gels approved by Health Canada in 2011, quickly gained popularity. Their advantages include bypassing first-pass hepatic metabolism, reducing the risk of thromboembolic events,[5] absence of metabolites, improved absorption and bioavailability, and more stable systemic delivery compared to oral preparations. Despite that both formulations have shown to be equivalent in their efficacy to relieve VMS,[6] transdermal options continue to be favoured by women and prescribers to this day.

Micronized progesterone, developed in Europe in the late 1970s, became available in Canada in 1999 and quickly replaced MPA as the progestogen of choice for women on estrogen with a uterus. It metabolizes into allopregnanolone, which has a strong affinity for Gamma-aminobutyric acid (GABA) receptors, contributing beneficial effects on sleep.[7] In addition, findings from the French E3N study suggest that micronized progesterone may have a more favourable breast cancer risk profile compared to other progestogens.[8]

A novel MHT combining CEE with bazedoxifene, a tissue selective estrogen complex (TSEC), has been available in Canada since 2017. This formulation of CEE and a TSEC that acts as an antagonist on endometrial and breast tissue and an agonist for bone, is beneficial for osteoporosis prevention. This combination offers a unique formulation appropriate for most women, including those with specific considerations.[9]

Tibolone, a selective tissue estrogenic tissue regulator (STEAR), available in Europe since 1985, made its debut in Canada in 2020. This complex molecule metabolizes into components with estrogenic, progestogenic, and androgenic properties, making tibolone an oral preparation equipped to address distinct symptoms of menopause such as mood changes and hyposexual desire disorder (HSDD).[10] It has also demonstrated a favourable risk profile with regards to breast and colon cancer.[11]

Lastly, since early 2024, estradiol and micronized progesterone have been combined into

• Hormone Therapy remains the most effective treatment for vasomotor symptoms (VMS) and the genitourinary syndrome of menopause (GSM) and has been shown to prevent bone loss and fracture.
• The risks associated with hormone therapy differ depending on factors such as type, dose, duration of use, route of administration, timing of initiation, and whether a progestogen is used.
• For women younger than 60 years or within 10 years of menopause onset without contraindications, the benefit-risk ratio is favourable for treating bothersome VMS and preventing bone loss.
• For women initiating hormone therapy more than 10 years from menopause onset or over age 60, the benefit-risk ratio appears less favourable because of the greater absolute risks of coronary heart disease, stroke, venous thromboembolism, and dementia.
• Longer durations of therapy should be for documented indications such as persistent VMS, with shared decision-making and periodic re-evaluation.
• For bothersome GSM symptoms not relieved with over-the-counter therapies, low-dose vaginal hormonal therapies are recommended.

Table 1. Hormone Therapy Position Statement; *Adapted from Faubion et al., 2022*[2]

a single oral preparation.[12] Although both therapies have been available for decades, this new combination simplifies administration, improves compliance, and reduces dispensing fees by consolidating treatment into a single product.

Non-hormonal Treatment Options for Special Considerations

Following the WHI publication, MHT prescriptions rapidly declined, and a new trend quickly emerged to meet the needs of menopausal women afflicted with ongoing symptoms. Non-hormonal medications previously approved for other indications such as selective serotonin reuptake inhibitors (SSRIs), selective norepinephrine reuptake inhibitors (SNRIs), gabapentin, pregabalin, clonidine, and oxybutynin became popular options to target specific symptoms such as VMS, insomnia, and mood disorders. However, these options often produced unpleasant side-effects and lacked the efficacy offered by MHT.[14] Despite this, concerned healthcare professionals and menopausal women reluctantly accepted these 'safer' alternatives. Today, as MHT has regained its place as a first-line treatment for menopausal symptoms, non-hormonal options have remained valid alternatives for women who have contraindications to hormonal formulations.[15]

The discovery of neurokinin 3 receptors (NK3R) as key players in the generation of menopausal VMS offered a unique opportunity to develop a truly novel non-hormonal treatment option dedicated to the relief of the most common menopausal symptom. Thermoregulation in the mammalian hypothalamus is mediated by kisspeptin-neurokinin B-dynorphin (KNDy) neurons, which are normally inhibited by estrogen. During the menopause transition, declining estrogen levels lead to KNDy neuron overstimulation, eliciting shifts in the thermoneutral zone and triggering vasomotor symptoms.[16] Fezolinetant (an NK3R antagonist) and elinzanetant (an NK-1,3 receptor antagonist), have both shown efficacy comparable to MHT with few side-effects. Both were approved in Canada within the last year for the treatment of menopausal VMS in women who have contraindications to, or prefer not to use, MHT.[14]

Local Treatment Options for GSM

For women experiencing vulvovaginal and bladder symptoms, local vaginal treatments, available for years as estrogen creams, tablets, and rings, are deemed safe for use by all given their negligible systemic absorption. Recently, an estradiol vaginal suppository has been introduced, designed to adhere to the mucosa only centimetres beyond the introitus. This targeted placement improves symptom relief where it matters most, compared to existing products inserted deeper into the vaginal canal.

