

CADTH COMMON DRUG REVIEW

Patient Input

INSULIN DEGLUDEC (TRESIBA)

(Novo Nordisk Canada Inc.)

Indication: Diabetes Mellitus, type 1 & 2

CADTH received patient input from:

Diabetes Canada

Patient Commando

Type 1 Together

June 21, 2017

Disclaimer: The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations.

While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

1. About Your Patient Group

Diabetes Canada leads the fight against diabetes by helping those affected by diabetes live healthy lives, preventing the onset and consequences of diabetes, and discovering a cure. It has a heritage of excellence and leadership, and its co-founder, Dr. Charles Best, along with Dr. Frederick Banting, is credited with the co-discovery of insulin. Diabetes Canada is supported in its efforts by a community-based network of volunteers, employees, health care professionals, researchers, and partners. By providing education and services, advocating on behalf of people with diabetes, supporting research, and translating research into practical applications, Diabetes Canada is delivering on its mission. For more information, please visit: www.diabetes.ca.

2. Information Gathering

This submission was completed based on data collected through patient input surveys conducted in October 2016 and June 2017, distributed through social media and e-blasts. The former survey informed the section on the impacts of diabetes; the survey was answered by 790 Canadians with type 2 diabetes and 57 caregivers who care for people with type 2 diabetes. The latter survey, open to the Canadian public for two weeks from June 5 to June 17, 2017, gathered information from Canadians with type 1 and type 2 diabetes and their caregivers about their experiences with current drug therapies and the drug under review (insulin degludec). The survey was answered by a total of 329 Canadians, including 185 with type 2 diabetes, 19 caregivers for people with type 2 diabetes, 52 with type 1 diabetes, and 19 caregivers for people with type 1 diabetes.

Among respondents (based on 158 responses) to the June 2017 survey, 36% were diagnosed over 20 years ago, 35% over 11-20 years, 14% over 6-10 years, 10% over 3-5 years and 5% diagnosed between 1-2 years ago. A high proportion are older people: 37% over 70 years old, 37% between 55-69 years, 13% between 40-54 years, 7% between 25-39 years, and 5% under 24 years old.

3. Disease Experience

Impact of diabetes:

Diabetes is a chronic and progressive disease. Type 1 diabetes occurs when the body does not produce insulin or produces very little insulin. Type 2 diabetes occurs when the pancreas does not produce enough insulin or when the body does not effectively use the insulin that is produced. Common symptoms of diabetes include fatigue, thirst and weight change. High blood glucose levels can cause long-term complications such as blindness, heart disease, kidney problems, nerve damage and erectile dysfunction. The goal of diabetes management is to keep glucose levels within the target range to minimize symptoms and avoid or delay the complications.

Diabetes requires considerable self-management, including healthy eating, regular physical activity, healthy body weight, taking diabetes medications (oral and/or injection) as prescribed, monitoring blood glucose and stress management. Poor glucose control can result in acute crises and serious long-term complications.

For the majority of respondents, diabetes has negatively impacted all aspects of their lives and limited activities and opportunities including travel and career. Some felt that diabetes “dictates” their lives, that they are “held captive by diabetes,” and that diabetes is “overwhelmingly debilitating.” Diabetes management is “constant struggle” and “a 24

hour, 7 days a week job.” Many are frustrated that they cannot lead a “normal life” due to diabetes. Some lost their driver’s privilege, employment, independence and spontaneity in daily life in general. It is also challenging when a person needs to manage diabetes as well as other coexisting conditions.

Many respondents indicated they are experiencing complications as a result of diabetes, including neuropathy, foot complications, heart problems, eye problems/loss of vision, kidney problems (that resulted in kidney transplant and dialysis), skin ulcers, erectile dysfunction, amputation and depression. Other impact includes fatigue and lack of energy. There was also a frequent emphasis on the psychological and emotional impact of diabetes on the lives of respondents as well as those their family members, as a result of the need to adjust to changes in diet and lifestyle, stress and anxiety about hypoglycemia, daily medication and treatment management, strain on relationships with family, and financial burden. For individuals who have to manage diabetes and care for other members of the family, it is particularly difficult.

Below are selected quotes that demonstrate the challenges of living with diabetes:

“Diabetes affects my life in what I can and cannot eat, how much I eat of certain things, my vision, how I heal, I take longer to get over flu and colds since my immune system is weaker; it affects my memory, moods, I have to worry about monitoring blood sugars and if they get too high or too low; it affects my internal organs, my circulation, everything..... Increased insulin injections make it hard to lose weight...on and on it goes. Nerve damage; have to watch my feet, increased risk of heart attack, kidney failure.”

“It has been a horendous[sic] experience for me because you have to change your lifestyle eating exercising to balance sugar levels etc. Having to inject 2 types of insulins and taking 8 different medications & i also have kidney deteriorating[sic] but i try my best to enjoy life as much as possible. I’ve been diabetic since 1980”

“I have neuropathy in my legs and hands. I have diabetic neuropathy in my eyes. I can’t drive anymore and have to rely on help from family and Handi transit. I was off for a year with Charcot’s foot. I walk with a cane now. Before this happened I was walking 5 kilometers a day. I’m lucky if I get to the end of my driveway. Diabetes has taken away all my independence.”

“I have been diabetic for 48 years. I have been spending \$18,000/year for several years on insulin, needles and test strips and other supplies required for my diabetes.”

“It has been a constantly overwhelming learning curve. It has affected my mood and energy levels. I discontinued working and went on disability 5 years ago (multiple comorbidities). I find that most people, including family, do not understand the issues I face around living with diabetes.”

“My husband [who has type 2 diabetes] has lost his eye sight, can no longer help around the house and is angry/depressed. This affects his relationship with his family (daughter, grand children). Our intimate relationship is minimal due to the diabetes. His feet and circulation in general is not great. It is difficult to get him involved in anything and he seems to have lost the desire to interact with people.” (From caregiver)

“2 sons diagnosed at 6yrs and 18 months with Type 1... The past 16 years our lives have revolved around testing, insulin doses, food requirements, carb counting, balancing excercise[sic] and activity with insulin on board, sleepless

nights up testing to catch lows, not to begin to mention the added stress of caring for a child with the flu who has type 1.” (From parent of children with diabetes)

Respondents to the most recent survey (June, 2017) indicated they are currently experiencing the following symptoms/ conditions: (between 197-218 people answered this question)

- Hyperglycemia: 79% (sometimes for 59%, often for 20%)
- Hypoglycemia: 57% (sometimes for 49%, and often for 8%)
- High blood pressure: 44% (moderate for 38% and severe for 6%)
- High cholesterol: 40% (moderate for 32% and severe for 8%)
- Eye problems: 39% (moderate for 31% and severe for 8%)
- Foot problems: 34% (moderate for 25% and severe for 9%)
- Nerve damage: 27% (moderate for 19% and severe for 8%)
- Mental health problems: 21% (moderate for 15% and severe for 6%)
- Kidney problems: 21% (moderate for 16% and severe for 5%)
- Heart problems: 15% (moderate for 10% and severe for 5%)
- Damage to blood vessels or brain: 9% (moderate for 6% and severe for 3%)
- Liver disease: 7% (moderate for 4% and severe for 3%)

4. Experiences With Currently Available Treatments

Current therapies:

A total of 212 people with diabetes and caregivers that answered the June 2017 survey indicated experience with diabetes medications.

The medications that respondents were taking at the time of survey include metformin (87), GLP-1 agonist (12), SGLT2 inhibitor (25), combination of SGLT2 inhibitor with metformin (6), DPP-4 inhibitor (13), combination of DPP-4 inhibitor and metformin (19), sulfonylurea (30), TZD (3), TZD with metformin (6), TZD with Amaryl (3), TZD with DPP-4 inhibitor (2), meglitinide (3), acarbose (3), and orlistat (4). Some respondents indicated that they stopped using medications due to reasons other than end of clinical trials: metformin (12), GLP-1 agonist (2), SGLT2 inhibitor (5), DPP-4 inhibitor (4), combination of DPP-4 inhibitor and metformin (4), sulfonylurea (8), TZD (13), TZD with metformin (2), meglitinide (2), acarbose (2) and orlistat (1).

The insulin(s) that respondents were taking at the time of survey include: long-acting insulin (100), intermediate-acting insulin (20), short-acting insulin (11), rapid-acting insulin (91), and premixed insulin (9). Some people had to stop insulin due to reasons other than end of clinical trials: long-acting insulin (11), intermediate-acting insulin (15), short-acting insulin (10), rapid-acting insulin (4), and premixed insulin (2).

Diabetes types and use of long-acting insulins:

Among the 100 respondents who indicated current of long-acting insulins, 74 people have type 2 diabetes and 26 have type 1 diabetes; among the 11 respondents who indicated discontinued use of long-acting insulins, 2 have type 2 diabetes and 9 have type 1 diabetes.

Use of long-acting insulin with other insulin and/or oral medications:

Among respondents with type 1 diabetes who are using long-acting insulin (n=26), 1 indicated use of intermediate-

acting insulin, 2 are using short-acting insulin, and 21 are using rapid-acting insulin. Few are also using oral medications including metformin (1), sulfonylurea (1), DPP-4 inhibitor (1), DPP-4 inhibitor with metformin (3), and GLP-1 agonist (1).

