

**Remission of Type 2 Diabetes: A Mixed-Method Analysis of Lived Experience Perspectives
on Barriers and Facilitators**

By

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Abstract

Type 2 Diabetes (T2D) affects approximately 3.8 million Canadians and is a leading cause of many health complications. T2D remission refers to an HbA1c level <6.5% without glucose-lowering medications for at least three months. Evidence suggests a >15 kg weight reduction through lifestyle changes and/or bariatric surgery is associated with the greatest likelihood of remission. Although remission rates vary by intervention and individual factors, clinical trials reported estimated remission rates ranging from 30% to 60% of participants. However, few studies explored the lived experiences of those who achieve remission, and the barriers they might experience.

To address this gap, a two-phase explanatory sequential mixed methods study was conducted to explore barriers and facilitators of achieving and sustaining remission through lifestyle interventions. Quantitative data from 21 adult (57 ± 8 years; T2D duration: 4 ± 3 years) with lived experiences of T2D remission were collected to assess clinical outcomes; including health surveys, HbA1c, continuous glucose monitoring (CGM) metrics, and dietary records. From this cohort, a purposive sub-sample of 7 participants took part in a one-on-one semi-structured interviews. An inductive thematic analysis of interview data identified key factors influencing the remission process. Findings were integrated using joint display methodology to explore points of convergence and divergence between clinical indicators and lived experiences.

Analysis revealed that adapting lifestyle behaviors with ongoing self-monitoring and tailoring strategies to individual needs were central to sustaining remission. Quantitative results showed strong glycemic outcomes (mean glucose: 5.0 mmol/L; >92.2% time in range), regular physical activity (Godin Leisure-Time Exercise score ≥ 24), and good perceived health. These aligned with seven overarching qualitative themes: 1. “flexibility as freedom”, 2. self-reliance, 3. accountability, 4. “one size doesn’t fit all”, 5. “healthcare, not medical care”, 6. barriers inside and out and 7. “I’d rather be healthy”.

Participants reported enhanced physical and mental well-being, crediting self-motivation, accountability, and self-directed education. However, they also reported barriers, including limited healthcare and individualized support, social stigma and mental health challenges, highlighting divergence in mixed findings.

This research contributes to a growing body of evidence supporting lifestyle-based T2D remission and centering lived experience as essential for rethinking and improving T2D care.

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Dedication

I dedicate this thesis to my husband, Fahad
who was willing to leave everything behind for my dream &
To my Ma, who taught me how to dream.

Table of Contents

Abstract.....	2
Acknowledgement	3
Dedication	4
Table of Contents	5
List of Tables	8
List of Figures.....	9
List of Copyright Materials.....	10
List of Abbreviations	11
Chapter I.....	13
1.1. Introduction.....	13
1.2. Comparative Literature Review	19
1.3. Research Gaps and Rationale.....	31
1.4. Research Questions and Objectives	32
1.5. References	33
Bridge to Chapter II	41
Chapter II	42
2.1. Abstract.....	44
2.2. Introduction.....	45
2.3. Methods.....	46
Study design.....	46
Study participants.....	47
Health screening questionnaire and remission survey	47
Sleep quality	47
Physical activity.....	48
Health-related quality-of-life	48
Perceived stress	48
Dietary habits and macronutrient intake	48
Three-factor eating questionnaire	49

Continuous glucose monitoring	49
Statistical analysis	49
2.4. Results	50
Participants characteristics	50
Health-related quality of life	51
Sleep quality	52
Perceive stress.....	52
Remission	52
Dietary pattern and macronutrient intake	54
Eating habits.....	54
Food counseling and challenges in healthy eating	54
Behavioural domains of eating	54
Three-day food record.....	54
Glucose regulation and profiles	55
Relationships between glucose profiles and dietary parameters	58
2.5. Discussion.....	59
Descriptive characteristics of individuals achieving T2D remission	59
Perceived factors influencing remission.....	59
Dietary pattern and macronutrient intake	60
Glycemic control	60
2.6. Strengths and limitations	61
2.7. Conclusion	62
2.8. References	63
Bridge to Chapter III.....	68
Chapter III.....	69
3.1. Abstract.....	70
3.2. Introduction.....	71
3.2.1. Study Aim and Mixed Methods Approach.....	72
3.2.2. Quantitative Strand	73
3.2.3. Qualitative Strand.....	73
3.3 Methods.....	75
3.3.1. Mixed Methods Design and Procedures (QUAN → qual)	75
3.3.2. Phase 1 (Quantitative Design and Procedures)	75
QUAN Study Design	75

QUAN Study Participants	75
QUAN Data Collection Procedures	76
Measures	76
Statistical Analyses	77
3.3.3. Phase 2 (Qualitative Design and Procedures)	77
Qual Research Design	77
Case Selection	77
Data Collection Procedures	77
Thematic Analysis	78
Trustworthiness	78
Positionality	79
3.3.4. Integration of QUAN Results and qual Findings	79
3.3.5. Ethical Considerations	80
3.4. Results	81
3.4.1. QUAN Results	81
3.4.2. Qual Findings	82
Qual Study Participants	82
Thematic analysis	82
Theme 1: “One size doesn’t fit all”	87
Theme 2: “Healthcare not medical care”	88
Theme 3: “Barriers inside and out”	89
Theme 4: “Flexibility as freedom”	90
Theme 6: “Self-reliance”	92
Theme 7: “I’d rather be healthy”	93
3.4.3. Mixed Methods Findings	94
Integration	94
Meta-interference findings	95
3.5. Discussion	100
3.5.1. Key take aways from meta-inference	102
3.5.2. Strengths and Limitations	104
3.6. Conclusions	104
3.7. References	105
Chapter IV	109
4.1. Study Summary and Relevance to Practice	109
4.2. Future Directions	110
4.3. Final conclusions	110
4.4. References	111
Appendixes	113

List of Tables

Table 1.1. Diagnosis of T2D.....	13
Table 1.2. Comparative overview of key studies investigating approaches to Achieving T2D Remission.....	20
Table 2.1. Participants' baseline characteristics	51
Table 2.2. Macronutrient and total calorie intake	55
Table 2.3. Continuous glucose monitoring outcomes.....	56
Table 3.2. QUAN data collection tools and outcome measures	76
Table 3.3. Overreaching themes and their categories identified from thematic analysis	82
Table 3.4. Joint display of integrated findings.....	95

List of Figures

Figure 2.1. Health-related quality of life (EQ-5D-5L)	52
Figure 2.2. Ranking of contribution factors to achieve remission	53
Figure 2.3. Individual continuous glucose curves separated by diet type	57
Figure 2.4. Correlation between 24 h glucose concentration, A1c, and carbohydrate intake ...	58
Figure 3.1. Visual model of sequential explanatory mixed methods study design (QUAN → qual)	74

List of Copyright Materials

Chapter II. Copyright License	43
Appendix 8. Term of Use (EQ-5D-5L).....	128

List of Abbreviations

ADA- American Diabetes Association
BC - British Columbia,
BPD- Biliopancreatic Diversion
BMI- Body Mass Index
CGM - Continuous Glucose Monitor
CHO- Carbohydrate
CMNT- Chinese Medical Nutrition Therapy
DSE – Diabetes Support Education
DiRECT- Diabetes Remission Clinical Trial
DIADEM-I - Diabetes Intervention Accentuating Diet and Enhancing Metabolism – Intervention
FR- Food Reintroduction
GLP-1- Glucagon-Like Peptide-1
GP- General practitioner
HbA1c - Hemoglobin A1c or glycated hemoglobin
HIIT- High Intensity Interval Training
IIT - Intention to Treat
ILI- Intensive Lifestyle Intervention
LAGB - Laparoscopic Adjustable Gastric Banding
LCD- Low carbohydrate diet
LFD- Low Fat Diet
LCMD- Low Calorie Mediterranean Diet
MB – Manitoba
MBS- Metabolic/Bariatric Surgery
MI- Metabolic Intervention
OR- Odd Ratio
PCP- Primary Care Physician
PGD- Post Graduate Degree
Pharma-TCR - Pharmacist-led, Therapeutic Carbohydrate-Restricted
QUAN – Quantitative
qual- Qualitative
RCT - Randomized Control Trial
REDCap - Research Electronic Data Capture
RYGB - Roux-en-Y Gastric Bypass
RBP4- Retinol-Binding Protein 4
RR- Relative Risk
SGLT 2- sodium-glucose co-trans-porter 2
SDT- Self Determination Theory
T2D - Type 2 Diabetes

TIR- Time In Range

TAU - Treatment As Usual

TDR- Total Diet Replacement

UM- University of Manitoba

U-TURN - Does Intensive Lifestyle Intervention Reduce the Need for Glucose Lowering Medications in Patients With Type 2 Diabetes? The U-TURN Project

UBC - University of British Columbia

VLCD- Very Low Carbohydrate Diet

Chapter I

Overall introduction

1.1. Introduction

The burden of type 2 diabetes (T2D) has grown significantly in recent years and is one of the most prevalent chronic diseases in adults worldwide. T2D affects over 6% of the world's population, with higher rates in older adults and in certain ethnic groups. This condition can be defined as elevated blood glucose concentrations caused by a combination of insulin resistance and insufficient insulin production of pancreatic beta cells (1,2). Insulin resistance refers to a condition in which an individual's body does not respond well to insulin and cannot properly utilize blood glucose (3). According to Diabetes Canada, T2D can be diagnosed by any of the following criteria (4) listed in Table 1.1.

Table 1.1. Diagnosis of T2D

Fasting Plasma Glucose	≥ 7.0 mmol/L indicates T2D
Random Plasma Glucose	≥ 11.1 mmol/L indicates T2D
HbA1c test	≥ 6.5% indicates T2D
2hPG (2-hour plasma glucose) in a 75 g Oral Glucose Tolerance Test	≥ 11.1 mmol/L indicates T2D

This complex metabolic disorder is caused by a complex interplay of genetic susceptibility, environmental and lifestyle factors. Genetic factors primarily influence beta-cell function and insulin action, while lifestyle factors can exacerbate insulin resistance and affect glucose regulation systems. The global rise of obesity, central adiposity and a lack of physical activity are also a major contributors in the T2D epidemic (5). However, influence of lifestyle factors can be prevented with appropriate healthy dietary patterns, regular exercise, medication, and regular monitoring (6). Most research shows that the fat in the abdomen and around the organs, known as visceral fat, is most strongly associated with insulin resistance. Visceral fat produce adipokines hormones such as leptin and adiponectin. These hormones are key regulators of metabolism and insulin sensitivity. In a condition like obesity, excessive visceral fat leads to reduced production of adiponectin and increased secretion of pro-inflammatory adipokines (e.g., resistin and retinol-binding protein 4 (RBP4) which disrupts the metabolic homeostasis and promotes insulin resistance (7). This imbalance disrupts insulin signaling and promotes chronic inflammation which have effects on metabolism and insulin sensitivity that can lead to chronic diseases like T2D (3,8,9). A meta-analysis on the effects of weight loss in individuals with obesity indicated that 60-90% of T2D occurs due to excess body weight and reducing 10% of body weight leads to improved glycemic control and other comorbid risks (10).

Conventional Treatment Options

The conventional therapy of T2D includes lifestyle modification, pharmacological intervention and routine monitoring which typically follows a structured timeline and is guided by specific HbA1C levels (11). This approach focuses on managing the blood glucose concentrations to reduce the risk of associated complications. The first line treatment involves dietary changes, increased physical activity and weight management to improve insulin sensitivity (11). When lifestyle modification alone is not sufficient, oral antihyperglycemic drugs such as metformin, sulfonylureas, thiazolidinediones, glinides, glucose-dependent insulintropic polypeptide (GIP)/glucagon-like peptide-1 (GLP-1) agonists, sodium-glucose cotransporter 2 (SGLT-2) inhibitors are introduced to meet individuals HbA1c targets (11). Insulin therapy may be required for symptomatic or metabolically-decompensated hyperglycemia or if glycemic targets are not being met (12,13). Although, these pharmacotherapies are an effective choice for many individuals with favorable outcomes in glycemic control, weight management (14), reduced cardiovascular mortality, and slower progression of chronic kidney disease (15) they may not always directly aim to address the underlying metabolic issues and require many individuals to take medications lifelong.

Remission of Type 2 Diabetes

In recent years, there has been growing evidence that remission is possible for individuals with T2D (16-20). T2D remission is defined by Diabetes Canada as having an HbA1c level <6.5% without using any glucose lowering medications for at least three months (21). HbA1c levels measure the average blood glucose concentrations over the previous three months. An HbA1c level of < 6% indicates normal blood glucose, 6%–6.4% indicates pre-diabetes, and > 6.5% indicates T2D (13). The concept of remission challenges the belief that T2D is a chronic and progressive condition. According to the findings from recent clinical studies, a sustained weight loss of approximately 15 kg or more is often associated with remission of T2D. This level of weight loss can lead to remission in about 80% of individuals with obesity and T2D (16–19,22). The ability to achieve remission can vary based on factors such as the duration of T2D, baseline beta-cell function, and an individual fat threshold, which suggest that even individuals with a normal body mass index (BMI) can achieve remission with significant weight loss (23,24). A "fat threshold" refers to the concept that each individual has a personal limit for how much fat their body can safely store before metabolic complication arises. In 2024, Taylor et al (25) tested this hypothesis of individual fat thresholds and found that exceeding the personal fat threshold causes fat to build up in the liver and pancreas which may leads to T2D. The findings also suggest that reducing fat below this threshold can restore normal organ function and potentially lead to T2D remission. Weight loss can be achieved through different approaches like dietary modification, increased exercise, a combination of both dietary modification and exercise, or through metabolic/bariatric surgery (MBS). Regardless of the approach used to achieved remission, sustained weight loss seems to be crucial for maintaining T2D remission (17,26,27).

Metabolic Bariatric Surgery and T2D Remission

MBS has been shown to be a highly effective treatment for achieving remission of T2D, often more significant than conventional medical and lifestyle interventions (28-30). The Alliance of Randomized Trials of Medicine versus Metabolic Surgery in Type 2 Diabetes (ARMMS-T2D) study by Kirwan. J et al (31) showed that the remission was achieved in 37.5% (60/160) in individuals who received surgery versus 2.6% (2/76) in those receiving medical/lifestyle therapy over three years ($p < 0.001$). The participants in the surgical group were younger on average than the medical/lifestyle therapy group while both groups had a similar duration of T2D (9 ± 6 vs. 9 ± 6 years). These factors may have influenced the remission outcome of the trials, as younger individuals often have better remaining β -cell function, which can improve the chances of T2D remission (31).

Ten years follow-up data from a randomized clinical trial compared metabolic surgery to conventional medical therapy in individuals with T2D. In the surgery group, 37.5% (15/40) maintained remission after 10 years, while no participants in the medical therapy group (0/15) achieved or sustained remission (32). Specifically, 50% of patients (10/20) who underwent biliopancreatic diversion (BPD) and 25% of patients (5 out of 20) who had Roux-en-Y gastric bypass (RYGB) remained in remission. However, there was no difference between the two surgical procedures ($p=0.19$). In the broader intention-to-treat (IIT) analysis, the remission rates were 5.5% for those on medical therapy, 50% for BPD surgery and 25% for RYGB surgery. The relative risk (RR) of achieving remission compared to medical therapy was 9 times higher for BPD (95% CI: 1.3–63.5) and 4.5 times higher for RYGB (95% CI: 0.58–35.0). Overall, BPD and RYGB were more effective ($p = 0.002$) than medical therapy in achieving long-term remission, with BPD showing the highest success rate (32). A meta-analysis of 16 studies, including 5 randomized controlled trials (RCTs), found that bariatric surgery enhances the likelihood of remission by a substantial margin, with odds ratios ranging from 9.8 (95% CI: 6.1 to 15.9) to 15.8 (95% CI: 7.9 to 31.4) when compared to conventional medical therapy (33).

MBS is mostly recommended only to non-pregnant adults with a BMI $\geq 35 \text{ kg/m}^2$ or higher due to the limited evidence on remission rates and long-term effect of bariatric surgery on T2D individuals with non-severe obesity (21). However, recent studies found that MBS has similar effects even in individuals with a BMI between 30 and 35 kg/m^2 (34,35). A meta-analysis by Jae Hyun Bae et al. demonstrated that MBS is similarly effective in individuals with both severe and less severe obesity, with similar remission rates observed across different BMI categories (BMI $< 35 \text{ kg/m}^2$ and BMI $\geq 35 \text{ kg/m}^2$). This study analyzed a total of 81 studies in which 23 focused on individuals with a BMI below 35 kg/m^2 and 58 on those with a BMI of 35 kg/m^2 or higher. After 12 months, T2D remission rates were 59% (95% CI: 0.49 to 0.70) for individuals with BMI $< 35 \text{ kg/m}^2$ and 61% (0.55 to 0.67) for those with BMI $\geq 35 \text{ kg/m}^2$, showing no difference between the two groups (36). Another meta-analysis (35) of seven RCTs in individuals with class I to III obesity (BMI 30- 35 kg/m^2) concluded that T2D remission is higher in MBS compared to medical therapy

after 36 months of follow up, regardless of the obesity class (RR = 6.65 [95 % CI: 2.24-19.79]; 5 trials, 404 patients). It is also important to mention that the quality of evidence assessed in this meta-analysis was limited and had a high risk of bias (35).

While MBS can be an effective treatment for inducing remission in T2D, it is often accompanied by significant concerns, including surgical risks, long term nutrient deficiencies and the potential for future malnutrition (37,38). A systematic review found that MBS may lead to deficiencies in iron, vitamin B12, folate and other micronutrients (39). A meta-analysis of 18 studies reported that in a sub-group analysis, MBS may increase the risk of alcoholic cirrhosis after surgery (40). It is also worth mentioning that many clinical trials did not align with the definition of T2D remission and are more focused on glycemic control rather than weight loss and reducing glucose-lowering medications (41). This procedure is still not widely accepted by, and accessible for, many individuals with T2D (42-25). A study on public delivery of MBS found that there is an unequal delivery of MBS within Ontario, with living farther distances from, or not having, a bariatric facility within the same health region having negative effects on delivery (46). Similar MBS programs are offered in Manitoba, but due to demand exceeding capacity wait times are long. In a survey (47) of primary care physician (PCP) referrals to bariatric surgery in Manitoba, 33.3% of respondents (1000 surveys administered, 131 responses, 13.1% response rate) indicated their biggest concern for care was the wait time. Wait times in Manitoba were more than 5 years but have now improved to 1 to 2 years (47–49). This suggests that MBS is not a feasible population wide strategy for T2D remission and should be reserved for individuals who are not able to achieve remission via lifestyle interventions.

Lifestyle Intervention and T2D Remission

Although MBS may lead to better remission outcomes, recent focus has shifted towards lifestyle interventions to achieve weight loss and remission from T2D. This is because the weight loss achieved through lifestyle interventions is comparatively safer, more cost effective, and less invasive than surgical options (50,51). Various lifestyle interventions have been shown to achieve remission of T2D (17,52). These interventions primarily focus on diet and physical activity, which have been shown to effectively control blood glucose concentrations and reduce weight, leading to improved quality of life for individuals with T2D (52). Various dietary approaches, such as low-energy diets, low carbohydrate diets, and the Mediterranean diet, have been effective in promoting T2D remission. Intensive dietary interventions, particularly those with very low energy intake, have shown higher remission rates compared to moderate caloric restrictions (17,52-54). The remission rate is comparable to those of MBS but with fewer side effects (53). However, remission achieved through lifestyle intervention is likely less durable over the long term compared to surgical outcomes. Intensive interventions have shown remission rates as high as 46% (17,27). Exercise is another important component of lifestyle intervention in achieving remission. Regular exercise improves insulin sensitivity, promotes weight loss, and lowers postprandial glycemia in individuals with T2D (55-57). A meta-analysis of studies examining the effectiveness of lifestyle

interventions for T2D remission found that a combination of both dietary approach and exercises like high intensity interval training (HIIT), walking, aerobic and resistance training are potentially more effective in achieving T2D remission (52).

One of the most widely cited cluster randomized trials focused on T2D remission, the Diabetes Remission Clinical Trial (DiRECT) (17,19) used an intervention called the Counterweight-Plus weight management program which uses an intensive low energy diet. This program included total dietary replacement (TDR) of 825-853 kcal/day for 3 months followed by food reintroduction phase of 2-8 weeks and a maintenance phase supported with structured monthly visits. This study included a total of 306 participants. The remission rate in the intervention group was notably higher compared to the control group. At 12 months, the remission rate was 46% (68 of 149) in the intervention group compared to 4% (6 out of 149) in the control (OR 19.7, 95% CI: 7.8–49.8; $p < 0.0001$). At 24 months, over 30% of participants sustained remission. After 2 years, the remission rate was 36% (53 of 149) in the intervention group compared to 3% (5 out of 149) in the control (aOR 25.82, 8.25 to 80.84; $p < 0.0001$). Weight loss of 15 kg or more was recorded in 36 (24%) of participants in the intervention group at 12 months and at 24 months, 64% and 70% remission was achieved in participants who lost >10 kg and >15 kg, respectively.