Prasterone, a Canadian innovation, is a vaginal suppository containing dehydroepiandrosterone (DHEA), which converts into estrogen and testosterone intracellularly, addressing the hormonal needs of all local receptors. It is currently the only vaginal product without boxed warnings.[17] Finally, ospemifene, an oral selective estrogen receptor modulator, specifically targets vulvovaginal estrogen receptors to relieve GSM.[18] It is especially convenient for women with mobility limitations or who wish to avoid vaginal applications.

The Future Looks Bright

Discovered in 1965, estetrol was initially explored as a promising menopausal hormonal treatment option that was abandoned following the WHI publication. Later, estetrol was combined with drosperinone and introduced as an oral

Contraindications to systemic estrogen therapy	• unexplained vaginal bleeding • acute liver dysfunction • estrogen-dependent cancer • coronary heart disease • previous history of stroke • history of thromboembolic disease
Contraindications to progestogen therapy	• unexplained vaginal bleeding • breast cancer

Table 2. Contraindications to MHT; *Adapted from Yuksel et al., 2021*[3]

Type of Estrogen Standard Doses	Trade Names
Oral Conjugated estrogen (CE) 0.3–0.625 mg daily	Premarin
17β estradiol 0.5–1.0 mg daily	Estrace/generics
Transdermal 17β estradiol 25, 37.5, 50 ug patch twice weekly 25, 50 ug patch once weekly	Estradot/generics Climara
17β estradiol 1-2 pumps of gel daily 0.25, 0.5, 0.75 mg gel, one sachet daily	Estrogel Divigel
Type of Progestogens **Standard Doses**	**Trade Names**
Oral Micronized progesterone 100 mg capsule x 1-2 daily every night at bedtime	Prometrium/generics
Medroxyprogesterone acetate 2.5–5 mg daily	Provera/generics
Combination Products **Standard Doses**	**Trade Names**
17β estradiol + norethindrone acetate (NETA) 0.5 mg + 0.1 mg tablet daily	Activelle LD
17β estradiol + NETA 1.0 mg + 0.5 mg tablet daily	Activelle
17β estradiol + drosperinone 1 mg + 1 mg drosperinone tablet daily	Angeliq
17β estradiol + micronized progesterone 1 mg + 100 mg capsule every night at bedtime	Bijuva
17β estradiol + NETA 140 ug NETA + 50 ug estradiol patch twice weekly 250 ug NETA + 50 ug estradiol patch twice weekly	Estalis Estalis
CE + bazedoxifene 0.45 mg CE + 20mg bazedoxifene tablet daily	Duavive
Tibolone 2.5 mg tablet daily	Tibella

Table 3. Systemic MHT products in Canada; *Adapted from Canadian Menopause Society MHT products in Canada publication. 2025*[13]

contraceptive in 2022. Estetrol distinguishes itself by its lack of first-pass hepatic metabolism, absence of metabolites, higher bioavailability, and a longer half-life. It offers beneficial effects on lipids, carbohydrate metabolism, and bone turnover. Estetrol induces apoptosis in breast cancer cells and, at higher doses, demonstrates antitumor effects in end-stage breast and prostate cancers while alleviating VMS often associated with other hormone receptor blockers used as adjuvant therapy. It has significant efficacy for managing VMS and GSM and should become available in Canada in 2026 as a stand-alone estrogen therapy, to be combined with a progestogen for women in need of endometrial protection.[19]

Conclusion

In Canada, there are currently 10 million women over the age of 40, and on average, they will spend 40% of their lives beyond menopause. Most will experience symptoms impacting their wellness and QOL for a decade, and for others these symptoms will persist indefinitely. The impact and cost of unresolved symptoms, on personal health, wellbeing, relationships, productivity at work, and on community and society at large, cannot be overstated.[20] With a deeper understanding of hormonal physiology over the last two decades, the development of a broad range of safe treatment options for all, and renewed interest in this field, medical professionals are now better equipped than ever to provide adequate care and support for all menopausal women.

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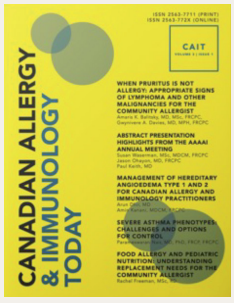

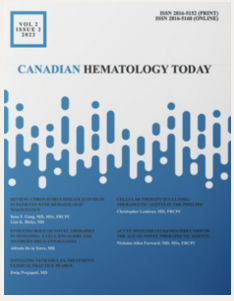

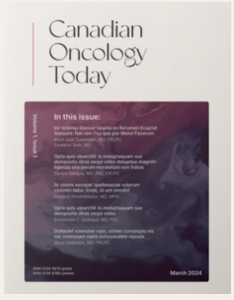

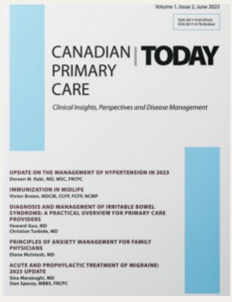

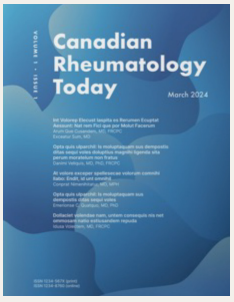

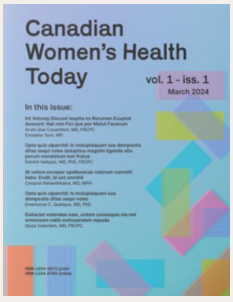

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