Among respondents with type 2 diabetes who are using long-acting insulin (n=74), 6 indicated use of intermediate-acting insulin, 7 are using short-acting insulin, 43 are using rapid-acting insulin and 3 are using premixed insulin. Some are also using oral medications including metformin (41), sulfonylurea (13), DPP-4 inhibitor (5), DPP-4 inhibitor with metformin (5), GLP-1 agonist (8), SGLT2 inhibitor (16), SGLT2 inhibitor with metformin (4), TZD (2), TZD with metformin (4), TZD with amaryl (2), TZD with DPP-4 inhibitor (2), meglitinide (2), acarbose (2) and orlistat (3).

Impact of current therapies:

When asked to compare experience before and after starting current treatment for diabetes, more than half of the respondents noted improvement in meeting target BG levels (fasting, post-prandial, upon waking) and A1C levels, and many respondents noted reduced side effects. Between 155-168 people answered this question.

- Meeting target fasting blood glucose levels: 60%
- Meeting target blood glucose levels after eating: 56%
- Meeting target blood glucose levels upon waking: 52%
- Meeting target hemoglobin A1C levels: 55%
- Avoiding hypoglycemia (low blood sugar): 46%
- Maintaining or losing weight: 33% (14% responded “worse”)
- Gastrointestinal issue (diarrhea, nausea, vomiting, pain): 24%
- Thirst, dehydration: 27%
- Yeast infection, urinary tract infection: 24%
- Lung or upper respiratory infection: 26%
- Bone fracture: 19%
- Organ damage (pancreas, liver, kidney, heart): 19%

Below are some direct quotes from respondents who commented on what works well, and not so well, with current therapies:

“Convenience and accurate no guessing on medications. really like the delivery system.” (person with type 1 diabetes, diagnosed 3-5 years ago, aged 70 years or older, who takes a long-acting insulin, metformin and sulfonylurea, noted improvement in fasting BG and A1C levels)

“[What works well:] Controlled postprandial and fasting blood sugar [What doesn't work well:] weight gain” (person with type 2 diabetes, diagnosed 6-10 years ago, aged 55-69 years, who takes metformin, sulfonylurea, a DPP-4 inhibitor and a long-acting)

“Able to adjust mealtime, less incidences of hypoglycemia and better awareness of dropping blood sugars” (person with type 1 diabetes, diagnosed 20 years ago, aged 40-54 years, who takes a rapid-acting insulin)

“My insulin pump and Dexcom system are of significant help ... [but] schedules, poor food choices (on the go) irregular

hours or activities... insulin doesn't always work as quickly or as slowly as anticipated.” (person with type 1 diabetes, diagnosed 11-20 years ago, aged 25-39 years, using a rapid-acting insulin)

One person with type 1 diabetes commented on the difficulty in twice-a-day insulin injections and preference for “a long acting insulin once a day”. A caregiver for someone with type 1 diabetes noted that the long-acting insulin he is taking “often wears off resulting in highs.”

5. Improved Outcomes

When asked about what they hope **new diabetes medications** can help address, the majority of respondents would like to see improvement and consistency in blood glucose control and avoidance of long-term complications, without weight gain, side effects and damage to organs. Reduced use of insulin and medications, less frequent injections and affordability are also seen as benefits. A respondent noted the hope to “feel well and normal.” When it comes to long-acting insulins, a respondent would like “long lasting and convenience. A basal that will last as long as it claims to.”

“I hope it gives us more freedom at mealtime by acting like a non-diabetic's blood sugar.” (person with type 2 diabetes, diagnosed 11-20 years ago, aged 55-69 years, who takes Metformin (4 per day), a rapid-acting insulin before meals, a long-acting insulin once a day, and a SGLT2 inhibitor once daily, and indicated improvement with current therapy)

“hope to cure it and/or reduce the need for insulin” (person with type 2 diabetes, diagnosed 11-20 years ago, aged 55-69 years, who takes metformin, a long-acting and rapid-acting insulin)

“When used as intended, along with monitoring of carb intake, activity will result in more consistent blood sugar results, avoiding hypoglycemic/hyperglycemia events and better pt compliance” (person with type 1 diabetes, diagnosed 20 years ago, aged 40-54 years, who takes a rapid-acting insulin)

“[It is challenging] timing insulin to cover carbs without spiking or crashing blood sugar levels...I hope for smart insulin. Where I can take one shot a day to cover all my blood sugar changes” (person with type 1 diabetes, diagnosed 6-10 years ago, aged 25-39 years, taking a long-acting, short-acting and rapid-acting insulin through CGM and injections)

“Keeping tighter control means higher incidence of hypoglycemia, so I have to check sugars more often and consume more food/sugar when I'm exercising or having a low...[I hope for] Improved control of blood glucose while avoiding major swings towards hyper or hypoglycemia; avoid weight gain; be linked with longer term health outcomes (e.g. reduced risk of heart attacks, etc.)” (person with type 1 diabetes, diagnosed 11-20 years ago, aged 25-39 years, taking a rapid-acting insulin)

6. Experience With Drug Under Review

Among survey respondents, 15 people indicated they are taking insulin degludec through manufacturer supply or clinical trial, including 4 with type 1 diabetes and 11 with type 2 diabetes. Among the 4 people with type 1 diabetes, 1 person takes it on its own, 1 person takes it with other diabetes medication(s), and 2 people take it in combination with other insulins. Among the 11 people with type 2 diabetes, 1 person takes it on its own, 4 people take it with other diabetes medication(s), 1 person takes it in combination with other insulins, and 4 take it with other insulin(s) and medication(s).

Compared with the other long-acting insulins, respondents found insulin degludec helps them to stabilize blood glucose. Comments include:

“it is comfortable to manage because there is no peak time” (type 1 diabetes)

“Tresiba seems to better stabilize blood glucose levels during the day. I take it at night, before going to bed” (person with type 1 diabetes, taking Tresiba and a rapid-acting insulin, diagnosed over 20 years ago, aged 40-54 years)

“no risk of hypoglycemia vs. rapid-acting insulin” (type 2 diabetes)

“prefer degludec, more stable action, seemed to level out sugars better” (type 2 diabetes)

“very smooth, less nocturnal hypoglycemia, very little variation from day to day” (person with type 2 diabetes, diagnosed over 20 years ago, aged 70 years or older, taking Tresiba with a rapid-acting insulin, GLP-1 agonist, SGLT2 inhibitor, TZD, and metformin)

“since starting tresiba I have reduced from 25 units per day to 10 units per day, A1C from 8.5 to 6.5.” (person with type 2 diabetes, diagnosed more than 20 years ago, aged 70 years or older, taking Tresiba with a rapid-acting insulin and SGLT2 inhibitor)

“I have personally been using this insulin for about a year (bringing it in from abroad), I have found it easy to use and titrate and have had a reduction in hypoglycemia as well as an improvement in A1c (as it has allowed me to increase basal insulin dose without increasing hypoglycemia)... I believe that insulin degludec provides an advantage over other basal insulins” (person with type 1 diabetes)

One person with type 2 diabetes did not have positive experience with Tresiba, and one switched back to another long-acting insulin after taking Tresiba for 9 months.

7. Anything Else?

Diabetes is a disease that requires intensive self-management. To achieve optimal blood glucose levels, individualization of therapy is essential, including selecting the drug or combination of drugs, route of administration (oral, injection, pen or pump), how frequently the patient monitors blood glucose and adjusts dosage, the benefits and risks that the patient experiences and/or tolerates, and the lifestyle changes the patient is willing or able to make. There are clear expectations that new drugs should offer good blood glucose control to prevent hyperglycemic and hypoglycemic episodes, as well as longer term control, with minimal side effects and long term damage to organs, at affordable costs and hope for a healthy and longer life. Many people with diabetes also hope for less dependence on insulin and medications. While current therapies (insulin alone, or combined with medications) have generally led to improvement for many people with diabetes in blood glucose and A1C control, respondents hoped for better long-acting insulins to help them lead a life without frequent interruptions of daily management.

Respondents who tried insulin degludec (Tresiba) reported more stable blood glucose and reduced risk of hypoglycemia, although it may not be the most appropriate treatment for everyone. The survey responses reinforce the understanding that different people with diabetes require different medications to help effectively manage their disease. Their clinical profile, preference and tolerance of therapy can direct physicians to the most appropriate drug therapy. Based on reported benefits, insulin degludec (Tresiba) is an important option for some people with type 1 and 2 diabetes to achieve more effective management of diabetes and better health outcomes.

Appendix 1: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

Yes, a consultant (Jane Tsai) supported the development of this submission.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

Yes, a consultant (Jane Tsai) supported the development of this submission.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Please find attached a list of organizations who have provided financial support to Diabetes Canada along with the amount provided.