After 2 years, the DiRECT study invited 101 participants to continue receiving support for three more years. Out of those, 95 participants agreed and were placed in the extension group while 54 participants stopped receiving the intervention. After 5 years of continued support, the extension group had higher remission rate than the non-extension group (34% vs 12%, $p < 0.0001$). On the other hand, the intervention group (including those who stopped at 2 years) had better outcomes than the control group with remission rates 27% vs. 4% respectively ($p < 0.0001$) (16). Overall, the findings from the DiRECT study shows that continued support has better long-term outcomes in sustaining remission.

Another clinical trial on intermittent fasting using Chinese medical nutrition therapy by Yang et al (58) with a total of 72 participants found that the remission rate in the intervention group was notably higher compared to the control group following standard dietary guidelines. The intervention group was following intermittent fasting using Chinese Medical Nutrition Therapy (CMNT). After 3 months of follow-up, 47.2% (17/36) of individuals achieved remission in the CMNT group, whereas only 2.8% (1/36) achieved remission in the control group (odds ratio [OR] 31.32; 95% CI: 2.39-121.07; $p < 0.0001$). At the 12-month follow-up, almost half of the participants (16/36) returned to a nondiabetic state and were in remission. About 65% (11/17) of participants in the CMNT group who achieved remission had a duration of disease longer than 6 years. This highlights the potential of intermittent fasting combined with dietary guidelines in achieving T2D remission.

The Look AHEAD study (59), conducted at 16 clinical centres across the United States, included 4,503 participants. It implemented an intensive lifestyle intervention (ILI) that aimed to reduce total calorie intake to 1200-1800 kcal per day by lowering total and saturated fat. This study focused on calorie intake reduction and increased physical activity. The goal for physical activity was to gradually increase from 50 min/week to 175 min/week by six months. Type of exercise included walking or similar exercises and strength training. Lifestyle intervention participants achieved partial or complete remission of 11.5% at 1 year and 7% at 4 years. Rate of remission (15% to 21%) were higher in those with substantial weight loss or fitness change, shorter duration of T2D, lower HbA1c levels at baseline, and those not using insulin.

The Diabetes Intervention Accentuating Diet and Enhancing Metabolism-Intervention (DIADEM-I) trial (18) conducted in Qatar, randomized 158 participants equally between the intervention (78/158) and control groups (78/158). The intervention group underwent intensive lifestyle interventions which included TDR and personalized dietary and exercise plans (10000 steps/day with gradual addition to reach 150min/week). TDR (800-820kcal/day) was maintained for 12 weeks in the intervention arm. In the final IIT, 147 participants were included where 70 participants were in intervention group and 77 in the control. 61% of intervention participants achieved remission followed by significant weight loss of 15% at 12 months compared to 12 % of control participants with 1% of weight loss (OR 12.03 [95% CI: 5.17- 28.03], $p < 0.0001$).

In the two year follow up of Does Intensive Life Style Intervention Reduce the Need for Glucose Lowering Medications in Patients With Type 2 Diabetes? (U-TURN trial) (60) study conducted in Denmark, 87 participants were assessed with 59 in the intervention group (U-TURN) and 28 in the control group (standard care). This intervention incorporated individually tailored dietary plans and intense exercise regimens. The intervention was stopped at 12 months and was not provided during the follow up period. The dietary plan involved energy intake restriction during initial 4 months (5%-60% carbohydrate, 15%-20% protein, 20%-35% fat with <7% saturated fat) and then balanced energy intake till 8 months. The exercise regime included supervised resistance and aerobic exercise for 30 to 60 minutes, 5 or 6 days per week. Both groups received T2D management counselling. Remission was examined in a secondary analysis at 24 months where 23% of participants (14/59) in the intervention versus 7% (2/28) in the standard care group met the criteria for partial or complete T2D remission. This corresponds to an odds ratio (OR) of 4.4 (95% CI: 0.8–21.4), indicating higher odds of remission in the intervention group compared with standard care, although this difference was not statistically significant ($p = 0.08$). The author assumed that the five participants lost to follow up had experienced a relapse.

The above findings from different trials supports that lifestyle interventions offer a non-pharmacological approach that may lead to significant improvements in glucose profile and in achieving T2D remission. However, social support and self-monitoring are important facilitators of successful lifestyle interventions, and these factors are often underexplored in these studies

(61,62). Remission potentially reduces the need for T2D medications, leading to cost savings and decreased potential for side effects. Apart from the need for reduced antihyperglycemic medication, remission can potentially improve quality of life and decrease T2D related complications such as heart disease, kidney damage, nerve damage and vision problems (52,63). One study on participants' perceptions of the quality of life associated with T2D reported that people with T2D expressed a willingness to give up 12% of their remaining lives in exchange for a lifetime of health without T2D. In this study, 220 out of 292 participants with T2D were first asked how many years they expected to live and then how many of those years they would be willing to trade away in return for receiving a technology that would permanently rid them of their T2D (64).

1.2. Comparative Literature Review

To synthesize the findings discussed above, Table 1.2 provides a comparative overview of major studies investigating lifestyle-based approaches to T2D remission. Relevant studies were identified through targeted searches on PubMed, Google Scholar and UM Libraries using combinations of keywords such as “lifestyle intervention”, “type 2 diabetes”, “type 2 diabetes remission” “low carbohydrate diet” “very low carbohydrate diet”, “total diet replacement”, “ketogenic diet”, “diabetic diet”, “behavioural change”, “physical activity”, “training”, “resistant training”, “high intensity interval training”, “walking”, “postprandial glucose”, “bariatric surgery”, “gastric bypass”, “conventional treatment”, “medical treatment”, “HbA1c”, “glucose”, “time point”, “CGM” and “insulin”. The search was set limited between the year from 2010 to 2025, published in English and specifically focusing on studies conducted in adult (>18 years old) human subjects without geographical restrictions. Shown in Table 1.2, the summary is organized by year.

Table 1.2. Comparative overview of key studies investigating approaches to Achieving T2D Remission

First author, year, country	Study Design	Sample -Total (I/C)	Study group	Duration (I/F)	Outcomes	Key remission strategy
Punthakee et al., 2024; Canada (65)	Open-label RCT; Multi-centre	100 (50/50)	<u>Intervention group:</u> Metabolic Intervention (MI) involving a low-calorie formula diet, activity prescription, medication reduction. <u>Control group:</u> Usual care (UC) following Diabetes Canada guidelines including lifestyle advice and glucose-lowering medications as needed. Medications (e.g., metformin and fixed-ratio insulin degludec/liraglutide) were used selectively in the intervention group. Most were withdrawn, and metformin was the only one allowed as needed.	12 months	At 12 months, remission of T2D was achieved in 41% of the intervention group where 7% of the control group ($p < 0.001$). At 12 months, the average weight change was -8.2 kg in the intervention group while -1.8 kg in the control group ($p < 0.001$)	Lifestyle intervention (Intensive metabolic intervention with low-calorie diet, reduced medication, increased physical activity)
Durrer C. et al., 2021; Canada (66)	Pragmatic, community-based parallel-group RCT; Multi-centre	188 (98/90)	<u>Intervention group:</u> Pharmacist-led, therapeutic carbohydrate-restricted (Pharm-TCR group) followed the Ideal Protein low-carbohydrate, energy-restricted meal plan, targeting <50 g carbs,	12 weeks	35.7% of participants in the Pharm-TCR group discontinued all glucose-lowering medications, compared to 0% in the TAU	Lifestyle intervention (pharmacist-led, therapeutic

			~110–120 g protein, and ~850–1100 kcal/day, supplemented with whole foods. Weekly in-pharmacy visits included support from a lifestyle coach and pharmacist. <u>Control group:</u> TAU (Treatment As Usual) group received standard T2D care, routine pharmacist-led medication advice and printed materials based on the 2013 Diabetes Canada Clinical Practice Guidelines for diet and lifestyle.		group ($p < 0.0001$; 95% CI: 25.9% to 44.8%). 17.3% of Pharm-TCR participants achieved an HbA1c $<6.5\%$ without any glucose-lowering medications, indicating remission-level glycemic control ($p < 0.0001$; 95% CI: 9.7% to 24.7%). 4 adverse event were reported related to hypoglycemic events in the Pharm-TCR group.	carbohydrate-restricted)
M.E. Lean et al., 2024, 2019, 2018; Scotland, England (16,17,19)	Open label Cluster RCT; Multi-centre	306 (157/149)	<u>Intervention group</u> (Counterweight-Plus weight management programme)-received TDR for 3 months (825–853 kcal/day; 59% carbohydrate, 13% fat, 26% protein, 2% fibre) followed by FR phase of 2-8 weeks (about 50% carbohydrate, 35% total fat, and 15% protein) and a maintenance phase supported with structured monthly visits. Physical activities were usual at TDR phase and	(18 weeks/12months, 24 months, 5 years)	At 12 months, the remission rate was 46% (68 of 149 in intervention), and at 24 months, over 30% of participants sustained remission. At 12 months, weight loss of 15 kg or more were recorded in 36 (24%) of participants in the intervention group. At 24 months, 64% and 70% remission was achieved in participants who	Lifestyle intervention (TDR and Physical activates)

			<u>Control group</u>- Standard T2D care. All diabetic medications were stopped at the start of the intervention. After 2 years, 101 participants were invited for continued support for 3 more years. 95 participants agreed and were placed into the extension group.		lost >10 kg and >15 kg, respectfully. At 5 years, extension group had higher remission rate than the non-extension group (34% vs 12%, $p<0.0001$). T2D remission is possible in individuals with a longer disease duration (6 years).	
Yang et al., 2022; China (58)	Open label-parallel design RCT; Multi-centre	72(36/36)	<u>Intervention group</u> (Chinese Medical Nutrition Therapy (CMNT))- 6 cycle of 15 intervention days. Each cycle includes a diet with 5 modified fasting days (~840 kcal/day) with a habitual mealtime. Next 10 days include an ad libitum diet which followed Dietary Guidelines for Diabetes in China (2007 edition) <u>Control group</u>- followed Dietary Guidelines for Diabetes in China (2007 edition) for the entire period. Guideline includes ≥ 5 g fiber per serving with low glycemic index carbohydrates. approximately 50% to 65% of total energy intake from carbohydrates, 15% to 20% from	(3 months/1 year)	After 3 months of follow-up, 47.2% (17/36) of individuals achieved remission in the CMNT group, whereas only 2.8% (1/36) achieved remission in the control group. At 12 month follow-up, 44% (16/36) participants in CMNT group-maintained remission during the follow up when they were following ad libitum diet instead of CMNT diet. 65% (11/17) of participants who achieved remission in the intervention group had a duration of disease longer than 6 years.	Lifestyle intervention (Intermittent fasting with maintenance diet)

			protein, and approximately 20% to 30% from fat. The saturated fatty acid intake was not to exceed 7% of total calories. During the follow up, both groups consumed ad libitum diet. Both groups were supervised by trained nurses.			
Sattar et al., 2022, UK (67)	RCT as proof of concept with an expanded observational study	25 (13/12)	<u>Intervention group</u> (Counterweight-Plus weight management programme)- received TDR (an 825–853 kcal/day formula diet) for 3-5 months, followed by FR phase of 6-8 weeks and a maintenance phase supported with the care of their GP. <u>Control group</u>- Standard T2D care. All diabetic medications were stopped at the start of the TDR.	(4.5months-6.5months / n/a)	The remission rate in the intervention group was significantly higher compared to the control group, with 38%(5/13) remission in the intervention group and none in the control group (p=0.039) The body weight loss in the intervention group was significantly higher compared to the control group, with an average [mean(SD)] of -7.7 (7.2%) versus -1.2 (1.4%) (p=0.005).	Lifestyle intervention (TDR)
Dambha-Miller et al.,2020, England (68)	Prospective cohort	867 (452/415)	<u>Intervention group</u> (multifactorial treatment)- frequent consultations, 30-min annual review, three 10-min consultations with a general practitioner and nurse, provision of educational materials and	(1 year /1year, 5 years)	Modest weight loss (>10%) in 1 st or first 5 years of diagnosis is strongly associated with T2D remission. Remission was	Behavioural change with multifactorial treatment.

			guidelines, and practice-based academic detailing sessions, encouraging earlier use of medication to improve control of risk factors, with a local diabetologist and a general practitioner opinion leader who described treatment algorithms and targets. <u>Control group</u> (routine care)- were advised to follow current UK T2D management guideline.		achieved in 257 participants (30%) at 5-year follow-up.	
Unwin et al., 2020, Norwood, UK (69)	Quasi-experimental study	128 (n/a))	<u>Intervention group</u>- education on low carbohydrate diet and physiological response of glycemic response. Person centered consultation (once every 6 weeks) and lower CHO diet educational resources were provided to the participants who chose low carbohydrate diet. A log was kept for the participants to compare before and after treatment.	(23 months/ 6 years)	59 (46%) out of all participants achieved remission at 23 months duration. 93% of 71 individuals with prediabetes achieved normal HbA1c level. Improvement in serum triglycerides of about 30%.	Lifestyle intervention (Low carbohydrate diet) with person centered educational approach.

Taheri et al., 2020, Doha, Qatar (18)	Open-label, Parallel group RCT; Multi-site	147 (70/77)	<u>Intervention group</u> (Intensive lifestyle intervention group)- received a TDR for 12 weeks (800-820 kcal/day, 57% CHO, 26% protein, 14% fat, 3% fiber, ≥ 2 L water) and a weight-loss maintenance phase for 12 weeks followed by gradual food reintroduction combined with physical activity support (initially 10000 steps/day followed by advised unsupervised 150min/week activity). Participants managed their own energy restricted diet and lifestyle changes for 6 months. Participants were monitored by dietitians and personal trainer once every 2 weeks. <u>Control group</u> (Usual medical care)- received usual diabetes care. All diabetic medications were discontinued at the beginning.	(12 months/ 24 months)	60% of all participants achieved remission followed by significant weight loss at 12 months and 30% of participants achieved normal glycemic levels.	Lifestyle intervention (TDR and physical activity)
Ried-Larsen et al., 2015,2019, Denmark (60,70)	Assessor-blinded, Parallel group RCT; Dual centre	93 (62/31)	<u>Intervention Group</u> (U-TURN intervention)- participants were provided individually tailored dietary plan (5%-60% carbohydrate,15%-20% protein,	(12months / 24months)	This study found that a 12-month lifestyle intervention consisting of high exercise volume and dietary counselling can lead to	Lifestyle intervention (antidiabetic diet and intense

			and 20%-35% fat, with <7% saturated fat) with energy intake restriction during initial 4 months and then balanced energy intake till 8 month. Additionally, participants received supervised resistance and aerobic exercise for 30 to 60 minutes, on 5 or 6 days per week. <u>Control group</u> (standard care)- pharmaceutical therapy and lifestyle advice. Both groups received diabetes management counselling.		partial or complete T2D remission (23% in intervention group and 7% in standard care). Physical fitness increased in the intervention group, but there were no significant differences in indices of glycemic control, lipidemia, or body composition after 12 months. Remission was examined in a secondary analysis	physical activity)
Umphonsathien et al., 2019, Thailand (71)	Quasi-experimental study	19 (n/a)	<u>Intervention group</u>- intervention consists of 3 periods. 2 weeks (-2 to 0) of run in period (VLCD-600kcal/day), Calorie restriction period for 8 weeks (0 to 8) (participants who has 90% compliance to the VLCD diet during run in period were included) and 4 weeks (8 to 12) of transition period (participants received gradual higher calorie intake of 800 kcal/day on week 9, 1000 kcal/day on week 10, 1200 kcal/day on week 11, and 1,500 kcal/day on week 12)	(2 weeks, 8 weeks/ 12 weeks)	At 8 weeks, almost 79% (15/19) of participants received remission. At 12 weeks remission remain same. IIT analysis showed that remission was achieved in 75% at both 8 weeks and 12 weeks. HbA1c levels were decreased by 1.2% (13 mmol/mol), 2.3% (26 mmol/mol), and 2.2% (24	Lifestyle intervention (VLCD)

					mmol/mol) at weeks 4, 8, and 12, respectively.	
Dave et al., 2019, Mumbai, India (72)	Quasi-experimental study	45 (n/a)	<u>Intervention group</u> (lifestyle intervention)- participants were provided with dietary counselling (ADA 2011 guidelines), exercise counselling (minimum 45 minutes, 6 days a week), educational counselling. After 1 year, participants were in usual care, as per the clinic standard operating procedures.	(1 year/ 5 years)	At 1 year, 26.8% (n = 12) achieved weight loss $\geq 10\%$, 20% (n = 9) achieved 5–10% weight loss and 44.4% (n = 20) achieved $\leq 5\%$ weight loss. At 5 years, weight regain was reported but the regained weight was still lower from baseline. Mean HbA1c ($\pm$ SD) was 79 ± 4 mmol/mol ($9.4 \pm 2.5\%$) at baseline, 42 ± 1 mmol/mol ($6.0 \pm 0.5\%$) at year one and 48 ± 1 mmol/mol ($6.5 \pm 1.2\%$) at year five. At 1 year, 53.3% (24) and 17.8 % (8) participants achieved partial and complete remission, respectively. At 5 year, 26.8% (11) and 19.5% (8) participants achieved partial and complete remission, respectively.	Lifestyle intervention with multidimensional counselling.

Bhatt et al., 2017, India (73)	Quasi-experimental study	12 (n/a)	<u>Intervention group</u> (LCD meal replacement) – participants were provided with 1000 kcal/day diet using 3 servings (30g) of meal replacement protein formula ([Protototal Whey; containing 378.5 kcal, 48 g whey protein, 41 g of CHO, and 2.5 g of fat) with 150 ml of skimmed milk, one regular meal, 3 L of fluid/day and 2–3 small homemade snacks. This diet includes 60%, 30%, 10% energy from CHO, protein, and fat, respectively. All diabetic medication was stopped from day 1 (except in 2 participants) From 2nd week, participants were advised moderate intensity and resistance training.	(12 weeks/ 12 weeks)	At 12 weeks, 50% of participants with high baseline hyperglycemia (median HbA1c 9%) achieved HbA1c levels in the nondiabetic range (<6.5%) without the need for glucose lowering medications.	Lifestyle intervention (LCD and physical activity)
Esposito et al., 2009, 2014, Italy (74,75)	Single centre RCT	215 (108/107)	<u>Intervention group</u>: Low Calorie Mediterranean Diet (LCMD)- Rich in vegetables and whole grain, low in red meat replaced by poultry and fish. 50% energy from CHO and 30% energy from fat (main source of added fat 30-50g of olive oil).	(4 years/ 4 years, 8 years)	At year 1, the prevalence of remission in the LCMD group was 14.7% (95% CI 13.0–16.5%), whereas it was 4.1% (95% CI 3.1–5.0%) in the low-fat diet group. At year 6, the prevalence of remission in the LCMD	Lifestyle intervention (LCMD, Low-fat diet and physical activity)

			<u>Control group:</u> Low Fat Diet (LFD) - rich in whole grains and restricted additional fats, sweets, and high-fat snacks. <30% from fat and <10% from saturated fat. participants were given 1800 kcal/day for men and 1500 kcal/day for women in both groups. Participants were advised to exercise 175 min/ week (moderate intensity). Participants were consulted by nutritionist and dietitian monthly for a year and then bimonthly afterward. Patients were newly diagnosed without medication.		group was 5.0% (95% CI 4.4–5.6%), while it was 0% in the low-fat diet group. At year 4, the incidence of requiring hyperglycemic medication were lower in LCMD (44%) than LFD (77%)	
Gregg et al., 2012, USA (59)	Ancillary observational analysis of a 4-year RCT; Multi-centre	4503 (2241/2262)	<u>Intervention group:</u> Intensive Lifestyle Intervention (ILI)- participants were provided with weekly group or individual session for first 6 month and then 3 sessions/month for 2nd 6 month). Total calorie intake was reduced to 1200-1800 kcal/day by lowering total and saturated fat intake. The goal for physical activity were 175 min/week.	(1 years/ 1,4 years)	Lifestyle intervention participants achieved partial or complete remission of 11.5% at 1 year and 7% at 4 years which is 3-6 times than the participants in DSE group. Rate of remission (15% - 21%) were higher in those with substantial weight loss or fitness change, shorter duration of diabetes, lower	Lifestyle intervention with moderate physical activity.