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Seema Nagpal, BSc Pharm, MSc. PhD

Position: Epidemiologist and Senior Leader,

Patient Group: Diabetes Canada

Date: June 2017

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1. Submitting Organization

Patient Commando Productions amplifies the patient experience as a guide to improve healthcare practice using multiple platforms:

- the most diverse online collection of patient stories in any medium that enrich our appreciation of the lived illness experience;
- accredited Continuing Medical Education that informs and trains healthcare professionals in narrative competency which evidence supports improved outcomes;
- develops unique collaborations between patients and healthcare professionals focused on improving disease specific therapeutic relationships;

Patient Commando views lived illness experience through the lens of the Social Model of Disability vs. a medical model. It offers no clinical data or advice, but rather supports and enables its community through the sharing of stories and experience, and facilitation of meaningful, relevant conversations.

www.patientcommando.com

2. Conflict of Interest Declarations

- a) *We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:*

Zal Press has received honoraria for speaking and delivering educational programs based on the authentic lived patient experience to AbbVie, Sanofi, Novo Nordisk, Astellas, and Actavis. He is Co-Chair of The Beryl Institute Global Patient and Family Advisory Council, a worldwide community of practice and thought leadership to improve the patient experience, with an international membership exceeding 50,000 that includes patient experience professionals, health care institutions and industry representing a broad cross section of pharmaceutical companies.

- b) *We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:*

This is not applicable. The quotes in this submission are the authentic, public comments from people living with diabetes (PWD). Analysis was conducted independently.

3. Information Gathering

Data sources include:

- personal interviews and facilitated group discussions
- conversation threads in social media platforms,
- the Patient Commando website story collection,
- community responses to our Experience Exchange program.

An inductive qualitative approach was used focusing on the narratives, where identified themes are linked to the data set rather than to theoretical perspectives.

4. Impact of Condition on Patients

Living with diabetes is a non-stop balancing act in living between extremes. But even with diligence, patients pay a price with multiple complications including heart disease, nerve damage (neuropathy), kidney damage (nephropathy), eye damage, foot damage, hearing impairment, and skin conditions. It is very complex and has a striking burden on the physical, emotional, social, and economic status of the person.

“THERE IS NO VACATION from Diabetes”.

“This year I discovered that there is no vacation from diabetes. I tried. I tried taking a summer off. Bad idea. I tried to take a week off. Still, a bad idea. Weekend? Nope. Not worth it. For those of you who can get away with it -- I don't know how you do it. But I found out that I'm diabetic and every day is a diabetic day. If I want to feel good about myself, feel up for the day, be at my best I have to follow my routine. I can't take a day off testing. I can't take a day off my eating routine. I can't just do what I want. When I do I pay for it.” [REDACTED]

Physical Threat: The management of blood sugar requires attention at both extremes – low (hypoglycemia) and high (hyperglycemia). Patients need to respond quickly as symptoms of low blood sugar — sweating, shakiness, weakness, hunger, dizziness, headache, blurred vision, heart palpitations, slurred speech, drowsiness, confusion and seizures – can be dangerous and affect activities such as driving a car. On top of this all consuming activity, patients live with increased risk of cardiovascular problems, amputation, reduced vision, chronic pain, wound management issues, and many other unforeseen and sometimes unpredictable complications. Patients need to be equipped with strategies to be prepared to manage serious and potentially life threatening events.

“Not being able to open the food while low. This is how I die.”

- *“I have severe hypoglycemic issues. In order for me to keep myself stable I'm eating something carb/protein balanced every 3 hours. If I eat higher carb, I crash in 2. I'm drinking a 30g protein shake before bed just to try and get through the night.”*
- *“About a minute after hitting the chair, I started to feel those symptoms of a hypoglycemic episode... starting to sweat, feeling chilly. I recognized what was going on and had prepped for dealing with it. I live alone. I got up and unlocked the back door then got my meter and measured my blood glucose again. I immediately called my buddy, and asked him to come over just in case I needed help. He's done that for me a couple other times so he knows what's going on. I keep cans of sliced fruit in heavy syrup in the refrigerator for just this situation. So I grabbed one, tore the top off and started drinking the heavy syrup. Right about then my buddy arrived.”* [REDACTED]
- *“Last week I had surgery to remove a lump in my breast. The surgeon called and said it was not cancer but a rare diabetes complication. I looked it up and it mainly happens with long time uncontrolled Type 1's. Well, I am a well controlled Type 2 for the past 8 years. I was also dx'd with Retinopathy and Diabetic Macular Edema last month.”* [REDACTED]
- *“Several years ago I experienced a sinus infection that led to hyperglycemia and greatly increased doses of insulin. During my first course of antibiotics I felt much better and my BG numbers started to improve. Within a day after stopping the antibiotics I had a relapse. I called the doctor and he ordered a second round of the same antibiotic. The second course knocked out the infection. Infections cause high blood glucose which in turn further entrenches the infection. It's a vicious cycle.”* [REDACTED]

- *“I’ll tell you what’s wrong with me. I’m losing my hair. I can’t hear in this ear. My teeth are falling out. I got torn rotators in both shoulders. I have carpal tunnel. I got arthritis. I got diabetes. I got bilateral knees (osteoarthritis), varicose veins and I’m pigeon toed. And an enlarged aorta. So that’s my story... I’m not really one to take care of myself like some people.”* [REDACTED]
- *“They do say having diabetes puts us at the same risk as someone who has already had a heart attack.”*
- *“I had my insulin levels checked. They weren’t low, they were off the charts. On a lab scale of 0 to 10, my insulin was 22 which puts me at 5 times risk for heart attack. I also have metabolic syndrome which coupled with high insulin puts me at 16 times risk for heart attack.”* [REDACTED]

Emotional: The fear of hypoglycemia is prevalent for many people living with diabetes. It is a constant shadow hovering over every aspect of life. A severe hypoglycemic episode is extremely traumatic and can heavily impact future treatment measures. Stigma associated with Diabetes manifests itself in people’s perception of self, disappointment with one’s own self-care efforts, the perception of others that Diabetes is the fault of the individual, and that obesity and bad food habits cause Diabetes. “Fat Shaming” comes not only from friends and family but surprisingly from health care professionals as well. For anyone with diabetes, experiencing negative emotions such as anger, frustration, guilt and shame is very common as is depression. “Diabetes Distress”, an attitude of feeling defeated by diabetes, affects a person in many ways.

“Hypoglycaemia is a constant fear for me, living alone. I don’t always feel my lows and have had it where I’ve passed out and then woken up hours later in the middle of the floor. That REALLY scares me, because what if I don’t wake up?” – [REDACTED]

- *“Lows are extremely disruptive and can be scary at times. I’m often worried about going low especially after drinking or exercise and before bed. I tend to over compensate and sometimes my blood sugars end up being on the higher end.”* [REDACTED]
- *“My question -- How do you handle mood swings when your BGs are climbing. My mom says I’m beginning to become unbearable to live with--anything and everything is ticking me off--at home and at work. I’ve always been a cool cucumber and let things roll off my back by cracking jokes, but lately I’m just down right irritable and constantly tired.”* [REDACTED]
- *“I’ll be the first to admit I watch a LOT of television. In my observations, the most common representations of diabetes are used as a comedic device or as a plot-pivoting clue. The former is no surprise, right? It might look like this: Character A sits on a couch eating a plate of donuts. Character B remarks “You’re gonna get diabetes.” [Insert laughter here?]. This first common representation of diabetes is one we in the diabetes online community have been trying to dismantle. We do not take this [mis]representation lightly, as it contributes to the stereotypes and stigma attached to living with diabetes.”* [REDACTED]
- *“I also have depression and am on 'happy pills'. It seems depression and diabetes are bedfellows.”* – [REDACTED]
- *“Doing the same diabetes-tasks over and over leads to burnout. Our lived-experience shows us this. If my insurance won’t cover alternative therapies like insulin pumps, continuous glucose monitors (CGMs), oral medications, etc, and or my doctor isn’t comfortable prescribing them, then how can I integrate a variety of novel tasks into my self-management toolkit that could potentially reduce the frequency of burnout?”*
- *When my self-management becomes monotonous and boring, I do experience maladaptive outcomes. My perception of self-worth decreases. That is to say that in burnout I literally feel like I matter less, am worth less, deserve less. Experiencing this sensation is incredibly maladaptive and generally leads to a slew of other problems. My health suffers, but so do my relationships, scholastic capacity, dependable-ness, and inner-drive.”* [REDACTED]

Social: Social interaction varies depending on age, gender, economic bracket. Diabetes complicates many social encounters. People suffer negative judgements of others. Peer pressure from friends in social situations can result in unwelcome consequences when combined with lack of control. The cost of diabetes to lower income individuals inhibits and restricts social engagement. Travel requires preparation. Food and drink are so often the focus of social interaction, requiring that each encounter be assessed through the lens of diabetes rather than through a person's preferences.

- *"Just before my friend pulled into the restaurant parking lot, she turned to me with a concerned look and asked, "Is it alright to eat here?" What she was asking was code for, "Is there anything on the menu you can eat?" The other person in the car, a friend of my friend's and a stranger to me, missed the subtext and asked, "Would you rather have Thai barbecue?" "No," my friend clarified for her. "Katherine's a diabetic."...Buzz kill." ██████████*
- *"The hardest thing is not being able to share an ice cream with my son, or have a small bowl of ramen soup. I feel like I have lost the joy of food. I used to LOVE to cook all sorts of dishes and I am experimenting but I feel really limited." ██████████*
- *"I was never going to feel 100%, always fatigued, lazy, no desire to visit with my friends, terrible hazy eyesight, resentful of my father's side of the family for giving the disease to me, suffering from what I call 'brain-fog' etc. Get the picture??" ██████████*

"I hate injections. If I eat a salad then I'm ok. If I eat a dish of protein. I'm ok. If I start adding other things... it's not good." - ██████████

- *"I am trying to find others who have eating disorders with type 2 diabetes. It seems really difficult to find anyone and I'm feeling really alone. It's difficult enough to find people who have type 2 at my age (I'm 33 and was diagnosed at 29). I actually have never come across anyone my age with type 2. I'm very ashamed of it and I'm very ashamed of the eating disorder (binge eating). I also have depression, so I'm just a mess. I don't care at all about taking care of myself and that just contributes to all of it. And it's another facet that people just don't get. Most people who get type 2 treat it as a learning experience. That just didn't happen with me. I've had people chastise me for that, too. I pretty much feel very alone amongst all of these circumstances. It would be nice to have someone to talk to." -*

Economic: Poorly managed health affects work opportunities. Disability as a result of complications such as limb amputation, the absence of employee benefits programs especially among lower income populations, interferes with capacity to self-manage and afford the costs of care and magnifies the physical impact of illness. Patients are forced into financial trade-offs of therapy vs. basic needs.

Treatment options are often determined not by the most effective therapy for the individual, but by the patient's insurance coverage and ability to afford the cost of a particular therapy.

- *"My doctor asked me 'What plan are you on?' It only occurred to me afterwards what a difference that question makes to the treatment chosen or available to a patient." ██████████*
- *"I've been really lucky to be under insurance my entire diabetes life but I'm getting to the point of that being over soon and I'm a little worried about it truthfully. I feel like diabetes is more of a financial disability than a physical one." ██████████*
- *"It has changed how I've looked for jobs though since I consider finding something with health benefits a huge priority (something most of my non-diabetic peers don't seem too concerned with). If I went back to university to do a PhD I would also probably look at their health insurance in pretty great detail before committing (something again most of my peers without a chronic illness wouldn't do)." ██████████*

- *“As a person with diabetes, I want tech advancement to happen because I want living with diabetes to be less of a burden on me. As an advocate, I want those innovations to extend beyond people like me who are privileged enough to have insurance, access to local knowledgeable doctors, friends in the diabetes community, access to higher education, and time to self-manage. As an advocate, I know that for our system to be just and fair, all who are interested ought to have access to the medicine and medical equipment.”* [REDACTED]
- *“So sad thought i lost 12 lbs what the scale said a couple weeks ago. Today i weigh in and only lost 7 after 2.5 months. Guess it is my fault not eating as carefully just don’t have the money to always buy good food. I just want to cry i so wanted to lose more.”* – [REDACTED]
- *“I’m on an extremely restricted budget s well, but I’m learning to cut the fat off my spending on food – I get most of my food organic. And I cook everything from scratch. I don’t buy things like cookies or ice cream. Fast food seems much more expensive to me.”* – [REDACTED]

5. Patients’ Experiences With Current Therapy

With any drug regimen, there is always a struggle for patient adherence. In terms of insulin, a lack of adherence comes at both an immediate and a long-term cost. Any improvement in this area, especially longer-acting insulins, help ensure that people living with diabetes are able to live happy and healthy lives without sacrificing their time and sanity. Self-titration is a common thing for patients living with type 1 diabetes. However, this is only possible through the assistance of a dedicated diabetes clinic team as the education required to make decisions is immense. Even with all of the correct knowledge, diabetes is still a guessing game at times as the exact same activities can produce drastically different blood sugars.

“I’ve been diabetic for 25 years and I’ve still forgotten my basal dose a few times recently. If my routine changes, then it’s just out of my mind and I might not remember for several hours. Having a small window to take a single daily dose is frustrating and makes life much more complicated.” [REDACTED]

- *“I take mine at night, only because I’m less likely to forget it then.”* – [REDACTED]
- *“I’ve struggled with giving insulin on my last year on the pump after five years of wearing it. I would just forget to bolus a lot. Not sure if that’s because I just got too used to or if it was because I was 19 (and my most rebellious stage of being a diabetic). I don’t have that problem with injections.”* – [REDACTED]
- *“When I was younger it was definitely tough sticking to an insulin routine. It was hard to motivate to properly count carbs and bolus accordingly.”* – [REDACTED]
- *“Adjusting insulin can be difficult because my schedule and activity levels tend to be inconsistent. Some days I need far more insulin than others. Maintaining a routine is something I need to work on for better management but I find it really difficult. I use temp basals and adjust my IC ratio with my omni-pod but it feels like I’m just guessing most of the time. Sometimes it works, sometimes it doesn’t.”* – [REDACTED]
- *“I struggle between maintaining tight control and having lows, because when I have tighter control I tend to have more lows. It’s easier to keep blood sugars somewhat elevated and not worry so much about lows, because you can still function. You can’t function when you’re low and you’re not going to pass out if your blood sugar is 10 or 12.”* – [REDACTED]
- *“I have had diabetes for 5 years now and I swear my energy level and strength keeps going down. I have tried all sort of vitamins etc and sometimes I feel better for a while but then I go back to being exhausted and fatigued again. Is this really just the way I will feel for the rest of my life everyday and nothing can be done?”* – [REDACTED]

- *“I depend on this meter. I get way too many bad readings. And those bad readings can cause me to do exactly the wrong thing. A false high when I am actually low can result in me injecting insulin causing a hypo. And if I am low and the meter says I am fine I can place myself at risk for a hypo. And exercise is one of those things that can induce both of these situations because it has such a strong and variable effect on my blood sugars. And having to take 3 tests just to get one confident reading, that is crazy.” – [REDACTED]*

6. Impact on Caregivers

A severe hypoglycemic event has a traumatic impact on those around the patient as the fear of a bad outcome begins to spread through the circle of care. Patients feel there is too much or too little attention paid to diabetes amongst loved ones. Relationships with family caregivers can become complicated when family members take on the role of “Diabetes Police”. Yet family members are often life saving interventionists, cheerleaders, managers and personal coaches. They suffer anxiety, stress and worry. The definition of family member/caregiver may be different for some patients, especially for isolated patients who need a caregiver backup strategy in case of a severe event.

For a good amount of time my Hubby has been in the good levels and he is starting to exercise. Now I'm so afraid that he will have a low. What does a low look like and if it happens what do I do to fix it? Also if he ever passes out from a low how do I bring him back and how dangerous is that if it happens.” – [REDACTED]

- *“What I do really hate is how [lows have] affected my interactions with others. Sometimes if people have seen you low especially family they assume you're a bomb waiting to go off, like the slightest breeze might make you low. My mom constantly tries to feed me and has many many times tried to talk me out of experiences that added a lot of value to my life because she fears I MIGHT go low.” – [REDACTED]*
- *“When I went on insulin, I hid it from my children. We went to NY and I had to tell them and my son said ‘How come I didn't know that?’ I would hide it. I would put it in a nice container, a nice bag, so it wouldn't look like insulin. I did that for about 3 months. When they finally knew I was on insulin, they were so sad.” – [REDACTED]*
- *“My husband woke up at 6 AM, said I looked comatose, took my blood sugar and it was 2.1. He called the ambulance but in the meantime, I had a seizure, lacerating my tongue. My husband was trying to give me glucose tabs but said I was spitting them everywhere, along with blood from my tongue. That was Tuesday; this is Sunday. Since then, my husband wakes me at 3 AM to take my blood sugar because it continues to be low during the night.” – [REDACTED]*
- *“My partner just got told that he is type 2 a little over a week ago and our whole world has been turned upside down. I am his nurse and everything as he is too afraid of needles to do any of the testing his self. Also I have been doing all the cooking and anything else for him. And trying to take care of the house work a full time job and we also have a 6-year-old son that I also have to take care of. I am trying to hold it together for him and be everything that everyone needs. But I have so much on my plate that I find myself not eating anymore and I have really forgotten what sleep is. It seems like all I do is think about what his last number was.”*
- *“I stood beside my mom in the hospital as she was being wheeled into the Operating Room to have her right leg amputated just below the knee. The amputation was necessary due to an infection that my mom and her doctors had been fighting for over a year and a half. They were unable to stay ahead of the infection and could not risk it spreading through the bone and getting above the knee. The only possible solution was to remove the leg to head*

off the infection and avoid even more serious future complications. I don't know how to put into words what it was like to see my mom whole one day and then missing a leg the next. It was such a helpless feeling. All three of her children were there with her. My brother, my sister, and I were all there. There was nothing that we could do but we were there if she needed us. She looked so vulnerable and weak that it was heartbreaking. This is the same mother who gave birth to us, raised us, protected us, and did all she could to support her children. There, lying in that hospital bed, now an amputee she appeared so fragile." – [REDACTED]

7. What Are the Expectations for the New Drug?

a) Based on no experience using the drug:

A single minor hypoglycemic event will take at least 20 minutes to treat successfully, with major events taking multiple hours or even days. This translates into time lost at work which negatively impacts earning potential as well as quality of life. Patients emphasize the gap in effectively controlling lows given their far ranging physical, economic, and emotional impact and consequences. Many patients also point out the challenges of adhering to specific routines indicating preference for simpler dosing.