			<u>Control group:</u> Diabetes Support Education (DSE) – 3 group session/ year focusing on multidimensional factor.		HbA1c levels at entry, and those not using insulin.	
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The data are presented in Mean (SD); I (Intervention), C (Control), F(follow-up), RCT (Randomized Control Trial), MI (Metabolic Intervention), TAU (Treatment As Usual), FR (Food Reintroduction), TDR (Total Dietary Replacement), CMNT (Chinese Medical Nutrition Therapy), CHO (carbohydrate), GP (General Practitioner), VLCD (Very Low Carbohydrate Diet), ADA (American Diabetes Association), LCD (Low Carbohydrate Diet), LCMD (Low Calorie Mediterranean Diet), LFD (Low Fat Diet), ILI (Intensive Lifestyle Intervention), DSE (Diabetes Support Education)

1.3. Research Gaps and Rationale

Findings from various lifestyle intervention bariatric surgery studies show there is a potential to achieve T2D remission. Yet, there are several notable research gaps that need to be addressed. In 2020, the Diabetes UK (76) published a research recommendation identifying the key research gap in T2D remission research. One of the key priorities for future research included identifying and understanding personalized treatment approaches based on individual variation including physiological and psychological and cultural needs. The recommendations also acknowledged the limited evidence on psychological impacts and the long-term sustainability of behaviour change following remission interventions.

Despite these emerging priorities, psycho-social factors such as emotional wellbeing, motivation, support and population specific insights into achieving T2D remission remain an under explored area (62). The role of psycho-social factors in achieving and maintaining remission through lifestyle interventions is very important because these factors are specifically crucial for sustained remission, where long term success equally depends on an individual's physiological and psychological wellbeing. Challenges such as stress, lack of support, and emotional difficulties can lead to relapse, even after initial success with lifestyle interventions (77). Most studies predominantly focus on physiological outcomes, often overlooking the impact of psychological and social support. In order to develop a person-centered targeted intervention and to improve remission rate and sustainability, the understanding of psychosocial challenges is crucial.

Additionally, there is limited understanding of how remission rates and predictors vary across different populations and countries as majority of the studies have been conducted in the United States, United Kingdom, and China. To our knowledge, there has been no mixed method study conducted on barriers and facilitators of T2D remission in Canadians. This indicates the need for more comprehensive studies in diverse cultural and geographical settings.

Furthermore, no study has reported continuous glucose monitoring (CGM) data to assess glycemic control and real time fluctuation of blood glucose concentrations among individuals who have achieved remission. CGM is a wearable device that continuously monitors interstitial glucose concentrations at frequent intervals, providing real-time data both day and night. Incorporating CGM data is important to have better understanding how lifestyle interventions influence glycemic patterns in individuals in remission from T2D.

Addressing these research gaps could significantly enhance the understanding and management of T2D remission. Consideration of psycho-social factors, population-specific studies, long-term durability assessments, and personalized treatment approaches are critical areas for future research that need to be addressed to enhance understanding and treatment strategies.

1.4. Research Questions and Objectives

The overarching aim of this study was to integrate quantitative data and qualitative findings to develop a meaningful understanding of effective strategies, as well as the barriers and facilitators experienced by individuals who achieved and maintained T2D remission through lifestyle intervention.

The secondary aim of the study was to examine the 24-hour glucose profiles of those people using continuous glucose monitors (CGM) to see if the different remission strategies associate with their glycemic control.

To address the research gap in the literature, this study explored the following research question:

1. What types of barriers and challenges do individuals who achieved T2D remission face during this process?
2. What dietary and physical activity strategies were commonly used to support remission?
3. How do these lifestyle strategies impact an individuals' glycemic outcomes?

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Bridge to Chapter II

The following chapter comprises a manuscript that provides a broad overview of the characteristics and quantitative lifestyle factors of T2D remission in lived experiences who achieved remission through lifestyle interventions. This chapter focuses on the clinical metrics such as blood glucose data, CGM metrics and health screening surveys. This chapter aimed to examine the CGM profiles and dietary patterns of lived experience of T2D. Tahmina Rahman contributed to investigation, data validation, and visualization. Alexis Marcotte-Chénard was the lead author of the manuscript and was responsible for formal analysis, investigation, validation, and visualization. Barbara Oliveira contributed to conceptualization, funding acquisition, and critical review. Paula Rocha supported investigation, data validation, visualization, and data curation. Sean McKelvey and Tom Elliott were involved in conceptualization, funding acquisition, project administration, validation, and visualization. Jonathan P. Little and Dylan MacKay served as the principal investigators and contributed to conceptualization, supervision, funding acquisition, project administration, validation, and visualization. All authors approved and contributed to the final manuscript.

Chapter II

Manuscript 1

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“Characterization of individuals achieving type 2 diabetes remission in real-world settings: Bridging clinical evidence and patient experiences”

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2.1. Abstract

The objectives of the study were to (1) describe characteristics and lifestyle factors of individuals who have achieved type 2 diabetes (T2D) remission (sub-diabetes glucose levels without glucose-lowering medications for ≥ 3 months) through changes to diet and exercise behaviour in real-world settings; (2) investigate continuous glucose monitoring (CGM) profiles of these individuals and explore how dietary pattern may influence glucose regulation metrics. This cross-sectional study recruited individuals living with T2D who achieved remission via changes to diet or exercise behaviours. Various questionnaires were used to assess overall health, and participants wore a blinded CGM for 14 days to assess glucose profiles and filled out 3-day food records. A total of 21 adults (57 ± 8 years of age) who were recently diagnosed with T2D (4 ± 3 years) with a A1c of $5.7 \pm 0.4\%$ volunteered to participate. Participants achieved remission through various means (e.g., combination of diet and exercise/ physical activity) and self-reported following different diets, including 52% following a low-carbohydrate or very low carbohydrate diet, 14% following a “ketovore/carnivore” diet, 10% using a meal replacement diet, 5% following Weight Watcher’s diet, and 19% no defined dietary pattern. The 24 h average CGM glucose value was 5.0 [4.8–5.6] mmol/L (median [IQR]) with 92 [85–97]% of time spent in range (between 4.0 and 9.9 mmol/L). The 24 h average CGM glucose ($r = 0.692$; $P = 0.001$) and A1c ($r = 0.470$; $P = 0.049$) were correlated with the daily percentage of energy intake from carbohydrate. Remission of T2D appears achievable through various means, including adoption of different dietary approaches and a more active lifestyle underpinning the importance of a patient-centred care.

2.2. Introduction

The prevalence of T2D continues to escalate around the globe, imposing a significant burden on healthcare systems (1). The emerging concept of T2D remission may provide new hope for individuals living with T2D to effectively manage their condition without the reliance on medication. The evidence supporting T2D remission has led to the publication of a Clinical Practice Guide- lines chapter on T2D remission by Diabetes Canada, which defines remission as having glycated hemoglobin (A1c) < 6.5% for three consecutive months without the use of antihyperglycemic medications (2). Although achieving remission is more likely in younger individuals with shorter duration of T2D (i.e., with residual beta cell function), this marks a pivotal shift in the management of T2D, away from the common conception is that this condition is “chronic and progressive” (3,4). The possibility of T2D remission developed from evidence following bariatric surgery (5,6). Indeed, several studies have documented that bariatric surgery (e.g., Roux-en-Y gastric bypass) can induce remission for a prolonged period (1–5 years) for 30%–63% of patients (7).

These promising results opened the possibility of achieving remission through other strategies. In 2018, Lean and colleagues published the primary results from the DiRECT (Diabetes Remission Clinical Trial) study, where 49 primary care practices across Scotland and England, comprising 306 participants living with T2D, were cluster randomized to usual care or a weight management program including a low-calorie meal replacement diet over 12–20 weeks with subsequent food reintroduction and support for long-term weight loss maintenance (8). After 1 year, 46% of the individuals in the weight management program achieved remission (A1c < 6.5% for 2 consecutive months) compared to 4% in the usual care group (8). Similarly, the DIADEM-I study directly randomized 147 participants into either a control group receiving usual care or an intensive lifestyle intervention group, also comprised of a low-calorie total diet replacement phase, food reintroduction, physical activity support, and a weight loss maintenance phase (9). Remission of T2D was observed in 61% of participants in the intensive lifestyle intervention group as opposed to only 12% in the control group after 12 months. Combined, the results from the DiRECT and DIADEM-I studies showcase that intensive low-calorie meal replacement interventions generating significant weight loss are efficacious to induce T2D remission.

Although the most robust evidence for T2D remission is via bariatric surgery and total dietary replacement, other nutritional strategies may also help individuals achieve remission. Athinarayanan and colleagues (2019) (10) have compared the efficacy of an individualized very low carbohydrate high-fat ketogenic diet compared to usual care (10) in an open-label non-randomized trial. Participants (n = 262) in the intervention group followed an individualized very low carbohydrate diet facilitated by web-based software telemedicine and online resources while 87 participants received usual care. After 2 years, 17.6% of the individuals in the very low carbohydrate diet group achieved remission compared to 2.4% in the usual care group (10).

Similarly, in a quasi-experimental single-arm study, Saslow et al. (11) demonstrated that out of 743 participants with $A1c \geq 6.5\%$ and who received a digitally delivered low-carbohydrate dietary program, 26.2% were able to reduce their A1c below the T2D threshold after 1 year while taking no glucose-lowering medications or just metformin (11). Results from the Look Ahead trial, a large multicentre RCT involving 4488 individuals, also showed that a multicomponent lifestyle intervention (i.e., reducing calorie intake, increasing physical activity level, and behavioural strategies) could induce remission, with $\sim 11\%$ of participants in remission after 1 year compared to only 2% in the control group (12). Four years later, the prevalence was still higher in the intervention group (7.2% vs. 2.1%) and this difference remained at 12 years (3.7% vs. 1.9%; (12)). Similarly, secondary analysis from the U-Turn trial showed that 23% of individuals performing ~ 300 min per week of supervised combined aerobic and resistance exercise training coupled with an individualized calorie-reduced dietary plan achieved remission compared to 7% in the usual care group after 24 months (13). While the quality of evidence may vary, these studies highlight the potential for achieving remission through various lifestyle strategies including low-calorie meal replacement, low-carbohydrate diets, and a multicomponent approach that integrates diet and exercise.

Despite the increasing evidence showcasing the potential for T2D remission, a notable gap remains between research settings and real-world patient experience. Indeed, based on our experience, partnerships with people with lived experience (<https://www.diabetesremission.ca/>) and testimonials available on social media, people living with T2D may be actively seeking remission through various means with varying levels of support from healthcare providers. In this context, we designed this study to better understand the various means through which individuals living with T2D are pursuing remission to bridge the gap between clinical practice and patients' realities. Therefore, the purpose of the study was to describe the characteristics (e.g., age, sex, etc.) and lifestyle behaviours (e.g., dietary patterns, physical activity levels, sleep, etc.) of individuals who have achieved T2D remission through changes to diet and exercise behaviour in real-world settings. The secondary aim was to investigate the continuous glucose monitoring (CGM) profiles of these individuals and explore how different dietary patterns may influence glucose regulation.

2.3. Methods

Study design

This cross-sectional study recruited individuals with physician-diagnosed T2D who had achieved remission ($A1c$ less than 6.5% and absence of glucose-lowering pharmacotherapy for at least 3 months) through lifestyle interventions in real-world settings. Eligible participants demonstrating interest in the study received a copy of the informed consent via email. Upon acceptance, participants completed an eligibility questionnaire followed by a Zoom call where the investigator explained the details of the study. Participants were then asked to provide recent A1c (within 1 month) to confirm remission status. Following this confirmation, participants filled out various

questionnaires (e.g., Pitts- burgh Sleep Quality Index, Godin–Shephard Leisure-Time, EQ-5D-5L, etc.) to capture factors that could influence (or be influenced by) remission. Participants then received via mail a CGM device (Freestyle Libre Pro) with instructions on how to install the device as well as a 3-day diet record to assess typical dietary intake. Once the 14-day CGM data collection and food record were completed, participants sent the sensor and the food log back to the laboratory in a prepaid envelope. The current project was approved by the University of British Columbia ethics committee and the University of Manitoba Bannatyne Campus Research Ethics Board and was carried out following the Declaration of Helsinki and the Tri-Council Policy Statement. This study has previously been registered on ClinicalTrials.gov as a cohort study (ID: NCT06177210).

Study participants

Participants were recruited across a 1-year period using posters, via healthcare professionals (e.g., private physicians, dietitians, and pharmacists), from lists of individuals who consented to be contacted from previous research, and online advertising. Participants had to be previously diagnosed with T2D and have achieved diabetes remission through lifestyle intervention. Exclusion criteria included (1) have not been diagnosed with T2D previously; (2) have an A1c level $\geq 6.5\%$; (3) are taking any glucose-lowering medications; (4) are ongoing medical treatment for diseases such as cancer, auto-immune or inflammatory disease, liver, or kidney disorders; (5) are unable to follow remote guidance by internet or smartphone; and (6) are unable to read or communicate in English.

Health screening questionnaire and remission survey

A health screening questionnaire was developed to encompass a variety of questions to characterize the participants such as age, sex, weight, height, education level, marital status, occupation, work hours, medical history, comorbidities, medications, weight change, etc. For more information (see appendix 1). A custom T2D Remission Survey gathered information about how individuals achieved remission, and any perceived barriers and facilitators. This survey included open-ended questions such as “How are you currently maintaining remission?” and multiple-choice questions such as “Which members of your health care team did you contact regarding remission?” completed via RedCap (Research Electronic Data Capture), a secure, web-based software platform designed to support data capture for research studies. The complete list of questions is available in (see appendix 2,3)

Sleep quality

Sleep quality and disturbances over the past 1 month were evaluated using the Pittsburgh Sleep Quality Index (PSQI; (14)). The score for the different components ranges from 0 (i.e., no difficulty) to 3 (i.e., severe difficulty), while the global score ranges from 0 to 21 (higher scores

indicate a worse sleep quality). A cut-off score of 8 was used in this present study to distinguish between individuals experiencing poor sleep quality (≥ 8) and those considered good sleepers (< 8), which have been previously shown to have high sensitivity and specificity (14).

Physical activity

Physical activity level was self-reported using the Godin– Shephard Leisure-Time Physical Activity questionnaire, which assesses time spent in physical activities of different intensities during a typical 7-day period (15). The total weekly leisure activity score is computed to arbitrary units which allow the classification in the subsequent categories: (1) ≥ 24 units = active; (2) 14–23 units = moderately active; (3) < 14 units = insufficiently active/sedentary.

Health-related quality-of-life

The EQ-5D-5L is a standardized health-related quality-of-life questionnaire that evaluates five key domains of health: (1) mobility, (2) self-care, (3) usual activities, (4) pain/discomfort, and (5) anxiety/depression (16). Each dimension is assessed independently, with scores ranging from 1 to 5, reflecting the severity of issues (1=no problem; 5=extreme problem). The EQ-5D-5L score can also be interpreted using an index score based on time-trade-off valuations developed for the Canadian population ($n = 1073$), with score ranging from -0.148 for the worst (5555) to the best 0.949 for the best (11111) health states (Xie et al. 2016). Additionally, the EQ-5D-5L also contains a visual analog scale where participants can rate their perceived health status ranging from 0 (“The worst health you can imagine”) to 100 (“The best health you can imagine”).

Perceived stress

The Perceived Stress Scale (PSS) is a classic stress assessment instrument with a total of 10 items (17). Each question has five possible answers (0 = Never; 1 = Almost never; 2 = Sometimes; 3 = Fairly often; 4 = Very often) and evaluates the degree to which an individual has perceived life as unpredictable, uncontrollable, and overloading over the previous month. After reversing the score for questions #4, #5, #7, and #8, the total score is calculated by summing all questions (scores ranging from 0 to 40, with the higher score representing higher perceived stress).

Dietary habits and macronutrient intake

Participants were asked to complete a 3-day dietary record representing their usual eating habits over 2 weekdays and 1 weekend day (18,19). Participants were provided clear instructions on how to fill the dietary record, accompanied by an example on the food log to assist them in accurately reporting their food intake. Estimated total energy (kcal), carbohydrate, lipid, protein, and fibre intakes were estimated by using ESHA software (ESHA Research, Salem, Oregon). Furthermore, several questions were also asked to better characterize dietary habits and related outcomes such

as: (1) “How many times do you eat per day?”; (2) “What are the usual times of meals?”; (3) “Who does the cooking?”; (4) “Who does the grocery shopping?”; (5) “How many times during the week do you eat away from home?”; (6) “Do you have a current meal plan? If so, what is it?”; (7) “What is your biggest challenge to eating healthy?”; (8) “Have you ever received diet counseling? If yes describe.”

Three-factor eating questionnaire

The three-factor eating questionnaire (TFEQ) was designed to identify three behavioural domains (i.e., factors) of eating: (1) “cognitive restraint of eating”; (2) “disinhibition”; and (3) “hunger” (20). The score for each domain was calculated with the automatic scoring tool (21). Higher scores indicate a greater tendency to consciously restrict food intake, a propensity to overeat in response to external cues and emotional states, and a higher frequency and intensity of hunger feelings, for these three domains respectively.

Continuous glucose monitoring

A blinded CGM device (Abbot FreeStyle Libre Pro) was inserted by the participants into the upper arm area and worn for a total of 14 days. The FreeStyle Libre Pro is factory calibrated and therefore does not require capillary blood glucose calibration. Following the current guidelines, we presented the total number of days of sensor data obtained, mean glucose values, time in range (i.e., 3.9–10.0 mmol/L), time in tight range (i.e., 3.9–7.8 mmol/L), time below range (i.e., <3.9 mmol/L), time in level 1 hypoglycemia (i.e., 3.0–3.9 mmol/L), time in level 2 hypoglycemia (i.e., <3.0 mmol/L), time above range (i.e., >10.0 mmol/L), time in level 1 hyperglycemia (i.e., 10.0–13.9 mmol/L), time in level 2 hyperglycemia (i.e., >13.9 mmol/L), and glycemic variability (SD and coefficient of variation of mean glucose) (22). Hypoglycemic events were defined as any period of 15 min or more spent below the 3.9 mmol/L threshold. Hyperglycemic events were defined similarly, using a threshold of 10 mmol/L. Prolonged hypoglycemic or hyperglycemic events were defined as those lasting longer than 120 min. Also based on these guidelines, we also presented the 24 h data as well as the daytime and nighttime categorized as follows (nocturnal: 00:00–05:59; diurnal: 06:00–23:59). Although guidelines suggest CGM data collection over 14 days, we included CGM data with fewer days due to technical problems (e.g., CGM recording interruptions or devices falling off) for some participants. Raw data were analyzed using the Diametric platform (University of Exeter; (23)). In addition to the estimated A1c provided by the sensor (eA1c), a standardized laboratory A1c was also obtained within 1 month via family physician requisition or as part of a recent routine check-up.

Statistical analysis

No formal sample size calculation was performed for this descriptive cohort study as our aim was to recruit across 1 year and describe persons with lived experience achieving remission in the real-

world and not to perform any statistical comparisons between potential subgroups (which we could not know would exist a priori). The normality of the data was evaluated through visual inspection of quartile histograms and Q-Q plots. Cronbach's alpha coefficient was utilized to evaluate the interval validity of the PSS questionnaire. The specified heuristic cutoffs were employed to assess the internal consistency among items of the PSS questionnaire, with α values categorized as follows: Excellent ($\alpha \geq 0.9$), Good ($0.9 > \alpha \geq 0.8$), Acceptable ($0.8 > \alpha \geq 0.7$), Questionable ($0.7 > \alpha \geq 0.6$), Poor ($0.6 > \alpha \geq 0.5$), and Unacceptable ($0.5 > \alpha$). Exploratory correlation analyses between glucose variables (e.g., CGM-derived metrics, A1c) and aspects of dietary patterns (e.g., percentage energy from carbohydrates) were conducted using Pearson correlation coefficients. All analyses were performed using SPSS 28.0 software (IBM SPSS Statistics, Armonk, NY, USA) and the significance level was set at $P \leq 0.05$. Data are presented as mean $\pm$ SD when normally distributed and as median [IQR] if non-normally distributed.