- "Hypoglycaemia is awful for me. I over treat constantly. I go into lizard brain where it's just like "eat everything in sight" even if I logically know better. I hate the feeling of the weakness that's comes with lows." – [REDACTED]
- "I'd switch for the very reason of only one shot per day vs 2 halves, as literature states. I'm so not a night person. I often fall asleep without the 2nd shot." – [REDACTED]

b) Based on patients' experiences with the new drug as part of a clinical trial or through a manufacturer's compassionate supply:

While Tresiba isn't available in Canada yet, there are multiple people posting about their experiences with it online from other countries. The key themes from this international experience is that Tresiba makes adherence easier and provides better control that reduces the number of hypoglycaemic events.

Canadians are participating in these conversations and are anticipating the availability of the product.

- "All good no ugly. Levemir made me depressed, Lantus really burned and just slowly pulled me low overnight, Tresiba is super stable and I don't have to even take it at exactly the same time each day either. Love it all around." – [REDACTED]
- "If I'm 8 or below I can't sleep and end up going hypo in the morning. It's been so much better with Tresiba and the hypos have stopped. Just don't want to be defensively eating at night." – [REDACTED]
- "I am on Tresiba now and really the only difference for me has been that it is one less shot, but for me that is not a small thing lol. So I like it better." – [REDACTED]
- "I'm on Tresiba, it lasts longer, doesn't peak and you have more flexibility with taking it.... weekends I get my extra hour in bed without worrying about my shot 😊" – [REDACTED]
- "So all of a sudden my insurance isn't covering Tresiba..... they said that I "have to try 2 other similar kinds and fail at them" before I can go back to the one I am on currently (and doing well with now that I've adjusted!) Has this happened to anyone else recently? They want me to try both Levemir and Toujeo and "fail" at those before I can go back to my current one, which is Tresiba. I had been on Lantus for years and then in the last year switched to Tresiba." – [REDACTED]
- "Switched from Lantus to Toujeo. Same results. Not at goal. Then switched to Tresiba. Testings are more or less in the low 100s each and every day. Not fearing hypos like before and feel much better" – [REDACTED]

8. Additional Information

Treating The Whole Patient

There is an underestimation of the importance of managing glycaemia (in lieu of managing an A1C number) as the whole patient. Fear of hypoglycaemia and more commonly the fear of being judged do not always appear on a patients' chart. The reasons are multi factorial, but it is very clear from the patient voice that it is far more than just the clinical manifestations of the features and benefits of drug A vs drug B.

- Patients will often “Rationalize” for non – compliance” even though they have had poor control for years, so they don't provide accurate feedback: e.g. missing readings on the CGM; “I forgot my meter.”
 - “Diabetes is not even my most important problem” [REDACTED] (Concomitant disease: cardiovascular, Arthritis, GI, mental health issues)
- Bias against insulin
 - First thing heard by HCP's when insulin is prescribed. “but I feel fine!”
 - “Outcomes on Insulin are associated with bad events, not positive benefits” – [REDACTED]
 - Fear of hypoglycemia: Although they do not have it initially on their own unless they have experienced it, it arises when they have seen other family members or friends.
 - Financial Cost of testing supplies and insulin itself.
- Although Treatment choice is a popular topic for Patient self-management:
 - HCP's do not know all the options on the CDA guideline for treatment algorithms, so why would a patient.
 - Patients (Type2 in general and the ‘working poor’ in particular) are given what they can afford or what their drug plan will allow: Most common questions PRIOR to prescribing: “What coverage do you have?”
 - Treatment options: “It's not their decision.” – Diabetes Educator.

Finally, patients raise system issues that affect decisions and choices across the continuum of care and experience:

- Fragmentation of the way diabetes is managed / paid for:
 - “Depending on the funding you're going to get in each area determines the kind of support you're going to get. Type 2's have a struggle while Type 1's have a different struggle.” – [REDACTED]
 - “I am still benefiting for being paid by company insurance but I am worried when I am not employed and I hear horror stories that medication/needles are not affordable to others. These people just do not buy the medication and these are the people who gets complications, i.e. heart attack.” - [REDACTED]
 - “I like to test often and I heard that our current system does not pay majority of it. I heard that they use the same needle 2 or 3 times to save money.”
- Alarms are being raised about patient access to the best treatment:
 - “My GP took care of me for over 3 years but I only got worse. Then he sent me to an endo and things started to turn around. I wonder if GP hung on to me cause he gets paid more because of all the visits I needed.”

1. About Your Patient Group

Type 1 Together brings together Canadians living with Type 1 Diabetes (T1D). We make T1D easier to live with through connections, sharing, and advocacy. Our website is: www.type1together.ca.

2. Information Gathering

Because there is considerable peer-reviewed and published T1D research specific to Canadians, we have deferred to that body of knowledge where appropriate. Our survey sought to supplement that data.

Type 1 Together reached out to the members of the Canadian T1D community via social media, email, and word of mouth. We invited members to complete an online survey in either English or French, and received 115 responses. We interviewed some members about their personal experiences.

Data were gathered in Canada during June 28 and July 16, 2017. The Canadian T1D community contributed 106 survey responses: 81 from people with T1D, 16 from parents (whose children may be adult), and 8 from caregivers. Respondents were well-distributed age-wise and geographically, although no participants responded from PEI, Northwest Territories, or Nunavut. One survey response was received from outside of Canada, and 8 responses were from people with type 2 diabetes.

Our respondents had tried a median of two basal insulins, and 54% were currently using an insulin pump.

Further, 4 people identified as having experience with insulin degludec via a clinical trial through BC Diabetes. To supplement this data, we reviewed diabetes community forum posts about insulin degludec.

3. Disease Experience

T1D is an autoimmune disease where your body stops producing insulin. People with T1D must take insulin to avoid a quick death. T1D is not caused by lack of exercise, poor diet, or lifestyle.

Insulin requirements are determined and affected by: consumption of carbohydrates, consumption of fat/protein, activity level, type of activity, the number of days since one was last active, caffeine intake, alcohol consumption, extent of “dawn phenomenon”, hormones, body weight, stress, illness, inflammation, menstrual cycle, pregnancy, insulin exposure to temperatures > 30 degrees Celsius, intra-subject absorption variability, injection location, presence of hyperlipotrophy or scar tissue in injection location, age of infusion site (if using an insulin pump), cortisone injections, ambient temperature, sleep, allergies, altitude, plane rides, smoking, current blood sugar level, and recent blood glucose levels (as a period of elevated blood glucose levels create insulin resistance). Both positive (such as being proposed to) and negative (such as fear) emotions can have dramatic effects on insulin requirements. Less commonly, using a vial or cartridge of insulin beyond 28 days can also negatively affect the potency of some insulins.

Taking too much insulin causes hypoglycemia (low blood sugar). Hypoglycemia is typically experienced as shakiness, anxiety, sweating, lethargy, confusion, rapid heartbeat, hunger, nausea, sleepiness, impaired vision, headaches, tongue/nose tingling, anger, crying, stomach aches and/or incoordination. Hypoglycemia can also cause seizure, unconsciousness, brain damage, and death.

Taking too little insulin in the short term causes hyperglycemia (high blood sugar). Hyperglycemia is typically experienced as nausea, extreme thirst, frequent urination, sleepiness, lethargy, anger, fatigue, increased appetite, dehydration, blurred vision, light-headedness, rapid breathing, rapid heart rate, vomiting, and/or difficulty waking up. Hyperglycemia can also cause rapid-onset coma and death.

Taking too little insulin in the long term increases the risks of diabetes complications: cardiovascular disease, heart attack, heart failure, atherosclerosis, peripheral vascular disease, high blood pressure, stroke, blindness, vision loss, vitreous hemorrhage, macular edema, glaucoma, cataracts, retinopathy, dementia, amputation, kidney failure, autonomic neuropathy, peripheral neuropathy, postural hypotension, gastroparesis, carpal tunnel, erectile dysfunction, fungal skin infections, hearing impairment, gum disease, skin ulcers, female infertility, and depression.

Mission impossible. T1D isn't like other diseases. It's certainly not like type 2 diabetes: our pancreases do not quietly help us out in the background. Insulin requirements can be affected by 30+ variables, and the responses are highly individualistic. It's not just a matter of figuring out how one variable affects you. It's not enough to know how having a cup of coffee affects your insulin requirements: it's knowing how a cup of coffee affects your insulin requirements on the nth day of your menstrual cycle, when you're stressed about work/school, and you haven't worked out in three days because you're fighting off a cold.

Frequently, it is not possible to predict how all variables affecting insulin requirements will affect you. With insulin requirements you struggle to predict and punishments for taking too much or too little, T1D pins us between a rock and a hard place. Too much insulin, and you can die quickly. Too little insulin in the short term, and you can die in a coma. Too little insulin in the long term, and you increase your risk of dying slowly in the future from diabetes complications.