2.4. Results

Participants characteristics

Between January 2023 to January 2024, a total of 21 individuals (14 females) living with T2D who achieved remission were recruited via various means (e.g., pharmacist and physician referral, posters, online advertising, etc.) from British Columbia, Canada. On average, participants were 57 ± 8 years of age, diagnosed with T2D for 4 ± 3 years (range from 6 months to 13 years), with a BMI of 29.6 ± 6.5 kg/m² and an A1c of $5.7 \pm 0.4\%$ (Table 2.1). Participants achieved remission 1.5 ± 2.3 years after T2D diagnosis (range from 1 to 110 months) and were in remission for 2.3 ± 2.3 years (range from 1 to 108 months) when included in the present study.

A total of nine individuals (43%) had a first-degree relative living with T2D (i.e., parents or siblings), seven individuals (33%) had second-degree relatives with a history of T2D (i.e., grandparent, cousin, aunt, and uncle), and five individuals (24%) did not report any family history of T2D. Half of the participants were employed full-time (48%) working 40 [40–50] h a week, while 14% were working part-time and 33% were retired. In terms of the highest level of education attained, among the surveyed individuals, seven (33%) pursued university education, four (19%) obtained post-graduate degrees, seven attended college (33%), and three (14%) completed high school. None of the participants included were smokers, while 43% were past smokers. The median weekly leisure-time activity score showed that the vast majority of the participants (76%) were considered active (score ≥ 24 ; Table 2.1). When participants were asked how often they see their family doctor, 10.5% responded once a month, 26% responded every 3 months, 53% responded twice a year, and 10.5% responded less than once a year.

Table 2.1. Participants baseline characteristics

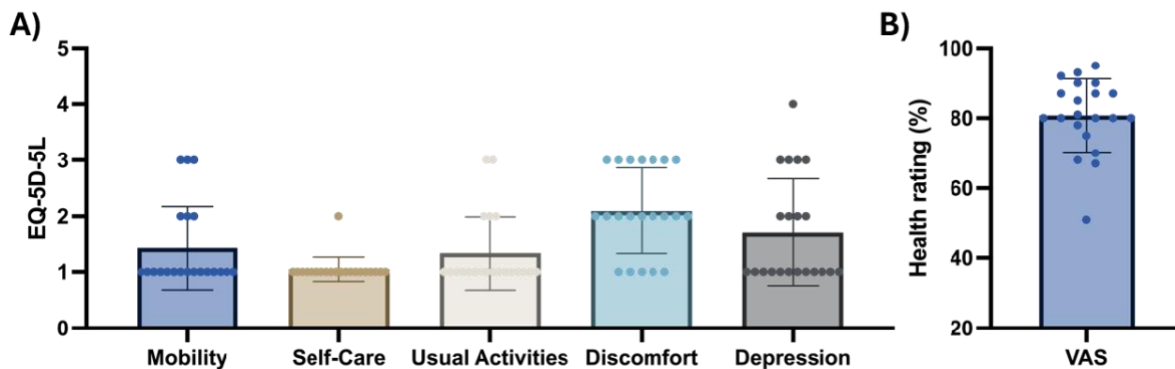
	Total sample (n = 21)
Biological sex (male/female (n))	7/14
Age (years)	57 ± 8
Height (cm)	173 ± 10
Weight (kg)	87.6 ± 18.4
BMI (kg/m ²)	29.6 ± 6.5
Time since diagnosis (year)	4 ± 3
Remission duration (months)	27 ± 27
A1c (%)	5.7 ± 0.4
Occupation n(%)	
Full time	10/21 (48)
Part-time	3/21 (14)
Retired	7/21 (33)
On disability	1/21 (5)
Smoking status (n (%))	
Current	0/21 (0)
Past	9/21 (43)
Physical activity (GLTE score)	
Strenuous exercise	0 [0–23]
Moderate exercise	20 [5–35]
Mild exercise	12 [3–18]
Weekly leisure-time activity score	42 [21–69]

Results are presented as mean ± SD or median [IQR]; BMI= body mass index; GLTE= Godin Leisure-Time Exercise.

Health-related quality of life

The mobility dimension of the EQ-5D-5L questionnaire was 1 [1-2], self-care 1 [1-1], usual activities 1 [1-1.5], pain and discomfort 2 [1.5-3], and the anxiety and depression dimension 1 [1-2.5] for (Figure 2.1A). The overall median index score calculated with Xie and colleagues' algorithm (24) was 0.86 [0.79-0.93]. The self-rated health status (ranging from 0 to 100) showed a median of 80 [76.5- 88.5]; (Figure 2.1B).

Figure 2.1. Health-related quality of life (EQ-5D-5L)



Results are presented as mean $\pm$ SD; A) 5 dimensions of the EQ-5D-5L ranging from 1 to 5; B) Visual analog scale for the perceived health; VAS= visual analog scale.

Sleep quality

The PSQI questionnaire revealed an average subjective sleep quality of 0.86 ± 0.7 , sleep latency at 0.90 ± 0.70 , sleep duration at 0.68 ± 0.67 , sleep efficiency at 0.42 ± 0.61 , sleep disturbance at 1.29 ± 0.56 and sleep medication at 0.29 ± 0.90 (Appendix 5. Figure S1A). Overall, participants had good sleep quality (5.3 ± 3.0 out of 21; Appendix 5. Figure S1B) with 5 individuals (24 %) having poor sleep quality (PSQI ≥ 8).

Perceive stress

The PSS questionnaire showed good internal consistency (Cronbach's $\alpha = 0.868$). Overall, the participant had an average score of 12.2 ± 6.7 out of 40, indicating an overall low stress level.

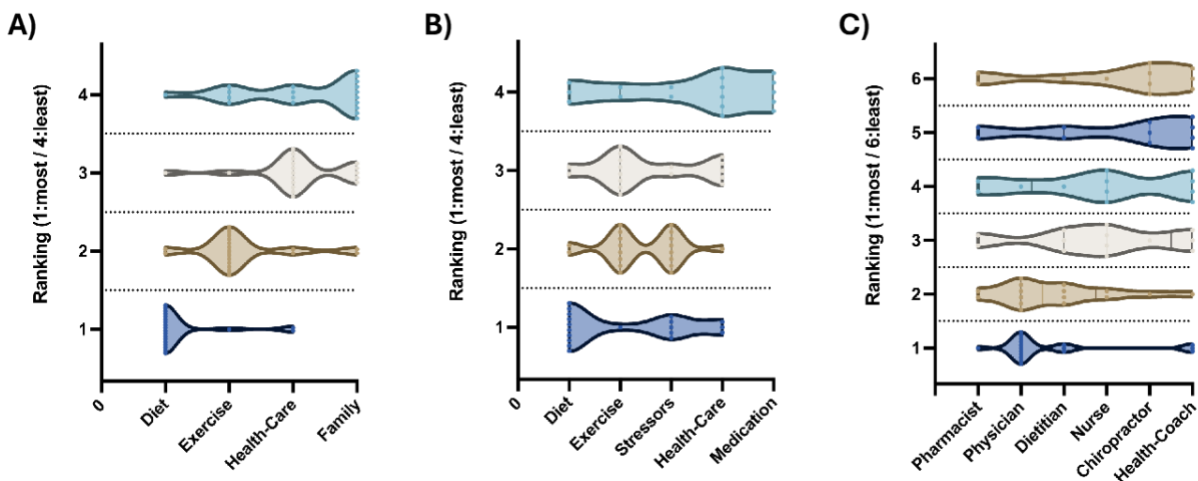
Remission

A total of 10 individuals (48%) achieved remission with mostly diet, while 11 (52%) achieved remission with a combination of diet and exercise. Before remission, seven participants (33%) were taking metformin, two participants (10%) were taking GLP-1 receptor agonists, and one (5%) was taking insulin. When participants were asked to rank from 1 to 4 (1-most important and 4-least important) contributing factors to putting their T2D into remission, most individuals put diet as first ($n = 18$), exercise as second ($n = 13$), health-care provider support as third ($n = 10$), and family support as fourth ($n = 11$; Figure 2.2A). Other important contributors were also mentioned by the participants such as fear (e.g., fear of not being there for their kids, fear of losing a limb, fear of renal failure, etc.), fasting, reading and continuous education, finding exercise that you enjoy, and stress reduction. When participants were asked to rank from 1 to 4 (1-most important and 4-least important), what factors made it difficult to achieve T2D remission, most individuals mentioned maintaining dietary change as first ($n = 10$), while maintaining physical activity levels

and external stressors were ranked as second most important contributor ($n = 8$ for both). Detailed information is provided in Figure 2.2B. When queried about additional challenges, participants highlighted the abundance of conflicting information contradicting health and well-being, the cost of adopting a healthy lifestyle, and depression. Also, some individuals (23%) cited the lack of support from the medical team such as dietitians, doctors, and nurses.

When individuals were surveyed about whom they consulted regarding achieving remission, 17 (81%) reached out to their doctor, 2 (10%) to their dietitian, 2 (10%) to a nurse, and 4 (19%) did not consult any healthcare professional (some individuals consulted more than one healthcare professional). The discussion between the health professional and the participants ranged from a positive experience with open-minded conversation and support to a negative experience. One participant stated that the doctor told them that they were risking kidney failure if they did not start taking metformin again. Meanwhile, another doctor borrowed a book about a low-carb diet from a participant and subsequently experimented with a low-carb diet alongside their patient to understand the experience better. When participants were asked to rank from 1 to 6 (1 -most important and 6 -least important), what health professional was mostly involved in their remission process, the most important seemed to be the physician followed by dietitian and nurse (Figure 2.2C). Finally, when participants were asked “How are you currently maintaining remission?”, the most important themes that emerged were dietary patterns and physical activity level (Appendix 3).

Figure 2.2. Ranking of contribution factors to achieve remission



Data are presented as Violon plot with individual data presented as a dot; A) Contributing factors to achieve remission; B) Difficulty to achieve remission; C) Professional involved in your remission; 1 is considered the most important factor and 4-6 the least important factor.

Dietary pattern and macronutrient intake

Eating habits

A total of seven participants (33%) reported following a low- carbohydrate diet, four (19%) a very-low carbohydrate diet, three (14%) a very-low carbohydrate diet that was described as a carnivore/ketovore diet, four (19%) reported no specific dietary pattern (e.g., described as “eating healthy”), two (10%) followed a low-calorie diet using meal replacement products, and one (5%) was following a Weight Watcher’s diet. Participants ate on average 3.0 ± 1.0 times a day with most (81%) participants reporting not eating after dinner (6:00 pm). The vast majority of our sample were cooking for themselves ($n = 20$; 95%) either alone ($n = 17$; 81%) or with a significant other ($n = 3$; 14%). Similar results were obtained when asking who did the grocery shopping with 71% ($n = 15$) of our sample were doing it by themselves, while 29% ($n = 6$) were doing it or alternating with a significant other. On average, individuals ate away from home 1.5 ± 1.0 per week with most people eating out one (74%) or two times (16%).

Food counseling and challenges in healthy eating

The majority of participants (62%) had food counseling with a registered dietitian primarily occurring at the time of their T2D diagnosis. Documented experiences ranged from neutral feedback about diabetes education to negative experiences (e.g., “It went badly”, and “did not work for me, and actually raised my blood sugar”). When participants were asked, “What is your biggest challenge to eating healthy?”, several themes emerged such as the “time and busy schedule”, the “associated cost”, the need to “consume more vegetables”, the “emotional eating/craving and loving carbohydrate”, and “eating out/social events” (complete descriptions are available in Appendix 4).

Behavioural domains of eating

The median score for the first domain of the TFEQ (i.e., cognitive restraint of eating) was 9.0 [5.5–11.0], indicating moderate severity. The median scores for the subsequent domains, disinhibition and hunger, were 6.0 [1.0–7.5] and 3.0 [0.5–4.0], respectively, (Appendix 5. Figure S2), both suggesting a low level of severity (21).

Three-day food record

The 3-day food log record showed that on average participants consumed 1653 ± 482 kcal per day. The average macronutrient distribution (percent total energy intake) was $31 \pm 16\%$ from carbohydrates, $22 \pm 7\%$ from protein, and $47 \pm 11\%$ from fat (Table 2.2). Individuals reporting following a carnivore/ketovore diet ($n = 3$) consumed an average of 1363 ± 425 kcal per day, with $11.5 \pm 4.6\%$ energy from carbohydrates, $30.0 \pm 4.3\%$ from protein, and $58.5 \pm 5.7\%$ from fat. People eating low-carb diet ($n = 7$) consumed an average of 1682 ± 394 kcal per day, with $31.5 \pm 15.8\%$ energy from carbohydrates, $20.3 \pm 6.8\%$ from protein, and $48.2 \pm 11.8\%$ from fat, while people eating very low-carb diet ($n = 2$) consumed an average of 2308 ± 388 kcal per day, with $26.1 \pm 10.3\%$ energy from carbohydrates, $23.6 \pm 5.3\%$ from protein, and $50.3 \pm 5.0\%$ from fat.

The two individuals following a meal replacement diet had varying total calorie consumption (720 vs. 2128 kcal per day; 22.5% vs. 39.3% carbohydrates; 17.5% vs 34.7% protein; 42.8% vs. 43.2% fat, respectively). Finally, individuals that did not specify a dietary pattern (i.e., healthy eating; n = 4) consumed 1608 ± 309 kcal per day, with $47.5 \pm 8.8\%$ energy from carbohydrates; $16.0 \pm 4.2\%$ from protein, and $36.5 \pm 4.9\%$ from fat.

Table 2.2. Macronutrient and total calorie intake

	Total (n = 18)	Min–Max
Total calorie intake (kcal)	1653 ± 482	720–2582
Carbohydrates (g)	134 ± 85	24–283
Net carbohydrates	113 ± 73	21–244
Protein (g)	85 ± 30	47–177
Fat (g)	86 ± 32	35–154
Carbohydrates (%)	31 ± 16	7–60
Protein (%)	22 ± 7	10–35
Fat (%)	47 ± 11	30–65

Data are presented as mean $\pm$ SD and as minimum (Min) and maximum (Max); net carbohydrates include only the carbohydrates that can be digested and converted into glucose, which is calculated by subtracting dietary fibre from total carbohydrates.

Glucose regulation and profiles

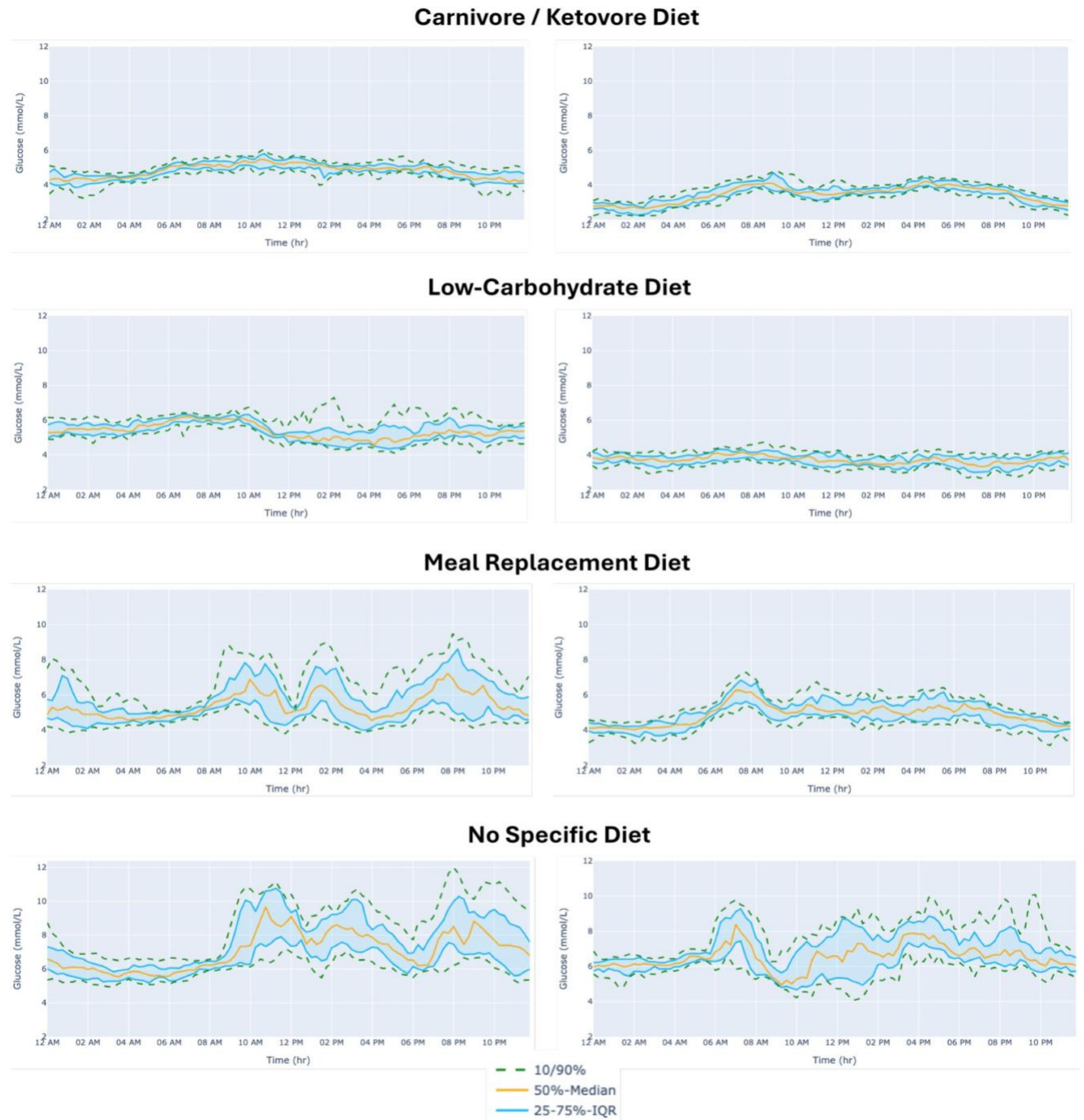
Out of the 21 participants included in the present study, 18 had complete CGM data with an average wear time of 13.2 ± 2.0 days (mean $\pm$ SD). The 24 h average glucose level was 5.0 [4.8–5.6] mmol/L with more than 90% of the time spent in range (Table 2.3). The CGM detected hypoglycemic events in seventeen out of the eighteen participants (median of 7 [2–13] events per participant). Prolonged hypoglycemia (≥ 120 min) was detected by CGM in six participants. Only six participants had CGM detected hyperglycemic events (median of 0 [0–2] events per participants), with no instances of prolonged hyperglycemia detected. Visual inspection of the 14-day CGM profiles shows that certain types of diet appear to result in lower average glucose and lower glucose variability (Figure 2.3). Specifically, the participants following a very low carbohydrate carnivore/ketovore diet appeared to have the lowest 14-day CGM average glucose and SD (3.8 ± 1.0 mmol/L; 0.83 ± 0.30 respectively; n = 3) followed by low- and very-low carbohydrates diet (5.0 ± 0.6 mmol/L; 0.84 ± 0.25 n = 9), meal replacement diet (5.2 ± 0.5 mmol/L; 1.11 ± 0.35 ; n = 2), and no specific diet (i.e., healthy eating: 6.6 ± 1.1 mmol/L; 1.43 ± 0.37 n = 4).

Table 2.3. Continuous glucose monitoring outcomes.

Variables	24 h	Diurnal	Nocturnal
Data availability (days)	14 [13.8–14]	NA	NA
Average glucose (mmol/L)	5.0 [4.8–5.6]	5.2 [4.8–5.7]	5.0 [4.2–5.4]
SD	0.98 [0.70–1.22]	0.91 [0.71–1.26]	0.63 [0.52–0.99]
CV (%)	19.9 [14.8–22.9]	18.2 [14.5–23.2]	14.8 [11.8–17.4]
eA1c (%)	4.8 [4.7–5.1]	NA	NA
Min glucose (mmol/L)	2.4 [2.2–3.33]	2.56 [2.22–3.40]	2.86 [2.22–3.67]
Max glucose (mmol/L)	9.2 [7.4–11.1]	9.16 [7.39–11.1]	6.95 [5.36–9.06]
MAGE	2.2 [1.5–3.1]	2.30 [1.49–3.27]	1.39 [1.03–2.23]
Time in range (3.9–10 mmol/L; %)	92.2 [85.2–97.0]	93.6 [85.3–96.8]	92.4 [68.8–98.7]
Time in tight range (3.9–7.8 mmol/L; %)	87.9 [68.0–93.5]	90.0 [59.8–94.8]	88.1 [68.8–96.7]
Time below range (<3.9 mmol/L; %)	6.5 [1.6–14.7]	4.7 [1.6–11.1]	7.0 [0.7–31.2]
Time below range (lvl.1: 3.0–3.9 mmol/L; %)	5.0 [1.0–12.1]	3.8 [1.3–9.2]	5.7 [0.7–16.7]
Time below range (lvl.2: <3.0 mmol/L; %)	1.2 [0.0–3.5]	0.8 [0.0–2.4]	0.9 [0.0–6.9]
Time above range (>10.0 mmol/L; %)	0.0 [0.0–0.4]	0.0 [0.0–0.5]	0.0 [0.0–0.0]
Time above range (lvl.1: >10.0–13.9 mmol/L; %)	0.0 [0.0–0.39]	0.0 [0.0–0.5]	0.0 [0.0–0.0]
Time above range (lvl.2: >13.9 mmol/L; %)	0.0 [0.0–0.0]	0.0 [0.0–0.0]	0.0 [0.0–0.0]

Data are presented as median [IQR]; n = 18; SD, standard deviation; CV, coefficient of variation; MAGE, mean amplitude of glycemic excursions; lvl, level; NA, not applicable; data presented as mean ± SD is available in appendix 6).