Balancing insulin is like walking on a tightrope. Blindfolded. In unpredictable and gusting winds. Where different parts of the tightrope have different widths and tensions.

How wide is that tightrope? According to Diabetes Canada guidelines, we should aim for a glucose range of 4 to 7 mmol/L, fasting or before meals. Converting mmol/L to mg/dl facilitates our calculations, and gives us a range of 72 to 126 mg/dl. For the majority of the day, we're trying to target a range of $(126 - 72 =)$ 54 mg/dl, or 0.54 grams per litre. Since the average adult has 5 litres of blood, we're trying to control blood glucose fluctuations within 2.7 grams. That's less than the amount of sugar in a single Life Savers candy for an adult, and it's reduced even further for a child.



Is it any wonder so many people with T1D struggle to cope?

How well are we doing? *Not well.* The DAWN2 (Diabetes Attitudes, Needs, and Wishes) study looked at the experience of 8,596 people diagnosed with diabetes, and 2,057 of their caregivers. The study took place in 17 countries across four continents. In 2016, data were also published summarizing the experiences of the Canadian participants with T1D¹, who had an average age of just 37 and had been living with T1D for an average of 21 years. Key findings included:

- 73% had diabetes complications such as stroke, kidney disease/kidney failure, eye damage/blindness, nerve damage, heart disease, and depression.
- Under-employment was significant: 9% were unable to work, and 14% were unable to work full time due to their T1D.
- More than a third identified they had experienced discrimination because of their T1D.
- 1 in 3 people assessed their quality of life as either “neither poor nor good”, or worse.

- T1D negatively affected many dimensions of functioning: 71% reported negative impact on physical health, 51% reported negative impact on finances, 54% reported negative impact on leisure activities, and 66% reported negative impact on emotional well-being.
- Nearly half (48%) registered high levels of diabetes distress, defined as “significant emotional distress that interfered with diabetes outcomes”.

Let’s put that last point into different words: *nearly half of people find T1D so crushing that their emotions interfere with their ability to manage their diabetes.*

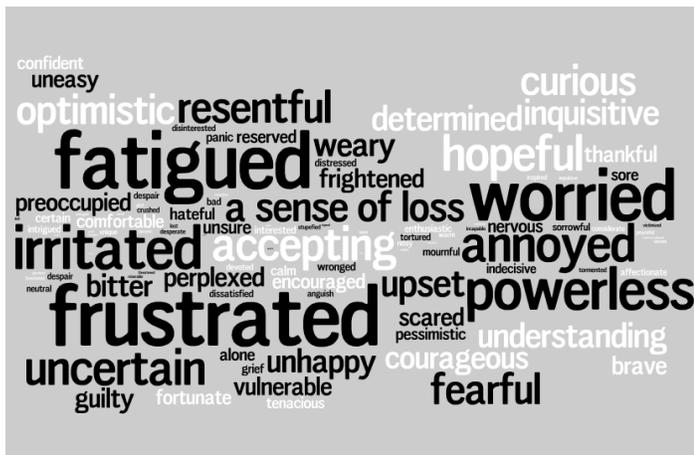
Caregivers are also affected by diabetes. DAWN2’s analysis of Canadian caregiversⁱⁱ found that:

- 33% experienced high diabetes distress
- 40% were very worried about hypoglycemic events
- 26% experienced a “moderate” to “very large” burden.

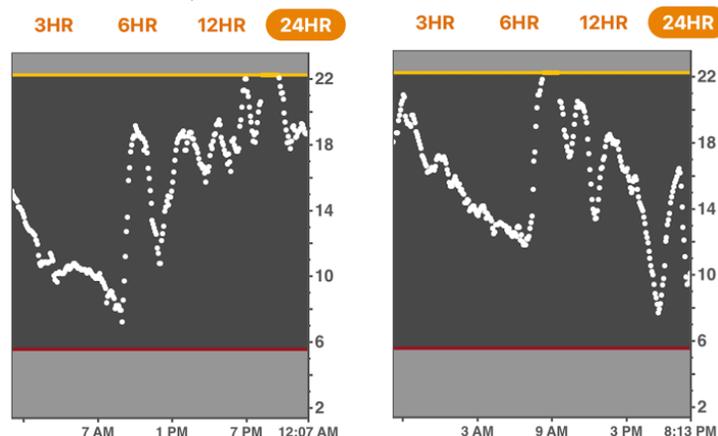
The emotional experience of the T1D community is overwhelmingly negative. We asked the T1D community to pick ten choices from a list of 112 emotions (of which 56 were positive and 56 were negative) to indicate how they felt about diabetes. We’ve illustrated their responses using font size to indicate relative frequency. Words in a black font indicate negative emotions, and words in white indicate positive emotions.

In both official languages, the themes of anger, helplessness, fear, and depression outweigh optimism and resiliency.

(Not enough French surveys were completed to obtain the variety experienced in the English results set. Consequently, the range of font sizes is less dramatic in the French version.)



T1D is a family struggle. The continual decision-making required by T1D gives families thousands of decisions to argue over, and can cause significant interpersonal strain.



One caregiver of a person with T1D on multiple daily injections expressed feelings of guilt, shame, helplessness, and anger regarding glucose levels, despite working diligently with an endocrinologist to optimize insulin doses. He described continuous glucose monitor tracings that “look more like something a polygraph machine would put out”, and provided the adjacent images as examples. He feared relationship and family breakdown if he pushed too hard.

Managing T1D well means walking a knife-edge of carefully calibrated insulin guesses/doses, very frequent glucose testing, exercise, healthy eating, calculating carbohydrate intake, omnipresent mindfulness of the 30+ variables that affect insulin requirements, and emotion (particularly fear) management. Managing T1D well requires extraordinary behavioral commitments and being attentive to it 24 hours a day, every day of your life. Even when you’re sleeping.

We do not have the tools we need. People with T1D need tools and technologies that make T1D safer, easier to manage, and less psychologically distressing to live with, not just over the weeks/months typical of a clinical trial, but over our lifetimes. We need to safely reduce and eliminate our risks of dying quickly or slowly developing diabetes complications from too much or too little insulin.

4. Experiences with Currently Available Treatments

Glucose levels are typically not well-managed. The “A1c” (glycosylated hemoglobin A1c) test approximates average blood glucose levels over a period of months. Lower A1c levels lead to lower levels of long-term diabetes complications, but also increase the risk of hypoglycemia.

In 2014, the American Diabetes Association lowered their A1c targets in children. One year later, they found average A1c levels unchanged, and remaining significantly above targetⁱⁱⁱ.

How do adults do? It is often quoted that the average A1c in adults with T1D is 8.0%, well above the goal of 6.5 set “for most patients” by the American Association of Clinical Endocrinologists. A recent study attempting to correlate A1c levels with average glucose level supported this statistic, finding an average A1c of 7.99% in 120 patients with T1D^{iv}. An A1c level of 8.0 increases the risk of diabetes complications. This risk is neither low nor theoretical: as stated above, 73% of Canadians with T1D that participated in the DAWN2 study had diabetes complications such as stroke, kidney disease/kidney failure, eye damage/blindness, nerve damage, heart disease, and depression.

Insulin management is an immense burden. Two in five people with T1D agreed that “My diabetes medication routine interferes with my ability to live a normal life”^v. People find it challenging to meet the demands of their diabetes medication routines. When asked “On how many of the last 7 days did you take all your diabetes medications exactly as agreed with your health care professional?”, the average of the answers was 6.11 days^{vi}. Significantly, more than two thirds were “very worried” about the risk of hypoglycemia^{vii}. A quarter of the group found it difficult to pay for their diabetes medication^{viii}.

Current treatments are not effective, increase stress, and require extraordinary levels of behavioural commitment continuously throughout the day. Of our survey respondents with T1D:

- 35% reported that they typically wake up *at least* twice a night because of T1D.
- 28% can “rarely” or “never” skip a meal or sleep through the night without going high or low (experiencing hyperglycemia or hypoglycemia).
- 16% report that any delay in insulin delivery affects their blood glucose levels. 30% can tolerate a delay up to 15 minutes.
- 75% reported they would be able to test less if their blood glucose levels were more predictable/stable.

Historic CADTH recommendations undermine the T1D learning process. T1D requires a lifetime of experimentation, skill development, and extraordinary learning. Learning is most effective when you develop and master skills, and then build up to developing and mastering progressively more challenging skills. Continually building on successes establishes deep cognitive connections and boosts confidence. CADTH recommendations seem to fail to take this into account, however. Consider someone wants to quit smoking. If you give them the least effective support and they fail, they may never try again. It’s similar with T1D. Unless you see success, under a crushing tonne of emotional burden, it is all too easy to decide that T1D is unmanageable. Not only does continually denying advancements reduce our sense of hope, but it also sets people up for failure.

The most relevant data is not clinical trial data over a period of weeks, but how people with T1D fare over their lifetime. And CADTH? We are not doing well! We need more help when it comes to T1D treatment options.