Figure 2.3. Individual continuous glucose curves separated by diet type



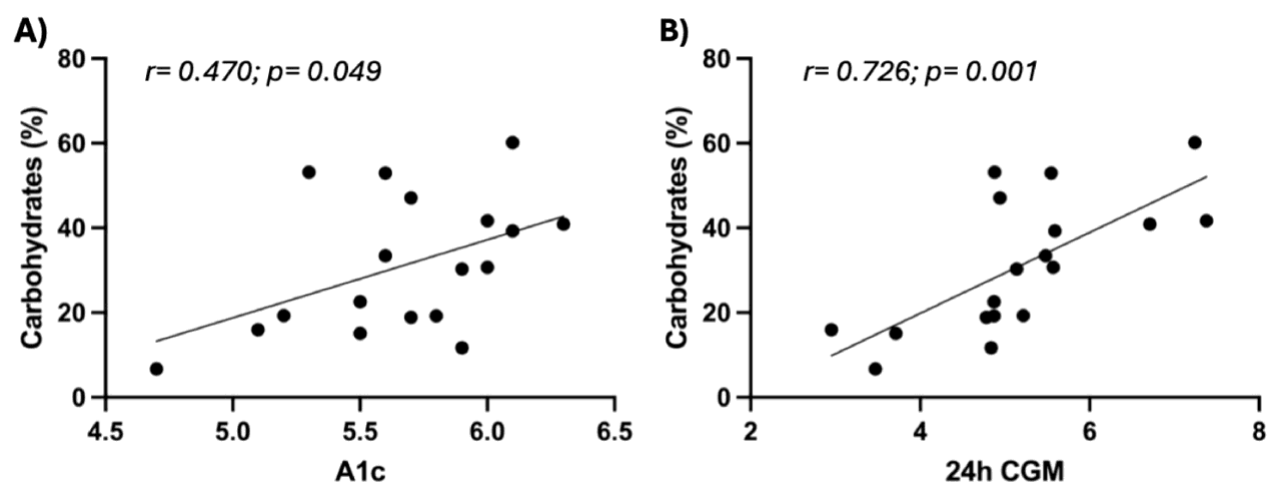
Results are presented as median (yellow); 25%–75% IQR (blue), and 10%–90% (green); each graph represent a single individual with an average of 13 days' worth of data; due to the self-reported nature of the dietary data, low-carbohydrate and very low carbohydrate diets are grouped together. In the low- carbohydrate section, the graph on the right represents a participant

who self-reported consuming a very low carbohydrate diet, but the 3-day food log shows ~33% energy from carbohydrate intake. Conversely, the graph on the left represents a participant who self-reported following a low-carbohydrate diet, with the food log indicating ~15% energy intake from carbohydrate

Relationships between glucose profiles and dietary parameters

Exploratory analyses revealed that the percentage of carbohydrates correlated with several glucose parameters, such as A1c ($r = 0.470$; $P = 0.049$), 24 h glucose concentration ($r = 0.726$; $P = 0.001$), glucose variability (SD: $r = 0.620$ $P = 0.006$; Figure 2.4) while total calorie intake was not correlated with any of the aforementioned parameters (all $P \geq 0.494$).

Figure 2.4. Correlation between 24 h glucose concentration, A1c, and carbohydrate intake



Correlation between A1c and carbohydrate intake in percentage ($n = 18$); (B) Correlation between 24 h continuous glucose monitoring (CGM) glucose concentration and carbohydrate intake ($n = 18$). The Y-axis represents the percentage of energy intake from carbohydrates.

2.5. Discussion

The objectives of the present study to shed light on the descriptive characteristics of individuals who had achieved T2D remission with changes to diet and exercise behaviour in real-world settings. The second objective was to describe glucose profiles using CGM and explore how dietary pattern may influence glucose regulation.

Descriptive characteristics of individuals achieving T2D remission

We had double the number of females volunteer to participate over the 1-year recruitment period when compared to males. This is not surprising as many studies have previously reported a major sex/gender disparity in healthcare utilization in individuals living with T2D (25) with greater scheduling and showing up to their medical appointments in women compared to men (26). Along those lines, females with T2D also tend to prioritize a balanced diet by increasing their intake of fruits and vegetables while reducing their consumption of meat (27). Therefore, the higher prevalence of females participating in the present study could partially be attributed to the proactive attitude exhibited by females toward managing their health.

The relatively recent diagnosis of T2D observed in the present study is in line with previous reports showing that lower time since diagnosis was a predictor of T2D remission (28). In the aforementioned DiRECT and DIADEM-I remission trials, inclusion criteria stipulated <6 and <4 years since diagnoses, respectively. Ancillary studies from DiRECT support the notion that some residual beta cell functional capacity is needed to achieve remission of T2D (29) and earlier time since diagnoses is likely increases the chances of sufficient beta-cell function/mass enabling remission. Therefore, it seems like initiating diet and exercise behaviour change early on in diagnoses, presumably related to residual beta-cell function, is an important consideration for individuals living with T2D to achieve remission. However, one participant in our study was previously taking insulin and had been diagnosed for 10 years prior to achieving remission, suggesting that it may be possible for individuals with long-standing T2D (including those taking insulin) to achieve remission through lifestyle changes.

Participants in this study exhibited relatively high self-rated health based on the EQ-5D-5L, adequate sleep quality based on the PSQI, and low-stress based on the PSS. Despite the cross-sectional nature of our design, these observations reveal that individuals who achieve remission of T2D through changes to diet and exercise behaviour appear to perceive their overall health as good.

Perceived factors influencing remission

To the best of our knowledge, this is the first study assessing different perceived factors that might influence the ability of individuals to achieve remission in real-world settings. An interesting finding is that half of our sample achieved remission with mostly diet, while the other half achieved remission with a combination of diet and exercise. This was also reflected when participants were asked to rank the most important factor to achieve remission, with most participants mentioning

diet first and exercise second. Despite diet and exercise both being considered as first line therapies in the treatment of T2D (30–32), individuals living with the condition tend to prioritize change in diet before exercising (33,34). Another interesting finding is that most people contacted their healthcare provider (a majority their physician; 81%) and that their experience varied significantly from a positive experience to a negative experience. Evidence from a sub study from the DiRECT trial where 34 individuals underwent qualitative evaluation on the overall process of remission, underlined the importance of continuous behavioural support from healthcare providers (35). Therefore, as the popularity of T2D remission grows, more healthcare providers should be knowledgeable and willing to help guide their patients in this endeavour.

Dietary pattern and macronutrient intake

Our findings indicate that multiple nutritional approaches (e.g., low-carbohydrate diet, carnivore/ketovore diet, meal replacements, non-specific “healthy” dietary patterns, Weight Watchers, etc.) may all be efficacious for achieving remission of T2D in real-world settings. However, regardless of the adopted diet in the present study, similar barriers (e.g., cost of healthy eating, lack of knowledge) to healthy eating were observed. These barriers help to reinforce the role of health-care providers in being knowledgeable and provide patient-centred care.

Average calorie intake assessed by 3-day food records was relatively low (i.e., 1653 ± 482 kcal). Although self-report food records usually underestimate the total energy intake by $\sim 15\%$ (36), individuals following meal replacement or low-carbohydrate diets usually have lower energy intake (37–39), so these values may still be reliable (40). Maintaining a lower energy intake is likely necessary, or at least a strong determinant, in achieving or sustaining T2D remission. Weight loss is a strong predictor in achieving T2D remission, notably via the reduction of ectopic adipose tissue in the liver and pancreas, which improve hepatic insulin sensitivity and β -cell function (41,42). It is well known that ongoing caloric restriction is needed to maintain weight loss (43), which seems to be reflected in the participants responses to factors associated with remission while highlighting the potential importance of ongoing behavioural support for T2D remission.

Glycemic control

Although CGM is now often used in clinical practice for the management of T2D, no official thresholds or values have been published related to T2D remission. To the best of our knowledge, this is the first study to describe the glucose patterns of individuals achieving remission in real-life settings. One interesting aspect is that even if all participants were under the 6.5% A1c cut-off for T2D remission (2), different 24 h CGM average glucose concentrations were observed ranging from 3.0 to 7.4 mmol/L (appendix 5. Figure S3). When compared to a similar subpopulation from The Maastricht Study (i.e., newly diagnosed T2D female (83%) aged 62 ± 8 with a BMI of 29 ± 4.4 ; $n = 197$), the average CGM-glucose concentration was 7.9 ± 1.6 mmol/L (44) compared to 5.2 ± 1.2 mmol/L in the present study. Along those lines, the glycemic variability (SD) in

individuals achieving remission was also lower than what is usually observed in individuals living with T2D ($SD = 1.0 \pm 0.4$ vs. 1.6 ± 0.7 , respectively; (44). Glycemic variability was especially low in individuals adhering to carnivore/ketovore or low-carbohydrate diets ($SD = 0.81 \pm 0.25$). Considering that long-term glycemic variability has been linked to the risk of stroke, myocardial infarction, and premature death (45), while short-term glycemic variability is linked to the risk of neuropathy (46), carotid intima-media thickness (47) and other diabetes-related complications (48), reducing glycemic variability for individuals in remission of T2D may be beneficial. Exploratory correlation analyses revealed that the percent- age energy from carbohydrates was positively associated with 24 h mean glucose and SD from CGM, as well as laboratory- based A1c. This suggests that individuals achieving remission may have better glycemic control when consuming low- or very low carbohydrate diets. Although there is some debate in the literature over whether lowering carbohydrate intake can independently (i.e., in the absence of weight loss) improve glucose regulation (49), these results are in line with the American Diabetes Association guidelines, which state that reducing overall carbohydrate intake has the most evidence for improving glycemia (50) and a Diabetes Canada position statement, which acknowledges that very low carbohydrate diets may be superior to higher-carbohydrate diets for improving glycemic control and reducing the need for glucose-lowering medications in the short-term (up to 12 months; (51).

Finally, an aspect of the CGM profiles of individuals in this study that warrants further investigation is the incidence of hypoglycemia. Indeed, 94% of our sample experienced hypoglycemic events detected by the Freestyle Libre Pro, which resulted in an average time spent below range of $17.5 \pm 27.8\%$. Interestingly, individuals following a carnivore/ketovore diet seemed more susceptible to hypoglycemia, spending $60.3 \pm 37.2\%$ of their time below range ($n = 3$), compared to low- and very carbohydrate diet ($11.8 \pm 20.7\%$; $n = 9$), meal replacement diet ($7.7 \pm 6.1\%$; $n = 2$), and no specific diet ($3.0 \pm 5.2\%$; $n = 4$). Whether this degree of hypoglycemia has any deleterious effects should be explored, although we do note that none of the hypoglycemic events detected by CGM were associated with any reported symptoms and none were confirmed by finger prick sampling. We did not assess blood ketone values in any of the participants, but previous work (52) has shown that when ketone levels are high, blood glucose can be very low without any apparent symptoms. Furthermore, it is possible that the CGM algorithm is less accurate when blood glucose levels are so low and stable across the day leading to over-reporting of hypoglycemic events.

2.6. Strengths and limitations

This study serves as an initial exploration into some of the characteristics of individuals who have attained remission through lifestyle interventions in real-world settings. As such, it lacks the statistical power to compare various diets and patterns within the population, which would require larger-scale cohort or interventions studies. Also, all participants recruited were from British Columbia and Manitoba, Canada, which may limit generalizability. Furthermore, most of the

perceived factors influencing the achievement of remission were acquired using questionnaires, open-ended questions and a 3-day food record. Gleaning more insights on experiences of individuals through qualitative inquiry (e.g., semi-structured interviews) could have allowed a broader understanding of achieving remission in the real-world; we are planning to do this in a follow-up study. Along those lines, having device-measured physical activity and sedentary behaviour using accelerometers may have allowed us to better characterize individuals who achieved T2D remission and assess whether the timing or pattern of physical activity influences glucose regulation. These limitations are counterbalanced with the novelty of the research being the first to describe the achievement of remission with lifestyle changes outside research settings. Understanding the experiences of individuals who achieve remission, including their barriers and facilitators, could assist future research in optimizing approaches and help guide healthcare providers when implementing such approaches in their practice. The implementation of CGM data also allowed a better understanding of how different diets might modulate 24 h glucose and glycemic variability in this population, but further large-scale studies will be needed to determine if there are systematic differences in glycemic control with different approaches to T2D remission.

2.7. Conclusion

The present study highlights the feasibility of achieving T2D remission outside of research settings through various means, including dietary changes (e.g., low-carbohydrate diets, carnivore/ketovore diets, healthy eating, etc.) and a more active lifestyle. Based on our preliminary results, a lower percentage of total daily energy intake coming from carbohydrates seems to be linked with improved glycemic regulation in people who have achieved T2D remission. In addition to changes in diet, performing regular physical activity, and having good sleep quality seem to be common characteristics of individuals who have achieved T2D remission. Considering that most people reached out to healthcare professionals to discuss the possibility of T2D remission, it seems crucial that healthcare providers are adequately prepared to support their patients in this endeavour, while recognizing that maintaining remission over the long-term can be challenging.

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Bridge to Chapter III

The following chapter comprises a manuscript which provides a broad overview of the participants experiences of T2D remission who achieved remission through lifestyle interventions. This chapter focuses on the barriers and facilitators of putting T2D into remission. This study aimed to explore T2D remission in real world settings. Tahmina Rahman was the lead author of the manuscript and contributed to conceptualization, case selection, data collection, and analysis. Alexis Marcotte-Chénard was responsible for investigation, validation, and visualization. Barbara Oliveira and Rebecca Mollard contributed to conceptualization, funding acquisition, and critical review. Margherita Cameranesi contributed to conceptualization, data collection and analysis. Jonathan P. Little and Dylan MacKay served as the principal investigators and contributed to conceptualization, supervision, funding acquisition, project administration, validation, and visualization. All authors approved and contributed to the final manuscript.

Chapter III

Manuscript 2

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“Why do they say manage?” A Mixed Method Exploration of Lifestyle Driven Remission in Type 2 Diabetes

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3.1. Abstract

Type 2 diabetes (T2D) remission offers individuals the potential to achieve and maintain normal glycemic levels without pharmacological intervention. Clinical trials suggest that T2D remission is achievable through sustained lifestyle interventions such as dietary modification and physical activity. However, there is limited understanding of the real-world experiences of individuals who achieve remission through these methods. This study aimed to explore the lived experiences of individuals who have achieved T2D remission through lifestyle approaches.

This two-phase sequential mixed-methods study involved twenty-one adult participants (N=21) recruited from British Columbia and Manitoba, Canada. In Phase-1, quantitative data on T2D remission strategies and outcomes were collected through surveys, continuous glucose monitoring (CGM), and 3-day diet records. In Phase-2, eight participants were purposefully selected based on CGM variability (mean sensor glucose, standard deviation, and coefficient of variation) to explore the barriers and strategies. Seven participants (n=7) completed semi-structured one-on-one interviews. Qualitative data were analyzed using inductive thematic analysis, and the data were integrated using a meta-interference of joint display approach.

Eighteen of twenty-one participants (mean age: 57 ± 8 years; T2D duration: 4 ± 3 years) wore a CGM for an average of 13.2 ± 2.0 days. The median time in range was 92.2% (IQR: 85.2-97), with a median glucose level of 5.0 mmol/L (SD: 0.98, IQR: 4.8–5.6). Interview participants were divided into two groups using extreme case sampling, with four showing low variability and three showing high variability in blood glucose measured by CGM. However, the themes emerged collectively, reflecting similar experiences across both groups. Thematic analysis identified seven overarching themes associated with T2D remission. Flexibility in diet and exercise, need for personalized care and accountability were central, with participants emphasizing the role of personal research in managing diet, physical activity, and decision-making. Health improvements, fear of long-term medication use, and future complications were strong motivators for adopting and sustaining lifestyle changes. Participants also highlighted significant challenges, including limited support for remission related to dietary guidance, medication management, and social and psychological barriers.

The integration of both data highlights the role of informed decision-making, along with emotional and educational factors in sustaining long-term T2D remission.

3.2. Introduction

T2D remission is a recent increasingly discussed goal in diabetes care, referring to the sustained normalization of blood glucose concentrations without the need for glucose-lowering medications. The most widely accepted definition of remission is an HbA1c below 6.5% (48 mmol/mol) measured at least 3 months after stopping glucose-lowering medications, as outlined in recent American Diabetes Association consensus statement (1). Recent clinical trials showed that T2D remission is most often achieved through significant weight loss of >15% of initial body weight. This level of weight loss reduces fat in the liver and pancreas, restoring beta-cell function and insulin sensitivity for some (2–4). Additional predictors of T2D remission includes shorter duration of diabetes, lower baseline HbA1c, and fewer medications. It is achievable across different ethnic groups and is independent of baseline BMI, supporting the concept that individual fat tolerance is key (3–5). This amount of weight loss can be achieved through early lifestyle intervention or metabolic/bariatric surgery (MBS).

Evidence from clinical trials support the feasibility of achieving remission through structured interventions. The DiRECT trial showed that nearly half of participants who lost significant weight through a structured, low-calorie diet achieved remission at 12 months, with higher remission rates in those losing more weight (6–8). Similarly, the Look AHEAD (Action for Health in Diabetes) study reported remission rates of up to 11.5% at first year among those receiving intensive lifestyle interventions, compared to just 2% in the control group (9). Although remission was the secondary outcome of this study. The DIADEM-I trial, focused on individuals with early T2D in the middle east also showed significantly higher remission rates following structured lifestyle intervention compared to standard care (10). These trials consistently show that remission is more likely when intensive interventions are initiated early after diagnosis. However, the durability of remission mostly depends on maintaining weight loss and adherence to lifestyle changes over time.

Despite variation in study design or population, most clinical trials targeting T2D remission share several core components. These typically include a structured dietary intervention, physical activity, frequent and ongoing clinical or behavioural support and personalized goal setting. Effective dietary approaches include low-energy (very low-calorie) diets, very low or low-carbohydrate diets (VLCD/LCDs), and the Mediterranean diet (11). These diets are often implemented with a focus on calorie restriction to promote weight loss. These approaches improve insulin sensitivity and increase remission rates even more when combined with physical activity such as moderate intensity aerobic and resistance training (11). These trials also involve multidisciplinary care teams, including dietitians, diabetes educators and physicians as well as the use of self-monitoring tools and regular follow up visits. These elements are designed to work together to facilitate weight loss, improve metabolic function and promote long-term adherence (11).

However, the intensity, frequency and clinical oversight provided in trials may not always reflect real-world healthcare setting. This leads to the primary gap in T2D remission research, “how individuals achieve and sustain remission outside of a controlled trial environment.” Although the clinical potential for T2D remission is well established, little is known about how individuals navigate the process of achieving and sustaining remission outside of research settings. Most existing studies focuses on physiological outcomes, with minimal attention to psycho-social factors such as individual motivation, family and health care support and mental health (12). These factors may greatly influence the long-term success of lifestyle interventions. This gap in literature limits the understanding of real-world effectiveness and patient-centered care perspectives.

Another critical research gap is regarding the barrier and challenges faced by individuals in achieving remission. While many studies are focused on the effectiveness of lifestyle intervention or bariatric surgery, few address the barriers faced by participants during the process. To develop a person-centered targeted intervention, it is important to understand what works and what may get in the way of remission. Addressing these barriers is key to improving remission rate and long-term sustainability in real world settings.

3.2.1. Study Aim and Mixed Methods Approach

To address these research gaps, the overreaching aim of this study was to understand how individuals achieve and sustain T2D remission through lifestyle intervention in real world settings. While clinical trials have established the efficacy of structured interventions, there remains limited understanding of how individuals navigate the remission process independently from healthcare professionals. This includes identifying not only the effective strategies used to achieve and maintain remission but also the barriers, supports, and individual decision making processes that shape this experience.

To address the complexity of the study aim, a two-phase sequential explanatory mixed method design was employed (13). This design allows for the integration of quantitative (QUAN) and qualitative (qual) data to provide a comprehensive understanding of the phenomenon being investigated. Here, "QUAN" is used to denote the primary quantitative phase, while "qual" indicates the secondary, explanatory qualitative phase (13). QUAN is capitalized and qual is not to indicate that the qual phase follows the QUAN phase in this study and qual findings were used to explain QUAN results. The study began with the collection of QUAN data (e.g., different health screening surveys, dietary recall, CGM data) followed by qual interviews exploring the lived experiences of a subsample of QUAN study participants, including the strategies they used to go into remission in greater depth. The QUAL subsample was selected based on CGM data. Figure 3.1 shows a visual model of the mixed methods study design.

This mixed method approach was chosen to bridge the gap between measurable clinical outcomes and the rich, contextual insights that qualitative data can provide. This integration enhances the

interpretive power of the findings by linking objective health data (e.g., CGM metrics and quality of life) with the personal, social, and psychological processes that contribute to achieving and sustaining remission.

3.2.2. Quantitative Strand

The QUAN strand of this mixed method study was guided by the following research questions:

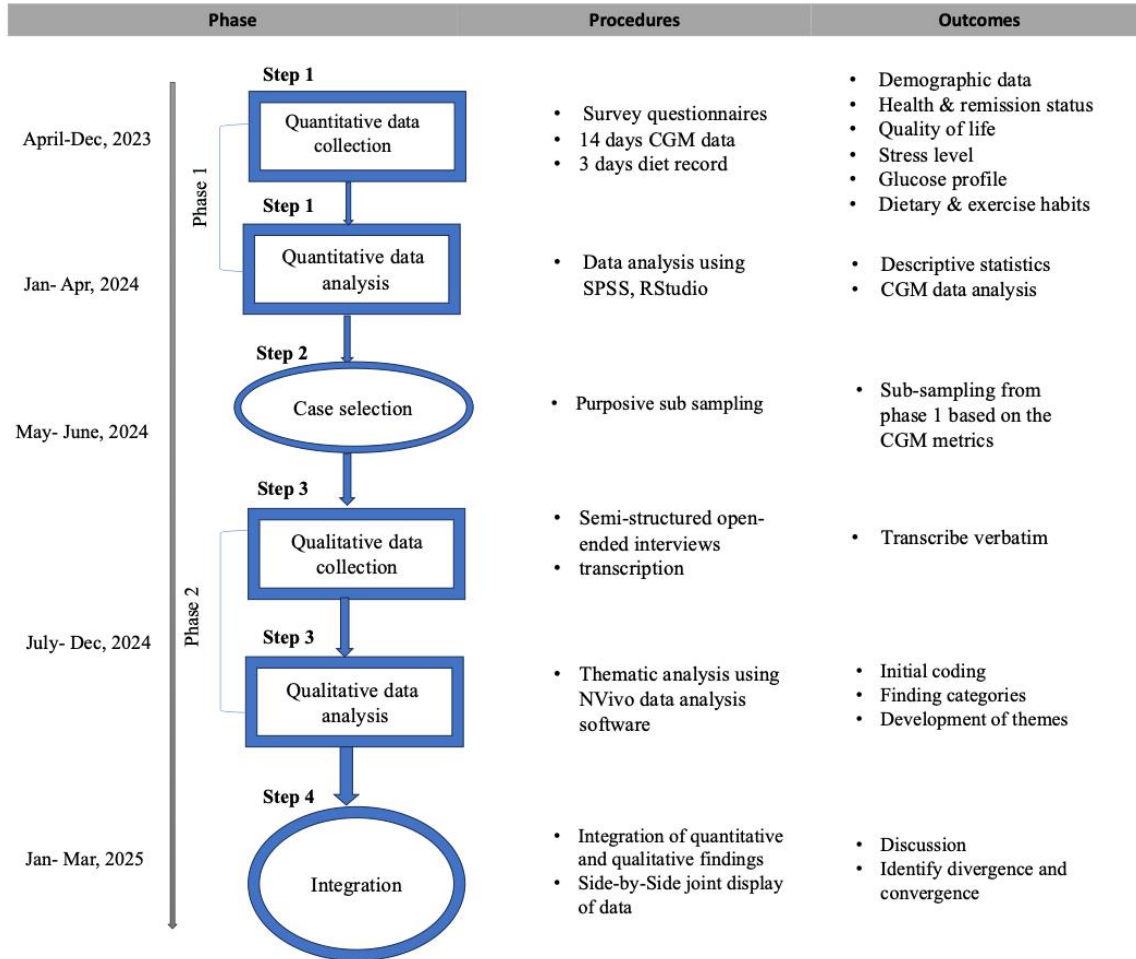
1. What strategies (e.g., diet and/or exercise) do Canadian adults report using to achieve and maintain T2D remission through lifestyle interventions?
2. How do these lifestyle strategies align with individuals' glycemic outcomes?

3.2.3. Qualitative Strand

Building on the QUAN findings, the qual strand of this mixed method study sought to answer the following questions:

1. What strategies do individuals use to effectively achieve and sustain remission?
2. What barriers and challenges do they encounter during this process?
3. How do they describe the support systems that facilitates or hinders their ability to sustain remission?

Figure 3.1. Visual model of sequential explanatory mixed methods study design (QUAN → qual)



3.3 Methods

3.3.1. Mixed Methods Design and Procedures (QUAN → qual)

This study employed a sequential explanatory mixed methods design to explore the process of achieving T2D remission in individuals who followed lifestyle changes as a remission approach. In this context, lifestyle changes refer to strategies aimed at improving health by changing daily habits such as diet, physical activity, sleep, and stress management (14). The study followed a two-phase design (QUAN → qual) where the QUAN and qual data was collected sequentially and analyzed independently. The qual subsample was chosen based on the QUAN data through a case selection method. The two sets of data were analyzed and interpreted separately and then merged during the last phase of the study (integration phase).

To implement this design, four procedural steps were followed (see Figure 3.1 for details). In **Step 1**, QUAN data were collected and analyzed. In **Step 2**, a sub-sample of cases were selected from the QUAN phase and connected to the **Step 3**, where qual data were collected and analyzed. In **Step 4**, the findings from both phases were merged in the integration phase.

3.3.2. Phase 1 (Quantitative Design and Procedures)

QUAN Study Design

The QUAN phase followed a cross-sectional research design in which participants from Manitoba (MB) and British Columbia (BC) were recruited and surveyed at one time point. The recruitment and data collection were primarily conducted using online data collection tools, thus the data collection was not restricted to any specific cities of the abovementioned Canadian provinces. In BC, participants were recruited by accessing past clinical trial records, stakeholders' networks, healthcare professionals, and online advertisement. In MB, participants were recruited by advertising the study using a poster and social media. See (15) for a detailed description of the QUAN phase.

QUAN Study Participants

A total of 21 participants were recruited across two provinces using specific eligibility criteria tailored to the objectives of this study. The participants were included if (1) they had previously been diagnosed with T2D and (2) had achieved T2D remission (HbA1c below 6.5% and no glucose lowering medications for at least 3 months) through lifestyle intervention. Remission status was confirmed using a recent laboratory HbA1c report submitted by the participant. The participants were excluded if (1) they had not been diagnosed with T2D, (2) had an HbA1c level higher than 6.5%, (3) were taking any glucose lowering medications, (4) were ongoing medical treatment for diseases such as cancer, autoimmune or inflammatory disease, liver, or kidney disorders, (5) were unable to follow remote guidance by internet or smartphone, (6) were unable to read or communicate in English.

QUAN Data Collection Procedures

Interested participants received an email from a study team member with information about the study, along with a link to an eligibility survey hosted on University of British Columbia (UBC) REDCap (16). Once eligibility was confirmed, participants were sent an electronic consent form. Upon acceptance, they were scheduled for a zoom call where the study procedures were explained in detail, and any questions were addressed before signing the eConsent form.

Participants were then asked to submit a recent laboratory copy of HbA1c to confirm the remission status. Upon confirmation, they were sent 6 different questionnaires (17-20) via UBC REDCap (see table 3.2 for details). Participants also received a study kit by mail containing a FreeStyle Libre Pro IQ- CGM reader and sensor (22), along with diet record forms (23). The CGM sensor was designed for self-insertion and included detailed instructions. However, participants were also offered a follow-up zoom call to guide them through the application process.

Participants wore the CGM for 14 continuous days and completed a 3-day diet record (2 weekdays and 1 weekend day) to assess food choices, macronutrient distribution, and diet types. Participants were sent a reminder to complete the dietary record by email.

Measures

Table 3.2. QUAN data collection tools and outcome measures

Based on the data collected, the following outcome measures were assessed.

Data Collection Method	Outcomes
Q1. Health Screening Questionnaire	Age, height, weight, biological sex, medical history, current health status and HbA1c value
Q2. Pittsburgh Sleep Quality Index (PSQI) (17)	Sleep quality and disturbances in previous month
Q3. Perceived Stress Scale (19)	Stress level over the past month
Q4. Godin-Shephard Leisure-Time Physical Activity Questionnaire (GSLTPAQ) (20)	Leisure time and exercise habit
Q5. EuroQol 5-Dimension 5-Level questionnaire (EQ-5D-5L) (Appendix 8 (18))	Quality of life
Q6. Three-Factor Eating Questionnaire (TFEQ) (21)	Eating behaviour
CGM sensor and recorder (22)	Confirmation of remission status, differences of glucose profile in different strategies, assessment of real time fluctuation in blood glucose

Diet Record (23)

Total calorie intake, macronutrient distribution
and dietary pattern

HbA1c (Hemoglobin A1c); CGM (Continuous Glucose Monitor)

Statistical Analyses

No formal sample size calculation was conducted, as the study aimed to describe real-world experiences of individuals achieving T2D remission over a one-year period, without pre-specified subgroup comparisons. Data normality was assessed visually using histograms and Q–Q plots. Internal consistency of the Perceived Stress Scale (PSS) was evaluated using Cronbach’s alpha. Exploratory correlations between glucose measures (e.g., CGM metrics, HbA1c) and dietary variables (e.g., % energy from carbohydrates) were analyzed using Pearson’s correlation. Analyses were performed in SPSS V28.0 (IBM; Chicago, USA), with significance set at $p \leq 0.05$. Data are reported as mean $\pm$ SD or median [IQR], as appropriate (15).

3.3.3. Phase 2 (Qualitative Design and Procedures)

Qual Research Design

The qualitative component of this study followed an interpretive description approach. This approach was used to explore participants lived experiences in achieving and maintain T2D remission that could inform practice and support patient-centred care. Qual data from this component were analyzed using thematic analysis approach (24), involving in-vivo coding, memo writing and theme development from participants’ narratives.

Case Selection

A subsample of eight participants who wore the CGM device and provided usable CGM data for an average of 13.2 ± 2.0 days were selected from Phase One. This subsample of study participants was purposively selected using extreme or deviant case sampling method (13,25). Specifically, we selected the four participants with the highest CGM values at the CGM assessment and the four participants with the lowest values. These values were the average sensor glucose, standard deviation, and coefficient of variance. To be selected, each participant had to have at least two of the targeted measures in the highest or lowest range. Out of the eight selected participants, only five consented to take part in the data collection which led to the selection of three more participants with higher or lower CGM values. Finally, seven participants participated in a one-on-one in-depth semi-structured interviews.

Data Collection Procedures

A flexible interview guide (see Appendix 7) including 25 open-ended questions was developed following the theoretical domain framework (TDF) to explore various influences on the experience of T2D remission, including behavioral strategies, psychological and social challenges, healthcare

system interactions and long term sustainability (26). This guide included questions that investigated domains explored in the TDF, such as psychological, social, physical, and economical factors contributing to T2D remission. The TDF is a psychological model used in behavioural research to understand the factors that influence human behaviour. TDF helps identify barriers and facilitators that affect people's ability to adopt new behaviours or change existing ones (26). The TDF in developing the guide was applied flexibly to avoid deductive approach and allow for the emergence of novel insights during analysis (27). Interview questions were modified during the interviews to focus on gathering more in-dept data. Interviews were audio and video recorded using UBC secure Zoom, which was also configured to generate verbatim transcripts of the interviews. Each transcript underwent a comprehensive review and verification process for verbiage review, speaker identification, formatting and punctuation to ensure its accuracy and to enhance rigour. Given the depth of the interview guide topics, each interview lasted between 1 and 1.5 hours, and three participants participated in a follow-up interview to capture their full experience.

Thematic Analysis

To analyze the data, an inductive thematic approach described by Braun & Clarke (24) was used. Participants were given a pseudonym before starting of the analysis. All identifying information was removed from the interview transcripts, memos, and reflexive notes before being imported into the qualitative analysis software. The data were analyzed thematically by two investigators (TR and MC) independently and concurrently. To begin, transcripts and memos were read multiple times to ensure thorough familiarization with the participant's narratives and context (24). Initial coding was conducted line by line, labeling short text segments using either gerunds or participants' own words (in-vivo coding), which helped retain the authenticity of participants' voices (24). As coding progressed, codes were compared, grouped, and refined through regular meetings between investigators. This collaborative process enabled the identification of patterns and the formation of broader categories, akin to axial coding, in which related codes were clustered around central concepts. These categories captured recurring experiences, barriers, and strategies described by participants. Through iterative analysis and ongoing discussions, categories were further distilled into overarching themes that represented key dimensions of the participants lived experiences with T2D remission (24). NVivo version 14.23.4 software (Lumivero, formerly QSR International, Denver, USA) was used throughout to organize codes, manage data, and support the identification of thematic patterns across transcripts. Data saturation was considered reached when no new codes, categories, or themes emerged from subsequent interviews, and when both investigators agreed on the identified themes indicating that the data were sufficiently rich and comprehensive (24).

Trustworthiness

In this study, the trustworthiness of the data was established through the four criteria of credibility, transferability, dependability, and confirmability (28). Credibility was ensured through in-dept interviews and follow up interviews to capture their whole experiences. NVivo software was used

to code, manage and organize qualitative data systematically which enables a transparent and rigorous coding process. Peer debriefing was also employed to verify the authenticity of the interpretations. Transferability was addressed by providing a thick description of the study participants' characteristics and their illustrative quotes. This allows readers to assess the relevance and applicability of findings to other settings. Dependability was supported through inter-coder agreement, triangulation of data and meta-interference of findings. Confirmability was established by maintaining a clear record of all analytical decisions, memos, and coding processes, ensuring that findings reflect the participants' experiences. To ensure that our findings remained grounded in the participants' lived experiences, we engaged in continuous reflexive practices throughout the study. This included memo writing, collaborative coding discussions, and ongoing dialogue with an expert in qualitative methods.

Positionality

As the lead author of the study, I approached this study with a strong interest in understanding how lifestyle interventions can contribute to T2D remission because I carry both loved and laboured experiences with T2D and its complications. As a researcher with a background in human nutritional sciences, my academic training and familiarity with the scientific literature informed my perspective that T2D can be addressed through sustainable, person-centered approaches beyond conventional medication-based management. I recognize that my educational and research backgrounds, as well as my existing knowledge of dietary and behavioural strategies, may have influenced how I interpreted participants' narratives. Although I do not have lived experience with T2D, I aimed to center the voices of our participants and interpret their experiences with accuracy, respect, and empathy. My goal was to understand how remission is achieved from a biological perspective as well as how it is experienced in daily life, shaped by individual, social, and systemic factors. By integrating both data (e.g., CGM values and participants' lived experiences), I sought to provide a comprehensive account of what real-world T2D remission looks like both biologically and experientially.

3.3.4. Integration of QUAN Results and qual Findings

In the final stage of the study, we focused on integrating the findings from Phase 1 and Phase 2 to enhance the depth and contextual understanding of the results. This integration process involved using the qualitative findings to provide explanations for the quantitative results (13). The data integration took place at two points of interface. First, a connecting approach was employed by purposefully selecting a subsample of participants from the quantitative phase to participate in qualitative interviews. The second point of integration occurred during the interpretation phase, where we used meta-inference through joint displays (13,29). The joint displays were created to identify points of convergence and divergence between both findings and to interpret the integration results.

3.3.5. Ethical Considerations

This study was approved by the University of British Columbia ethics committee and the University of Manitoba Health Research Ethics Board and was carried out following the Declaration of Helsinki and the Tri-Council Policy Statement. This study is registered on ClinicalTrials.gov as a cohort study (ID: NCT06177210). All the data were stored at the UBC secure storage, and a data sharing agreement was signed between the two universities.

3.4. Results

3.4.1. QUAN Results

The quantitative results are discussed in detail in Chapter 2 (15). In Summary, a total of 21 individuals (14 female and 7 male) in T2D remission were recruited between January 2023 and January 2024. The average age of the participants was 57 ± 8 and the mean T2D duration was 4 ± 3 years. Participants had an average BMI of 29.6 ± 6.5 kg/m² and an HbA1c of $5.7 \pm 0.4\%$. Participants achieved remission approximately 1.5 ± 2.3 years after diagnosis and had maintained remission for an average of 2.3 years at the study entry. Most participants demonstrated good health-related quality of life (median of 0.86 [0.79–0.93]), moderated to low stress levels and generally good sleep quality (an average score of 12.2 ± 6.7 out of 40). Dietary assessment revealed diverse eating patterns where 14(66%) participants reported following VLCD/LCDs, 4(19%) eating healthy, 2(10%) followed a meal replacement diet, and 1(5%) was following a Weight Watcher's diet. Participants reported eating three times a day on average, preparing meal themselves most of the time and limiting eating out.

Eighteen of the 21 participants wore CGM and completed the three-day dietary record. CGM data showed strong glycemic outcome with a 24 hour median time in range (TIR) of 92.2% [85.2-97.0] and low glucose variability. Visual inspection indicated that VLCDs, particularly carnivore/ketovore dietary styles were associated with the lowest average glucose concentrations and variability. Exploratory analyses demonstrated a significant positive correlation between carbohydrate intake and glycemic measures such as HbA1c ($r = 0.470$; $p = 0.049$) and average glucose concentration ($r = 0.726$; $p = 0.001$). Total calorie intake showed no such association ($p \geq 0.494$).

3.4.2. Qual Findings

Qual Study Participants

A total of seven participants (five biological males and two biological females), aged 45 to 68 years (mean 57.6 ±8.7 years), were included in the qualitative component of this study. All participants had achieved T2D remission through lifestyle intervention. Most participants (n=6) reported intentional weight loss as part of their remission process. Educational level varied, with most having completed college or university-level education and one participant holding a postgraduate degree. The majority were married (n=6), while one participant was single. Participants were either employed in management or technical professions (e.g., software programming), retired, or receiving disability support. This diverse group provided insight into real-world experiences of achieving and maintaining T2D remission through lifestyle strategies.

Thematic analysis

Thematic analysis of interviews revealed seven overarching themes (Table 3.3) that reflected participants' lived experiences in achieving and maintaining T2D remission. The qualitative subsample was purposefully selected from two glycemic pattern groups (high vs low mean glucose, CV and SD) based on CGM data. However, the findings were presented collectively, as the emergent themes were consistent across participants regardless of group. Among the seven themes, three themes captured key barriers, three described strategies and one represented motivation. These overarching themes were developed from categories that reflected individual, social and systematic influences. Many of the theme titles were derived directly from participants words.

Table 3.3. Overreaching themes and their categories identified from thematic analysis

Themes	Categories	Quotes
Barriers		
Theme 1. “One size doesn’t fit all”	1. Non-Supportive Healthcare Professionals	Quote 1: “My doctor said, ‘I am going to give you these medicines and you should probably lose some weight.’ Good advice but that’s like saying, ‘I think you should make some more money’. It’s kind of silly to say, ‘oh, you should lose it’.” (James; 57 yrs)
[Participants described feeling frustrated with a healthcare system they believed focused on standardized, medication-driven care that often	2. Person-centred care	
	3. Presence of Support	

overlooked remission as a goal. They emphasized the need for individualized, person-centred support tailored to their unique circumstances. While support from family and open-minded providers was helpful, many felt they had to advocate for themselves. Overall, participants called for a more flexible and supportive approach that acknowledges diverse paths to remission.]

Theme 2. “Healthcare, not medical care”

[Participants expressed deep skepticism toward conventional diabetes care, which they viewed as overly focused on medication and outdated dietary guidelines. Many felt that current standards lacked alignment with remission goals and were influenced by profit-driven interests. This mistrust led them to question medical advice, seek alternative approaches, and take greater responsibility for their own care. Their experiences reflect a desire for a healthcare model that prioritizes long-term health, transparency, and remission-focused support over routine medical management.]