Hypoglycemia is a major deterrent to pursuing a lower A1c. Nocturnal hypoglycemia is a significant issue. In one 48-hour study^{ix}, one third of participants experienced nocturnal hypoglycemia, with an average duration of 78 minutes for participants using insulin pumps, and 98 minutes for participants using injections. Up to 5% of people with T1D die overnight from “dead in bed” syndrome, which some researchers attribute to hypoglycemia^x. Hypoglycemia can also kill during waking hours.

Researchers examined Canadian absenteeism and healthcare utilization following hypoglycemia^{xi}. Although they did not provide separate numbers for T1D and T2D, they found that 9% of people with diabetes took sick leave from work/school following a hypoglycemic event, with a mean of 10 ± 36 days, and noted rates were greater in people with T1D. Late arrivals and early departures were also common responses to hypoglycemia, and were noted to be more frequent in people with T1D. These work/school absences can have harmful effects on careers and learning. In adults with T1D, hypoglycemia also impairs cognitive functioning during hypoglycemia and for up to 75 minutes afterward^{xii}. Taking 15-30 minutes to treat hypoglycemia, and 75 minutes to recover cognitively means that a person with T1D may be incapacitated for more than an hour and a half during their work/school day treating and recovering from just a single episode of hypoglycemia. Hypoglycemia is not limited to one episode per day: people with T1D can go low repeatedly. Indeed, our survey data found that 24% of respondents experienced *5 or more episodes* of hypoglycemia over 24 hours when having a “bad” day. Hypoglycemia can also cause you to lose your license and creates other career barriers (such as becoming a pilot). Is it any wonder 1 in 3 people with T1D experience discrimination?

Hypoglycemia can evoke a panic/emergency response and can lead to overcompensation in the short term, in the long term, or both.

- Short term, hypoglycemia often leads to blood glucose spikes as people with T1D, overcome by a tsunami of survival instincts, over-treat their low blood glucose level by ingesting more than the minimum required amount of carbohydrate, rather than iteratively, slowly, and scientifically treating with small amounts of carbohydrate and reassessing treatment requirements 15 minutes later. Consuming excess sugar to treat hypoglycemia leads to weight gain, and destabilizes blood glucose levels.
- Long term, fear of hypoglycemia can play havoc with both diabetes management and emotion management. According to Dr. Michael Vallis, “If you go through a period of two or three weeks, and [...] you have a series of two, three or four serious hypoglycemic episodes, the result of that is that you could spend the next 6 to 12 to 18 months hyperglycemic.”^{xiii} The incidence of severe hypoglycemia is estimated at 1.9-2.5 episodes per patient per year^{xiv}.

Fear of hypoglycemia can be debilitating. The Diabetes Online Community is well-networked and active on social media. When someone with diabetes dies, users change their profile pictures and avatars to a blue candle to observe the loss. It means that social media can frequently, and sometimes continuously, be filled with reminders of recent deaths. One mother of a young adult with T1D commented: “My heart stops. It could be us. I can't breathe. A candle brings the reality--the deadly nature of diabetes home in one seemingly tranquil image. Honestly I try not to investigate too much. There have been friends and children of friends lost. The stories are just too painful.” While social media can offer exceptional emotional support and dissemination of information, it can also worsen fear of hypoglycemia by dramatically heightening the sense that *it could be you*.

One second-year Nursing student commented that T1D makes her *continuously afraid of being alone*: “For fourteen years I've fallen asleep at night wondering if I'd wake up in the morning. Imagine feeling scared to be alone at any point in time, especially at night, because your blood sugar could go low, you could pass out, no one is there to get any form of glucose into your body, you seize and slip into a coma, and eventually die from a lack of glucose. Type 1 Diabetes is a 24 hour disease – there are no breaks in managing it. It is both physically and mentally draining. And no matter how well you try to control it, it will always throw a curve ball at you. You'd think after fourteen years of it you'd have better control – that you'd be experienced enough to manage any little thing thrown your way. But that just isn't the case.”

Our survey found that 37% of respondents with T1D were continually or typically fearful of going to sleep at night because of the risk of hypoglycemia.

Hyperglycemia increases your risk of future diabetes complications, but to some, dying slowly feels like a better choice than dying quickly from hypoglycemia. Those who focus on short-term outcomes may feel they “benefit” from hyperglycemia, future complications be damned. No one should have to make such choices.

5. Improved Outcomes

People with T1D want, would benefit most from, and deserve a full cure. That's the goal. A cure would provide profound and unimaginable relief in many aspects of functioning for both the person living with T1D and their family/caregivers.

We look for the following improvements in our treatment regimens:



Goal: Improved health/blood glucose management with less work. Is as effective, or is more effective.

- Automatically adjusts to blood glucose level without human intervention
- Has positive health side effects (such as cardiovascular risk reduction)
- Reduces likelihood of linked autoimmune conditions (celiac, thyroid, ...)
- Takes less time away from everyday life to manage
- Matches normal, individual metabolic needs
 - Can increase/decrease basal rates immediately, without delay.

Goal: Can eat a “normal” diet

- Don't need to count carbohydrates
- Don't need to worry about glycemic index or glycemic load
- Does not restrict diet

Goal: Increased safety

- Eliminates/reduces hypoglycemia
- Eliminates/reduces hyperglycemia
- Eliminates/reduces risk of complications (heart attack, stroke, kidney failure, blindness, amputation...)
- Easier to calculate dosages
- Fewer side effects (No cancer, no weight gain...)
- Safe and approved for use in all ages
- Less intra-subject absorption variability
- Associated with less glycemic variability
- Rapidly treats hypoglycemia
- Restores immune system to pre-diabetes functioning

Goal: Reduced emotional burden

- Non-invasive or minimally invasive continuous blood glucose monitoring
- Psychologically easier to live with. Less likely to cause diabetes burnout
- Don't need to live attached to a pump/infusion line, or medical appliance
- No/reduced behavioural demands
- Prescribed schedule easier to follow (fewer injections, injection flexibility / less worry about timing of next dose)
- Can sleep through the night without worry or needing to wake up (or wake up repeatedly) to check blood glucose levels
- Makes it easier for healthcare professionals to understand how to treat T1D
- No risk of ever losing driver's license

Goal: Reduced financial burden

- Free/more affordable drugs, technologies and supplies
- No/fewer injections per day
- No/fewer blood glucose tests per day
- Treatment causes less time off work
- Fewer health care appointments

Goal: Less pain

- Doesn't need to be injected; no/less injection pain
- Non-invasive or minimally invasive continuous blood glucose monitoring
- Medication doesn't sting

Goal: Equality and choice

- Access to my choice of therapies (a choice of: insulin, pump, meter/strips, flash glucose testing, continuous glucose monitor)
- Don't need to "fail" on one treatment to gain access to other treatment options
- People with diabetes can have any career they chose.

Some people wake up repeatedly during the night to check their blood glucose level. Even a small improvement, such as meaningfully reducing or eliminating nocturnal hypoglycemia, would mean that people with T1D could sleep through the night, and could go to sleep without fearing (or with less fear) that they will never wake up.

Cost is the primary trade-off when it comes to selecting treatments to manage T1D.

6. Experience with Drug Under Review

We received several comments from people who had participated in an insulin degludec clinical trial through BC Diabetes:

- "Blood sugar lowers more than before when taking Tresiba. No disadvantages. No side effects."
- "Through a clinical trial at BCDiabetes. Blood sugar more in control than before. No disadvantages. No side effects. Tresiba was fairly easy to use."

One respondent without insulin degludec experience noted: "Without having tried it the advantages of anything different is a pro. Each T1 is similar but different in where what works great for me may not work great on the next person. Choice and variety is always better."

Because insulin degludec is not currently available in Canada, we reviewed forum posts^{xv,xvi,xvii} on TuDiabetes, a popular online diabetes forum, for feedback.

- "My new A1c is 5.8!!!! I have never, ever been this low. The other great thing is I have not had 1 nighttime low, not 1 which is amazing to me. It is so nice to go to bed and not have to worry about lows." – Gail12, on 2016-07-23

- “It is quite marvellously flat. Even helped to level out some hormonal stuff, though how, I've no idea. When I combine tresbiba with low carb eating, I can almost forget I have diabetes, as I hardly need any bolus insulin.” – JustLookin, on 2016-08-24
- “No stinging, 24 hour solid coverage... we did try dosing every 36 hours and being able to skip a day sometimes but Tresiba really needs to be dosed daily. He injects it before bed and we don't have any hypo issues through the night. Good luck with the change! I don't know anyone who has regretted it.” – JT112, on 2016-08-24
- “I have been on Tresiba for almost six months and love it. No more random hypos and the release is super steady and predictable. Been on Lantus which Was crazy up and down. Toujeo little better. Tresiba far better.” – AlfrezzaGuy, on 2016-08-26
- “[...] we are all different. I have seen several posts from people who were not as pleased with their results from Tresiba. But I have not seen anyone have significant issues with it either. If you are having problems with stability it may be helpful.” – Randy5, on 2017-04-03

7. Anything Else?

Beyond A1c. The FDA hosted a public workshop during the summer of 2016 called “Diabetes Outcome Measures Beyond Hemoglobin A1c (HbA1c)”. To paraphrase a DiaTribe article^{xviii} on the subject: we need different outcomes to assess diabetes drugs and technologies. A1c does not capture hypoglycemia, and a single episode of hypoglycemia can be fatal. A1c is simply a single average and it does not capture glycemic variability. Different levels of glycemic variability can produce the same A1c, but at wildly different levels of safety and senses of emotional and physical well-being. A1c does not capture how different therapies affect quality of life.