1. Skepticism toward conventional diabetes management
2. Over reliance on medication
3. Financial influence on healthcare

Quote 2: *“As someone who is heavy, you know what you are not supposed to eat, you know what you should eat but its matter of have I guess the willpower or motivation to do it’.”* (Sarah; 61yrs)

Quote 3: *“I’m very lucky that I have a doctor who is a different doctor than I had when this all started.....Right now, [doctor’s Name], my doctor, she will spend half an hour, 45min with me. So we get to have real conversations and so that really facilitates far more understanding than most doctors in Canada.”* (Joey; 65yrs)

Quote 4: *“You’re managing and maintaining your disease which is progressive and incurable. This is what they said, ‘all you can do is manage it’. I just had to break away and say no”* (Joey; 65yrs)

Quote 5: *“I hate that term, ‘manage your diabetes’. They don’t wanna tell you could put it into remission. They wanna say manage. Why do they say manage? Because they want you chronically ill, and if you’re chronically ill, then you’re chronically a patient, or chronically a consumer of whatever drugs they are producing.”* (James; 57yrs)

Quote 6: *“They’re not going to be suggesting, “Try this method.” I think they prefer just prescribing the pills, and make it easier for them, and at the end of the day they probably make more money doing it that way.”* (David; 47yrs)

Theme 3. Barriers inside and out

[Participants described facing both internal and external barriers in their remission journeys. Emotional struggles such as self-reported anxiety, depression, and motivational lapses were compounded by social challenges, including a lack of understanding from others, judgment, and limited support. The described that physical setbacks such as injuries or co-existing conditions also disrupted their efforts and required additional planning and resilience.]

Quote 7: *“It was especially difficult because my wife and kids still ate carbs and candy”* (David; 47yrs)

Quote 8: *“I have had depression most my life and that is my main challenge.... sticking to diet”* (Joey; 65yrs)

Quote 9: *“I was doing a Zumba class, but cause I had my knee replaced in January. I'm not doing that one currently. Probably it'll be about a year before I can get back to that”* (Sarah; 61yrs)

Strategy

Theme 4. “Flexibility as freedom”

[Participants emphasized that their success with remission was rooted in flexibility rather than strict adherence to rigid dietary or exercise rules. Many described adapting different strategies to suit their personal preferences, routines, and social contexts. They expressed that this sense of control and freedom was supported by self-monitoring tools (e.g., CGM or other similar devices), which allowed them to make sustainable, individualized choices that supported their remission goals. This flexibility also helped them manage cravings and navigate

1. Flexible and sustainable dietary choices
2. Craving control strategies
3. Flexible and varied exercise routines

Quote 10: *After approximately five weeks, I went on an almost no-carbohydrate diet....Even if you're eating low-carb stuff, like certain vegetables, you're still getting carbohydrates”* (James; 57yrs)

Quote 11: *“If I can fit everything in, great. If not, I don't stress over it. Living a low-stress life is also important for health”* (John; 45yrs)

Quote 12: *“you say, ‘oh it's all about portion size. Only have half a muffin. Who eats half a muffin?”* (James; 57yrs)

challenges in a way that felt empowering rather than restrictive.]

Theme 5. Accountability

[Participants described a deep sense of personal responsibility to their remission journey. Many emphasized that sustainable change began with taking ownership of their health. They believed this internal motivation fostered consistent lifestyle habits and a commitment to long-term behavior change.]

1. Lifestyle commitment and personal responsibility
2. Confidence in remission maintenance

Quote 13: *“Actually, just being happy in your own body is pretty much what it was and then take every little bit at a time. Start one little thing and try and work with that.”* (Mia; 68yrs)

Quote 14: *I'm 100% confident (staying in remission using lifestyle approach). Unless there's some biological reason that I can't control without pills, then I'm very confident in it.”* (Alfie; 60yrs)

Quote 15: *“I'll die before I go back into diabetes, meaning. You will have to kill me to stop me from being healthy.”* (James; 57yrs)

Theme 6. Self-Reliance

[Participants reported taking an active, independent role in managing their remission. They mentioned using glucose monitoring tools to adjust their behaviors in real time and engaging in self-directed learning through research and peer networks. This empowered approach fostered a strong sense of control and ownership over their health.]

1. Body and glucose monitoring
2. Self-directed learning and research

Quote 16: *“I do read the medical research. I go to PubMed, research clinical trials and things like that.”* (Alfie; 60yrs)

Quote 17: *“ The only thing that I cared about measuring was my carbohydrates and watching what I eat did to my blood glucose”* (Alfie; 60yrs)

Quote 18: *“I joined the [online support group name], this is where I was getting information as well.I'd then go research it a little bit more.”* (John; 45yrs)

Motivation

Theme 7. “I'd rather be healthy”

1. Positive health outcomes

Quote 19: *“The results were so fast like within a week. That really took away that fear”* (Joey; 65yrs)

[Participants described being strongly motivated by the physical and emotional benefits they experienced after achieving remission, such as improved energy, reduced pain, and mental clarity. They believed these positive outcomes reinforced their commitment to lifestyle changes. They reported that fear of future complications and reflecting on past health challenges also played a powerful role in sustaining their motivation.]

2. Motivation from fear and reflection

Quote 20: *“I did not want to go the road of taking medication every day and then eventually going on insulin shots”* (James; 57yrs)

Quote 21: *“The biggest fear would be developing diabetes again and for some reason not being able to reverse it- being stuck taking medication”* (David; 47yrs)

Theme 1: “One size doesn’t fit all”

Category 1: Non-supportive healthcare professionals

Participants voiced strong dissatisfaction with conventional healthcare systems. They felt that standard diabetes care often offered generalized, medication focused solutions. Participants frequently described the healthcare system as dismissive and overly reliant on standardized approached.

*“If you are following standard care and not seeing results,
you should have an open mind and listen to your patients
and see what they are doing” (John)*

When asked for support regarding exercise or dietary plan, they often reported receiving generic support, limited in scope and not aligned with their individual needs.

*“My doctor always said, oh you should get out for a walk’ and
he was asking a man who was 300lb and
depressed to get out and do exercise.....
the way they recommend things is wrong” (Joey; 65yrs).*

Some said that their physicians’ lack of support, and encouragement of medication use is rooted in the doubt of patient’s ability to make lifestyle changes or sustain remission. These experiences created a sense of frustration and isolation, particularly among those who felt that the healthcare system failed to acknowledge their remission goal as a viable outcome.

Category 2: Person-centred care

Participants often described that the current care model mostly focuses on managing the symptoms and on prevention of future complications instead of promoting long-term strategies aimed at remission..

*“I tried so hard to find either a nutritionist or
a dietitian who would be keto friendly.” (Joey; 65yrs)*

They also emphasized that there is a diverse path to remission and the healthcare providers should be open minded to any approaches that can put T2D into remission. The remission model needs to be personalized to individuals need and address root causes rather than merely managing the symptoms. Participants expressed a desire for structured, multidisciplinary support in remission-focused interventions, including access to dietitians, exercise specialists, and psychologists. They mentioned that achieving T2D remission requires financial stability due to the costs associated with individualized dietary approaches, gym memberships, and self-monitoring tools. However, participants described that this initial financial investment ultimately translates into both personal financial and health gains in the long term by preventing complications and frequent medical care.

*“What is going to cost me financially down the road if I'm not healthy?
A lot more....Financial costs of being sick are tremendous.
It's a lot cheaper to buy good food than it is to buy expensive healthcare stuff, healthcare aids.”
(Alfie; 60yrs)*

They viewed their remission as contributing to a reduced financial burden on the healthcare system as well, due to fewer follow-up appointments and reduced need for intensive medical management.

Category 3: Presence of support

Participants also reflected on the role of support from family, peers and healthcare professionals. While some described positive, encouraging interactions, other expressed frustration at the resistance or skepticism they encountered from people around them. In some cases, participants independently took the initiative to educate family members or even their physician about lifestyle approaches and remission potential. Participants described feeling supported when physicians took the time to listen to them and remained neutral while they shared their progress or asked questions.

*“100% on board? No, but listens, you know.
She will listen to my explanations and the research that I provide her....
she listens so she's not person that you will do it this way.
She will listen to you and then have a discussion,
and I really appreciate that.” (Sarah; 61yrs)*

Theme 2: “Healthcare not medical care”

Category 1: Skepticism toward conventional diabetes management

There was a widespread criticism among participants of dietary guidelines from diabetes associations, which were perceived as outdated or overly high in carbohydrate. Participants believe that there is a need for guideline update that can be aligned with their remission need.

*“Every year we have the same discussion,
I understand she has to because of the medical obligation....
once again, I just say...the associations just haven't caught up yet with changing guidelines”
(Sarah; 61yrs)*

Participants questioned the current guidelines and challenged whether remission was truly achievable using them. They also expressed that health information, particularly regarding food and nutrition is often conflicting and unclear.

“I would challenge them to provide data...”

*how many people they put into remission using standard guidelines?....
if it didn't work, they'd blame the patients" (James; 57yrs)*

Category 2: Over reliance on medication

Many participants expressed skepticism toward traditional diabetes care which they view as heavily medication focused.

*"The easiest thing is to prescribe medication and
tell you to watch what you eat while continuing the pill." (David; 47yrs)*

They described that the physicians place them on medication immediately after diagnosis which for some, felt abrupt and led to feelings of confusion. In some cases, this approach was perceived to have worsened their condition.

Category 3: Financial influence on healthcare

A recurring belief among participants was that profit motives influenced medical recommendations, particularly around medication and dietary guidelines. Several participants questioned whether the food and pharmaceutical industries might influence clinical and dietary advice. Some perceived that if they did achieve remission, they would no longer be profitable clients for these industries. These perceptions deepened their commitment to self-education and alternative care paths.

*"The people producing metformin and insulin
and other diabetes-related drugs don't really want you to go into remission.
I'm not a good customer for them." (James; 57yrs)*

Theme 3: "Barriers inside and out"

Participants identified a range of psychosocial barriers to achieving and maintaining remission. This included lack of social support, judgment from others for their over enthusiasm, emotional eating and motivational dips.

*"I have to actually tone back some of my enthusiasm
when I am with my family and friends, because I get annoying." (Alfie; 60yrs)*

Participants' self-reported mental health challenges like depression or anxiety further complicated efforts, especially when combined with external stressors.

*"Some days, you're having bad day and instead of walking,
I might sit down with a glass of wine and a bag of chips" (Mia; 68yrs)*

Participants described experiences such as not being included in plans or having to bring their own food to social gatherings. They emphasized that their situation is not the same as having a food allergy, so others often do not understand their dietary choices. Some participants even reported receiving judgment from their own family members.

*“I guess cause it’s not an allergy.
People don’t see it the same.
They don’t see it as severe.” (Sarah; 61yrs)*

Physical challenges such as injuries or co-existing conditions occasionally disrupted their ability to exercise or prepare meals or to stick to the dietary plans. Participants described that these setbacks required creative problem solving and increased reliance on planning or support systems to stay on track.

*“I got a shoulder injury when I was in Mexico.
I tore my tendon, and I couldn't play for a bit (talking about physical activity).” (Mia; 68yrs)*

*“Quite often you have people that are obese not always but quite often,
they have all of the problems with diabetes, aching muscles, sore joints,
all that other stuff that all those things that come with it and exercise becomes challenging.”
(James; 57yrs)*

Theme 4: “Flexibility as freedom”

Category 1: Flexible and sustainable dietary choices

Dietary freedom was described being central to participants long term success. Many described moving away from restricted dietary plans and instead developed sustainable eating patterns that fit their lifestyles.

*“I don’t need to count anything anymore...
it’s so much easier to stick to. A lot of people think it’s limiting
but I find it freeing” (Alfie; 60yrs)*

LCDS and VLCDs were most commonly used among our participants but they modified these diets based on personal tolerance, preference and social context. Planning meals ahead of time, experimenting with different diets, avoiding restrictive portion control and cooking at home were cited as practical strategies.

*“I’ll make adjustments to manage my blood, glucose as best I can in that circumstance,
so I may skip breakfast and lunch that day, and only eat dinner.
Because I know I’m going to eat much later in the day,*

or I'll change the food that I may have chosen for that meal.” (Alfie; 60yr)

They experimented with different diets and, based on their CGM or glucose readings, identified which diets were more suitable for them and felt less restrictive and more sustainable. Some individuals found satisfaction in repeating meals, while others preferred variety. Some participants mentioned returning to LCDs whenever they felt they were slipping away from their goals.

Category 2: Craving control strategies

Participants acknowledged that cravings for sugar and processed carbohydrates were difficult to overcome initially. However, many learned to manage these cravings over time through mental boundary setting, increased protein intake and avoiding trigger foods like added sugars. They also mentioned that minimizing carbohydrate intake also reduced their cravings significantly. Social environments also presented challenges and participants developed adaptive strategies such as eating before going out, choosing healthier alternatives during holidays or adjusting the subsequent meals.

*“I don’t tell myself, “I’ll never have it.” I just say, “I’ll try not to.”
That’s more convincing to my body than forbidding something outright.” (John; 45yrs)*

Category 3: Flexible and varied exercise routines

Similar to dietary freedom, exercise routines were diverse as well. Most participants described their exercise routine as walking every day for at least 15 to 30 minutes. They also adopted flexible approaches such as post-meal walks, weight training, or strength training. Some practiced structured exercises like high-intensity interval training (HIIT). While others focused on integrating various forms of movement into their daily routine, such as walking the dog, biking, or swimming. What unified their approach was the emphasis on adaptability and sustainability than strict adherence to one exercise plans.

*“Walking outside for maybe 10-15min.
There's a bit of a gym in the house as well, so there's a bike.
We have a bike in the house.
So I'll just use the bike for like, maybe 15-20 min or something sometimes.....
I don't have a formula.” (John; 45yrs)*

Theme 5: “Accountability”

Category 1: Lifestyle commitment and personal responsibility

A strong internal sense of responsibility emerged as a defining characteristic among participants. Many reflected on the moments when they chose to take charge of their health, motivated by a desire to live medication free or to avoid health complications.

*“In the end, you can’t blame anything else.
You have to take responsibility for yourself” (David; 47yrs)*

This internal drive translated into consistent behavioural changes, including being consistent with eating pattern, regular activity, and mindful routines. Several participants discussed building self-acceptance, recognizing their limits and developing the discipline needed for long term change. Participants emphasized that at the core, they are the one who needs to make the change.

“Nothing tastes as good as being healthy feels” ~ (James; 57yrs)

Category 2: Confidence in remission maintenance

Participants generally expressed high confidence in their ability to maintain remission. They believe they know how to get back to remission if they have a relapse and will sustain their remission unless there is an external factor that will make them not being in remission. Many attributed their success to consistency and a mindshift toward health ownership. Self-acceptance and emotional resilience were also noted as important factors in staying committed to remission-friendly behaviours, particularly in the absence of external guidance.

“Oh, I’m sure I will like, unless there’s some major health issue that causes me to not be able to eat certain foods or a certain way.” (Sarah; 61yrs)

Theme 6: “Self-reliance”

Category 1: Body and glucose monitoring

Participants described a highly engaged approach to monitoring their glucose concentrations and bodily responses to food, stress, and activity. Many used CGMs or finger-prick tests to identify patterns in their diet and exercise routine. They described independently monitoring how foods and exercise affected their glucose levels and adjusting their diet and activity based on these observations. This empowered them to make real-time adjustments and fostered a sense of control over their health.

*“you just put on your arm (CGM) and
then just see what you do and see what the foods you eat,
I would try different foods, and then I’d see what it would do to my numbers.” (John; 45yrs)*

Category 2: Self-directed learning and research

Due to a perceived gap in professional support, most participants turned to self-directed learning. They read books, scientific literatures, joined online support groups to learn from peers who were

in the same journey as them, listened to educational videos online from different healthcare professional.

*“I do read the medical research.
I go to PubMed, research clinical trials and things like that.” (Alfie; 60yrs)*

When asked how they determined whether the information was evidence-based, participants stated that they always checked the sources, looked for journal citations, and verified the information themselves by searching through rigorous scientific journals.

*“On PubMed...I would have looked up ‘fibre and microbiome’
so just trying to get information and
see if any studies have been done on certain topic” (John; 45yrs)*

“Vast majority of my sources..... meta-studies, RCTs, and all that...” (James; 57yrs)

This independent learning helped them make informed decisions and fostered a sense of ownership over their remission journey.

Theme 7: “I’d rather be healthy”

Category 1: Positive health outcomes

Improved health and well-being were powerful motivators. Participants described enhanced energy, better sleep, weight loss, mental clarity, and improved social confidence. For many participants, these benefits reaffirmed the value of their efforts and helped sustain their behaviour change. They mentioned that they stayed motivated due to the factor that they were seeing rapid improvement in their physical and mental function.

*I remember at about, maybe 2 weeks after I started carnivore
I could sit at the kitchen table, cross my legs comfortably,
and talk to my kids without feeling pain.
I thought wait a minute, “Shouldn’t my leg be hurting by now?” but it didn’t. (James; 57yrs)*

Category 2: Motivation from fear and reflection

Participants reported fear of future complications such as taking medication, losing an organ and not being around for their children played a significant role in initiating change. Many also reflected on past unhealthy behaviours and used those reflections as motivation.

*“I don’t want to lose a foot.
I don’t want to go blind, and I don’t want to take insulin” (Mia; 68yrs)*

“The biggest fear would be developing diabetes again

and for some reason not being able to reverse it- being stuck taking medication” (David; 47yrs)

3.4.3. Mixed Methods Findings

The purpose of the integrated findings of this mixed methods study was to explore how individuals achieved and sustained T2D remission through lifestyle interventions in real-world settings. The study began with QUAN data collection and analysis which has been previously published (13), followed by qual interviews to provide context and depth to those outcomes. The findings here are presented thematically, with integration achieved through joining displays and narrative synthesis.

Integration

To gain a more comprehensive understanding of the experiences and outcomes of individuals, the QUAN and qual findings were integrated using a meta-interference approach. This process involved interpreting the connections between statistical patterns and personal narratives to discover a better understanding of the remission process. The integration was guided by joint display methodology which allows researchers to merge and visually compare data types in meaningful way (23). Through this approach, key domains of lifestyle modification and remission such as weight loss, diet, exercise, education, behavior or mindset, quality of life and system level factors were used to frame the synthesis. This domain was synthesized based on the existing literature on T2D remission that solely focuses on lifestyle interventions (6,7,11,29,30). This strategy aligns with best practices in mixed methods research where drawing meta interferences supports a richer interpretation of complex phenomena (28). The joint display (Table 3.4) presented below illustrates convergence and divergence of findings and how lifestyle behaviours and structural influences interacted to support or challenge the T2D remission journey.

Meta-interference findings

Table 3.4. Joint display of integrated findings

Domain	Quantitative Result	Qualitative Finding	Quote	Meta-Inference	Meta-Inference Type
Weight loss	16 (74%) participants reported intentional weight loss.	Participants mentioned that the desire to improve both physical and mental health, regain their energy, and enhance overall quality of life motivate them. Many were motivated by the fear of diabetes complications and dependence on lifelong medications, alongside encouragement from visible health improvements. This behavioural change was supported by self-directed learning and actively engaging in research. They developed personal strategies through ongoing self-monitoring of diet, blood glucose responses, and exercise impacts. Theme: “I’d rather be healthy” and Self-Reliance	[Quote 16-21]	Participants intentionally lost weight as part of a self-driven effort to improve their health and achieve T2D remission. This reflects self-education, awareness of the link between weight and glycemic control, and motivation to make lasting lifestyle changes. Moreover, this finding reflects that weight loss was a thoughtful, active, and knowledge-based process, not an incidental outcome of remission in the study participants.	Convergence
Education	Out of 21 participants, 7(33%) had university,	Participants engaged in self-education through books, online	[Quote 16-18]	Many participants were self-taught and used their	Convergence

4(19%) PGDs, 7(33%) college and 3(14%) had high school degree.

platforms, support groups, family, and learning from observing their own body. This initiative reflected a drive for personal empowerment and autonomy in managing diabetes.

education and digital literacy to make informed decisions, compensating for a perceived lack of guidance from the healthcare system.