Glycemic Variability. Researchers are suggesting and confirming that glycemic variability (GV) may be important health metric. Data show that GV is factor in the pathogenesis of diabetes neuropathy^{xxix}, and retinal damage^{xxx} in people with T1D. GV may be an independent risk factor for cardiovascular disease even in people *without* diabetes^{xxxi}. We worry that CADTH methodology may not give sufficient weight to this emerging predictor of diabetes complications.

Although current research may not unequivocally demonstrate the importance of reducing GV, the patient experience is clear: reduced glucose variability leads to greater predictability, reduced hypoglycemia, increased feelings of safety and an increased ability to manage glucose levels.

Sugar intake. The World Health Organization has issued a recommendation to reduce free sugars (monosaccharides (glucose, fructose) and disaccharides (sucrose or table sugar)) to less than 5% of daily calories when possible. An adult eating a 1700 calorie diet, should, therefore, try to limit their sugar intake to less than 85 calories, or 21 grams of carbs. When a person with T1D experiences hypoglycemia, the medically prescribed response is follow the “rule of 15”:^{xxxii} eat 15 grams of carbs of fast-acting sugar, wait 15 minutes, and re-test their blood glucose level. If the blood glucose level is still low, they repeat the action as needed: another 15 grams, another 15 minutes, and test again. Not only does hypoglycemia increase the number of strips people with T1D use, but it can also make it impossible to meet the WHO recommendation, even when avoiding 100% of free sugars throughout the day. We request that CADTH model the dimension of excess free sugar consumption and its deleterious effects on health in its analysis.

CADTH, you have recommended against coverage of every new basal insulin you have ever reviewed. You continue to recommend NPH, a basal insulin that waxes and wanes throughout the night and has significant intra-individual absorption variability^{xxxiii}, despite a goal of diabetes care being stable and predictable blood glucose. In the 1990s, the diabetes community referred to NPH as the “devil’s insulin” due to its unpredictable and untrustworthy nature. (Google

["devil's insulin"]: while many pre-web USENET newsgroup posts and early webpages from the 1990s and early 2000s no longer exist, you'll still find it referenced today.)

To put it *extraordinarily mildly*, we don't understand how you could repeatedly recommend that coverage of Lantus and Levemir be denied. As a community, we question your... well, everything. It's time to chart a new course in treatments for T1D.

As an article^{xxiii} in the British Medical Journal humourously pointed out, there are no randomized clinical trials of "parachute intervention" for people falling out of planes. It objectively reviews that not everyone who uses a parachute lives, and that not everyone who jumps without a parachute dies. Is CADTH willing to jump without a parachute until there is an adequate body of double blind, randomized, multi-national, placebo-controlled, crossover trials and sufficient analysis on parachute efficacy and economics?

The terror you would experience jumping out of an airplane possibly strapped to a "placebo parachute" is entirely similar to the fear a person with T1D experiences. Our data found that 13.7% of us go to bed, every night, fearing we may be unable to wake up when our alarms go off at 2:30 AM to check blood glucose levels. Every. Single. Night. If our finding holds for the entire T1D community, tens of thousands (and possibly over hundred thousand) Canadians fall asleep every night wondering if it will be the last time they (or their loved one) do so.

CADTH, people with Type 1 Diabetes need barrier-free access to medications and technologies that enable us to manage diabetes well over a lifetime. This includes knocking down the barrier of making people fail on NPH before they can access more reasonable, predictable and understandable options. We are doing poorly as a population, and things need to change.

CADTH, until you facilitate access to better quality medications and technologies, you are complicit in our declines.

Conclusion. On a population basis, our A1cs are typically not meeting target. Nearly half of us experience high levels of diabetes distress that interferes with diabetes outcomes, and majority of us have diabetes complications. People with T1D need predictable and reliable tools to manage their diabetes in a way that is emotionally and behaviourally sustainable over a lifetime. We need safer drugs and technologies to attenuate the high levels of emotional distress that interfere with diabetes outcomes.

Appendix 1: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

Type 1 Together requested clarification from Novo Nordisk, the drug manufacturer, regarding the CADTH application initially only being indicated for people living with T2D. As insulin degludec is presently unavailable in Canada, we also asked questions about its expected characteristics, and whether or not it would be indicated for use in children.

Novo Nordisk was exceptionally clear that they would not discuss or influence the contents of this document. No version of this document has been shared or discussed with Novo Nordisk.

We reached out to Dr. Michael Vallis, DAWN2 Lead Investigator for Canada, who provided us with copies his published papers.

Because insulin degludec is not currently available in Canada, we reviewed forum posts on TuDiabetes, a popular online diabetes forum, for additional feedback.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

Type 1 Together wrote the survey. We also wrote, coded, and hosted a webpage on our site to collect the survey data. We analyzed the data ourselves, using R.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

We have never received funding from any company or organization. To date, all costs have been paid by our leadership team.

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Jen Alexander

Position: Founder

Patient Group: Type 1 Together

Date: July 19, 2017

ⁱ **Diabetes Attitudes, Wishes and Needs Second Study (DAWN2): Understanding Diabetes-Related Psychosocial Outcomes for Canadians with Diabetes.** <https://www.ncbi.nlm.nih.gov/pubmed/26948024>

ⁱⁱ **Psychosocial and Management Experiences of Canadian Family Members Living with People with Diabetes: The Second Diabetes Attitudes, Wishes and Needs Study** <http://aperito.org/uploads/pdf/DRTOA-2-125.pdf>

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- iii **Change in hemoglobin A1c one year following the 2014 American Diabetes Association guideline update.**
<https://www.ncbi.nlm.nih.gov/pubmed/28528078>
- iv **Hemoglobin A1c and Self-Monitored Average Glucose: Validation of the Dynamical Tracking eA1c Algorithm in Type 1 Diabetes.**
<https://www.ncbi.nlm.nih.gov/pubmed/26553023>
- v **Diabetes Attitudes, Wishes and Needs Second Study (DAWN2): Understanding Diabetes-Related Psychosocial Outcomes for Canadians with Diabetes.** <https://www.ncbi.nlm.nih.gov/pubmed/26948024>
- vi **Ibid**
- vii **Ibid**
- viii **Ibid**
- ix **Nocturnal hypoglycaemia in Type 1 diabetic patients, assessed with continuous glucose monitoring: frequency, duration and associations.** <https://www.ncbi.nlm.nih.gov/pubmed/17381503>
- x **Causes of death in childhood-onset Type 1 diabetes: long-term follow-up.** <https://www.ncbi.nlm.nih.gov/pubmed/26996105>
- xi **The Canadian Hypoglycemia Assessment Tool Program: Insights Into Rates and Implications of Hypoglycemia From an Observational Study.** <https://www.ncbi.nlm.nih.gov/pubmed/28528246>
- xii **Delayed recovery of cognitive function following hypoglycemia in adults with type 1 diabetes: effect of impaired awareness of hypoglycemia.** <https://www.ncbi.nlm.nih.gov/pubmed/18039813>
- xiii **When the Going Gets Rough** (transcribed from an audio recording of a talk given at the 2003 Canadian Diabetes Association Professional Conference.)
- xiv **The Canadian Hypoglycemia Assessment Tool Program: Insights Into Rates and Implications of Hypoglycemia From an Observational Study.** <https://www.ncbi.nlm.nih.gov/pubmed/28528246>
- xv **Exciting news since switching to Tresiba.** <http://www.tudiabetes.org/forum/t/exciting-news-since-switching-to-tresiba/54986/11>
- xvi **Switching from Lantus to Tresiba or Toujeo.** <http://www.tudiabetes.org/forum/t/switching-from-lantus-to-tresiba-or-toujeo/60673/4>
- xvii **Who's Tried Tresiba?** <http://www.tudiabetes.org/forum/t/whos-tried-tresiba/55665/13>
- xviii **Going Beyond A1c – One Outcome Can't Do It All.** <https://diatribe.org/BeyondA1c>
- xix **Association between glycemic variability and peripheral nerve dysfunction in type 1 diabetes.**
<https://www.ncbi.nlm.nih.gov/pubmed/27465125>
- xx **Retinal neurodegeneration in patients with type 1 diabetes mellitus: the role of glycemic variability.**
<https://www.ncbi.nlm.nih.gov/pubmed/28238189>
- xxi **Is nondiabetic hyperglycemia a risk factor for cardiovascular disease? A meta-analysis of prospective studies.**
<https://www.ncbi.nlm.nih.gov/pubmed/15505129>
- xxii **Variability of insulin absorption and insulin action** <https://www.ncbi.nlm.nih.gov/pubmed/12450450>
- xxiii **Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials.**
<https://www.ncbi.nlm.nih.gov/pubmed/14684649>