Theme: Self-Reliance

Diet	14(66%) participants reported following VLCD/LCDs, 4(19%) eating healthy, 2(10%) followed a meal replacement diet, and 1(5%) was following a Weight Watcher's diet. Available CGM data showed average glucose concentration was 5.0 [4.8–5.6] mmol/L with more than 90% of the time spent in range. Participants following LCDs and keto/carnivore diet had the lowest average glucose and variability among all the dietary types.	Participants expressed strong preferences for low-carb, whole, unprocessed foods. They resisted portion control and restrictive models, preferring sustainable, simple meals. Many avoided sugar to reduce cravings and gain better control. They tailored meals to fit their cravings, physical needs, and lifestyle. Theme: “Flexibility as freedom”	[Quote 10-12]	Participants who achieved remission developed personalized routines tailored to their lifestyle, preferences, and physical needs. This alignment reflects that flexibility, not restriction was foundational to their success and sustainable dietary behaviour.	Convergence
Exercise	The Godin-leisure time score showed that	Exercise routines were flexible and self-paced, including	[Quote 10-12]	A flexible and adaptive exercise regimen, especially	Convergence

majority of the participants 16(76%) were active (score ≥ 24).

walking, HIIT, strength training, and post-meal movement. Participants emphasized building consistency over intensity, and adjusted plans based on energy levels and time.

Theme: “Flexibility as freedom”

walking supported long-term adherence to physical activity goal. Gradual integration of physical activity became part of daily life and promoted sustained glycemic improvements.

Mindset & behavior	Participants showed moderate conscious control over their eating (cognitive restraint score 9.0 [5.5–11.0]). They had low tendencies to overeat impulsively (disinhibition score 6.0 [1.0–7.5]) and low hunger-driven eating score 3.0 [0.5–4.0].	Participants described increased self-awareness, internal motivation, and discipline. They emphasized personal responsibility, routine building, and habit change. Mental strategies such as food boundaries, social adjustment, and structured planning were key to maintaining change. Theme: “Accountability” and Self-Reliance	[Quote 13-18]	A strong mindset rooted in accountability and consistency supported lasting behavioural change. Participants reframed their relationship with food and viewed their lifestyle as a long-term commitment rather than a temporary fix.	Convergence
Quality of life	The overall health-related quality of life, as measured by the EQ-5D-5L index score was 0.86 [0.79–0.93]. This score reflects a generally good perceived health status. The self-rated health status, assessed on a	Participants reported better physical, mental, and emotional well-being. Improvements in energy, appearance, and confidence were frequently mentioned. Social interactions and body image improved alongside health markers which	[Quote 19-21]	Participants linked lifestyle changes directly with improved quality of life. These improvements served as powerful motivators that reinforced lifestyle adherence and strengthened confidence in sustaining remission.	Convergence

visual analog scale from 0 (worst health) to 100 (best health), yielded a score of 80 [76.5–88.5], indicating that participants perceived their overall health positively.

gave them a positive feedback to changes.

Theme: “I’d rather be healthy”

Support	Quantitative data showed a high score of good perceived health status. Family support was ranked 4th out of 4 factors in remission contribution.	Participants shared complex social, psychological, and physical barriers that challenged their journey toward T2D remission. Social barriers included judgment from others when making dietary and lifestyle changes, often leading to feelings of isolation. Participants also faced internal struggles such as food cravings, low motivation, and mental health challenges like stress and depression. Physical barriers, including pre-existing conditions and plateaus in weight loss added further difficulty. Theme: “Barriers inside and out”	[Quote 7-9]	There were mixed findings related to support and barriers. While participants reported social and family barriers that aligned with the quantitative results, the findings related to psychological and physical challenges diverged between the quantitative and qualitative data. Participants reported feeling generally healthy, their qualitative accounts reveal an internal-external tension: feeling well yet facing ongoing struggles that threaten long-term sustainability. These multifaceted barriers also highlight that good perceived health status does	Convergence & Divergence
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				not necessarily equate to an absence of obstacles in remission efforts.	
Healthcare	13(62%) participants reported having a generic dietary counselling at the time of their T2D diagnosis. Healthcare support was ranked 3rd out of 4 factors in remission contribution.	Healthcare was often described as dismissive, non-personalized, and generic. Participants felt conventional care did not support their remission goal. Some turned to naturopaths, online communities, or self-education. Others expressed frustration with perceived outdated guidelines and lack of support for alternative approaches. Theme: “Healthcare, not medical care” and “One size doesn’t fit all”	[Quote 1-6]	Participants desire for more collaborative, patient-led, and open-minded healthcare models and ranking healthcare as 3 rd in the contributing factor suggests that the current healthcare framework may not align with the evolving needs of individuals seeking remission through lifestyle changes.	Convergence

The quantitative data used for this analysis are the same data used for Marcotte-Chénard et al (13); The data presented here are in median [IQR]. PGD (Post Graduate Degree), VLCD (Very Low Carbohydrate Diet), LCD (Low Carbohydrate Diet), CGM (Continuous Glucose Monitor), HIIT (High Intensity Interval Training)

3.5. Discussion

The findings of this mixed method study offer valuable contribution to the growing body of research on sustainable T2D remission that highlights the importance of individualized approaches, patient empowerment and system level factors in shaping health outcomes. Interestingly, although the qualitative subsample was purposefully selected from two glycemic pattern groups based on glucose variability (low vs. high) from the CGM data with the intention of exploring potential differences in experiences between these groups, the findings were ultimately presented collectively. This decision was based on the observation that the emergent themes were very consistent across participants, regardless of glycemic variability. One possible explanation is that all participants were already in remission as indicated by HbA1c levels below the diagnostic threshold for T2D ($\leq 6.5\%$) so the high and low variability within remission may not be that impactful. Additionally, the variability in the CGM data can be strongly influenced by artifacts such as sensor physical compression that creates glucose readings that may appear low but are not real or clinically significant. However, the consistency of themes across the low and high glucose variability groups is noteworthy and suggests shared experiences among individuals who have successfully achieved and maintained remission.

Individualized pathways to T2D remission

One of the central findings of this study was the considerable heterogeneity in participants dietary and exercise strategies which supports the overreaching theme “one size doesn’t fit all.” Quantitative data revealed that while LCDs or VLCDs were commonly associated with lower mean glucose, participants adopted and adapted these approaches in diverse ways to suit their preferences, tolerance and lifestyle. This was demonstrated through high TIR values, low glucose variability and participants own narratives. These findings are consistent with previous clinical studies on lifestyle interventions where they implemented an intervention with different dietary and exercise approaches (6,7,9,10). Qualitative insights further contextualized these findings by showing how participants navigated and personalized their dietary choices based on CGM feedback, perceived cravings and social environments. This self-experimentation stresses the importance of biofeedback and self-efficacy in promoting sustainable behaviour change. Here, biofeedback refers to participants’ independent observation of how their food intake and exercise affect their glucose levels, using tools such as CGM or other glucose measurement devices. They used this real-time information to adjust and tailor their lifestyle and behaviors accordingly. Importantly, participants emphasised that rigid dietary or exercise programs were not sustainable long term, and that flexibility and autonomy played crucial roles in remission maintenance. The literature supports this finding where personalized dietary approaches such as tailored low-energy or LCDs has shown higher remission rates than generic dietary advice (31). These approaches consider individual needs, preferences, and responses to specific foods or macronutrient compositions (31–33).

The role of self-education and accountability

A key emergent theme of this study was participants proactive engagement in self-monitoring and learning. Many described a self-directed approach to understanding how food, exercise, stress and sleep influenced their glucose outcome. Quantitative measures showed strong glycemic outcomes and stability which participants attributed to their self-monitoring and adaptation of their routines. Self-motivation and accountability are key psychological factors in achieving and sustaining T2D remission. They also influence how individuals manage lifestyle changes and overcome barriers in their remission journey. Higher self-motivation and a sense of accountability are linked to better self-management, improved health outcomes, and may lead to greater likelihood of remission (34). This finding also aligns with the self-determination theory (SDT) (35), which shows that autonomy and competence are critical for sustained motivation. The strong sense of accountability and health ownership observed in participants are the factors that are associated with long term success (36,37). When healthcare professionals encourage individuals to make their own choices and support their values, they felt more in control. This autonomy support increases individuals sense of ownership over their health behaviours, leading to more sustained lifestyle changes (37). Similarly, individuals who are motivated by personal values and internal goals rather than external pressure or guilt, are more likely to stick with healthy behaviours, diet and exercise, which are crucial for remission (38).

Perceived healthcare gaps and structural barriers

Despite achieving remission, many participants reported significant dissatisfaction with conventional healthcare systems. Categories such as “non-supportive healthcare professionals” and “skepticism toward conventional diabetes management” highlight a disconnection between patient experiences and current healthcare delivery models. Participants frequently described their remission goals as being dismissed or unsupported by clinicians, particularly in favour of standardized, medication focused care. These findings are congruent with critiques in the literature that question the alignment of current guidelines with real world remission outcomes where remission is often seen as motivational, but not always as a primary clinical goal.

In a qualitative study on physicians’ perspective on T2D remission in primary care, many primary care professionals mentioned viewing remission as a motivational tool but are skeptical about its long-term impact on clinical management. They cited concerns about relapse, ongoing cardiovascular risk, and the need for continued follow-up even after remission is achieved (39). There is reluctance to formally code remission in medical records due to fears of patient loss to follow-up and the perception that remission is often temporary. Professionals worry that focusing remission support on more motivated or affluent individuals could worsen health inequalities. Clearer guidance and evidence are needed to make remission support a clinical priority (39). This perception of many healthcare professionals that T2D diagnosis is irreversible, and remission is

only temporary was also reflected in our participants' experiences and perception, as many felt that their healthcare providers doubted their capability to achieve and maintain remission (22).

Additionally, participants raised concerns about the influence of the pharmaceutical and food industries on medical guidance, as well as the lack of multidisciplinary, person-centred care. Participants often mention that the healthcare providers are not adequately trained or do not have enough resources to guide individuals who seek T2D remission which are consistent with the previous findings in the qualitative study of DiRECT trial (40). The healthcare professionals included in this study mentioned that having a structured program helped them better support the individuals and resulted in positive outcomes (40). The participants in this study highlighted that the involvement of their healthcare professionals motivated them to participate in the DiRECT trial (40). This highlights an urgent need for healthcare systems to acknowledge that T2D remission can be a viable clinical goal and need to provide an integrated, supportive care pathway for both patients and healthcare professionals.

Social and psychological dimensions

The study also illustrated the psychological complexity of sustaining T2D remission. While quantitative data showed generally good quality of life and low stress levels, qualitative findings revealed ongoing social and emotional challenges. Participants reported feelings of isolation, judgement from peers and family, and struggles with mental health and motivation. These social barriers are often overlooked in clinical practice but may significantly influence the sustainability of lifestyle changes (12). This finding also points to a divergence between perceived health metrics and lived experiences which suggest that current quantitative measures may not fully capture the psychosocial burdens associated with long term remission and quality of life. The theme “barriers inside and out” emphasizes the need for psychosocial support as a critical component of future remission care (12,42). This domain not only addresses the gap in the literature on barriers of T2D remission but also raises an important question for future research, “how social support and mental health interventions can be tailored to sustain remission over time?”

3.5.1. Key take aways from meta-inference

- Flexibility was a consistent and strong theme across both qualitative and quantitative findings.
- Personalized, adaptable approaches were more sustainable than restrictive or prescriptive ones.
- The ability to experiment and tailor strategies based on those biofeedback helped them stay consistent and committed.
- Motivation was also reinforced by visible health improvements and a sense of control over their condition.

- A notable perceived gap exists between the person and the healthcare providers regarding the recognition and support of T2D remission.
- VLCD/LCDs or carnivore-style diets and regular walks were perceived as most effective when adapted to personal needs.

3.5.2. Strengths and Limitations

This study adds to the growing recognition that T2D remission is both possible and sustainable through individualized lifestyle interventions in real world settings. A major strength of this study lies in its mixed methods design, which enabled a holistic exploration of both clinical outcomes and patient perspectives. The integration of CGM data with rich qualitative narratives provides nuanced insight into the complexity of achieving and maintaining remission. This is the first study to our knowledge to explore CGM data in T2D remission lived experience individuals. However, the study also has limitations. A limitation of this study was the relatively small sample size and selected participants for the qualitative component. However, this size of sample was sufficient to fulfil the aim of this study and to capture the barriers and facilitators in the remission process. This sample also lacked diversity in terms of ethnicity, socioeconomic status, and geographic location. Sociocultural factors may influence dietary preferences, access to care, and perceptions of health and remission and the insights may not be fully transferable to populations with different cultural, educational and economic backgrounds. To partially address this limitation, our study participants were recruited from two different provinces in Canada. Although CGM data added valuable insights, the interpretation of hypoglycemia may not accurately reflect true clinical risk. Given that none of the participants were on glucose-lowering medications known to cause hypoglycemia, these findings may reflect physiological adaptation rather than clinically meaningful hypoglycemia. It may also reflect sensor limitations such as compression lows or arbitrary threshold cutoffs, rather than clinically meaningful hypoglycemia. Additionally, the study relied on retrospective accounts of participants' experiences with T2D diagnosis, remission strategies, and lifestyle changes. This may introduce recall bias, as participants could unintentionally simplify past events, particularly when reflecting on emotional or complex periods of their remission journey. To mitigate this limitation, the HbA1c values, CGM data, and 3-day dietary records were incorporated into the analysis. Another limitation was that although the qualitative subsample was purposefully selected from two glycemic pattern groups based on CGM data, the final analysis did not separate the findings by group because the emergent themes were consistent across participants. This may overlook subtle differences in experiences between groups. In addition, the exclusive focus on participants who achieved remission and could not capture the perspective of individuals who may attempted but did not succeed in sustaining remission. Their experiences could offer important insights into the barriers and limitation of remission process. The future research can address this gap by including these individuals and by exploring their perspective.

3.6. Conclusions

Our study findings suggest that T2D remission is not only related to diet and exercise, but also on self-efficacy, system level support and socio-emotional resilience. For the healthcare systems to effectively support remission, it is timely to think beyond a “one-size-fits all” model and toward patient-centered care that empowers individuals through education, autonomy and holistic support.

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Chapter IV

Overall Conclusions

4.1. Study Summary and Relevance to Practice

The findings of the present study reinforce that T2D remission may not only be possible but can be an achievable outcome for some individuals. This research showed that the strategy of achieving and sustaining remission is rooted in personalized, flexible patient empowerment (1). The mixed method findings also demonstrated that participants experienced both clinical improvements and enhanced quality of life. However, they also faced complex psychological and systemic barriers that are often overlooked in traditional care models (2).

Current clinical guidelines largely emphasize on glycemic control through pharmacological interventions and general lifestyle advice. As a result, remission is often viewed as temporary or secondary, rather than a sustainable and achievable goal through individualized lifestyle interventions (3). This can easily lead to perceived barriers in healthcare for many individuals who see T2D remission as a goal. In contrast, this study acknowledges T2D remission as a valid and sustainable outcome in motivated individuals. This recognition aligns with existing clinical evidence advocating for lifestyle interventions as a successful approach, (4–9) as well as with the participant narratives shared in this study.

This study further acknowledges, in line with existing literature that T2D remission may not be achievable for every individual with T2D even with strong behavioral efforts. Many participants in this study had already achieved remission at the time of data collection and described a strong personal commitment to lifestyle changes. They were also generally health-literate and engaged in self-education, which may not reflect the broader T2D population. However, it should be considered as a management option alongside existing treatment strategies and presented to patients as part of shared decision-making, empowering them with informed choices and to provide a greater sense of control over their condition. Yet, this acknowledgement leads to a question for future research and policy changes. “While this group of individuals may represent a small subset of the overall population with T2D, how well are their choices and approaches supported within current models of diabetes care? Are existing systems equipped to recognize and meet the needs of individuals who achieve remission outside of conventional pathways?”

If remission is achievable for some, health systems should consider where and how these individuals are accounted for in clinical guidelines, funding decisions, and long-term care planning to maintain inclusivity and individualized care in chronic disease management. This approach has the potential to reduce the perceived healthcare gap and systemic barriers between individuals with T2D and healthcare providers as well (10).

4.2. Future Directions

Based on the findings, this study presents a few key future implications. (i) Incorporating CGM and patient-led data interpretation into routine care may enhance individuals' ability to make real-time decisions about food, exercise, and medication. This echoes findings from emerging studies that highlight the effectiveness of CGM not only for glycemic control but also for increasing patient engagement and self-efficacy (11), (ii) The development of structured, flexible dietary and physical activity approaches co-designed with individuals which will prioritize their autonomy over uniformity, (iii) The study highlights the importance of recognizing the broader context in which individuals attempt remission. Barriers such as the monthly cost of CGM, gym memberships, and limited access to psychosocial support must be factored into intervention design. Future policy should aim to reduce financial barriers to remission-supportive resources, and (iv) Inclusion of remission as a formal goal for highly motivated and suitable individuals in clinical practice. This also require equipping healthcare providers with the appropriate training and resources to support this outcome. Future research should focus on scaling these approaches, evaluating their cost-effectiveness, and exploring system-level changes which is required to operationalize person-centered remission care in diverse healthcare settings.

4.3. Final conclusions

This research highlights the necessity of moving beyond pharmacological maintenance toward holistic and individualized care that supports remission as a realistic and empowering outcome for people with T2D.

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Appendixes

Appendix 1. Health Screening Questionnaire

Page 1

Health Screening Questionnaire

Thank you!

- 1) Age _____
- 2) Gender ☐ Male
☐ Female
☐ Non-binary
☐ Other
- 3) Self reported weight _____
(kg or lbs)
- 4) Self reported height _____
(in/ft or cm/m)
- 5) Last grade of school completed: _____
(e.g. high school, university)
- 6) Marital status ☐ single
☐ married
☐ divorced
☐ widowed
- 7) Occupation: _____
- 8) Work hours: _____
(eg. 40 hours/week, 32 hours/week)
- 9) Do you have any special dietary needs and/or observances? ☐ Yes
☐ No
- 10) If yes to above, which ones? _____
- 11) What is your current medical history?
E.g. hypertension, migraines, angina

(e.g. hypertension, migraines, angina)
- 12) What is your past medical history?
E.g. heart attack 5 years ago

- 13) Do you have familiar history of chronic diseases? ☐ Yes
☐ No

- 14) If yes to the previous question, which ones? ☐ Diabetes Mellitus
☐ Heart disease
☐ Dyslipidemia
☐ Hypertension
- 15) Please list all medications you are currently taking including over-the-counter products such as vitamins and mineral supplements. If possible, list the doses of the medications you are taking. _____
- 16) Do you have any allergies? If yes, please list what allergy and the type of reaction.
E.g. anaphylaxis with peanut butter _____
- 17) Do you smoke? If yes, how many packs per day do you smoke? ☐ Yes
☐ No
- 18) Have you ever smoked in the past? If yes, how many packs per day did you smoke? ☐ Yes
☐ No
- 19) When was your last physical examination? _____
- 20) How often do you see your family doctor? ☐ once a week
☐ every two weeks
☐ once a month
☐ every 3 months
☐ twice a year
☐ over a year
- 21) Have you been hospitalized within the last 12 months? ☐ Yes
☐ No
- 22) If "yes," describe what happened: _____
- 23) How many times do you eat per day? ☐ once a day
☐ twice a day
☐ three times a day
☐ four times a day
☐ more than four times a day
- 24) What are the usual times of meals? _____
- 25) Who does the cooking? _____
- 26) Who does the grocery shopping? _____

- 27) How many times during the week do you eat away from home?
☐ once
☐ twice
☐ three times
☐ four times
☐ more than four times
- 28) Do you have a current meal plan? If so, what is it?

- 29) What is your biggest challenge to eating healthily?

- 30) Have you ever received diet counseling
☐ Yes
☐ No
- 31) If "yes," describe:

- 32) Have you ever taken appetite suppressants? If yes, choose from the list.
☐ Amfepramone
☐ Sibutramine (Meridia or Reductil)
☐ Topiramate or Bupropion (Welbutrin)
☐ Liraglutide or Semaglutide (Saxenda or Ozempic or Rybelsius)
☐ Tirzepatide (Mounjaro)
☐ None the above;
- 33) When was your last significant weight change?

(E.g. 3 months ago, 1 year ago, 2 years ago)
- 34) Was the weight change intentional?
☐ Yes
☐ No

Appendix 2. Remission Survey

Page 1

Remission Survey - Lifestyle Intervention

Please complete the survey below.

Thank you!

Do you have a family history of type 1 diabetes, type 2 diabetes, or gestational diabetes?						
	Sibling	Parent	Grandparent	Cousin	Aunt/Uncle	No family history

Select from the following choices:	☐	☐	☐	☐	☐	☐
------------------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

What medications were you taking for your diabetes?					
---	--	--	--	--	--

	Metformin	Acarbose	Sulfonylureas (gliclazide, glyburide, glimepiride)	DPP-IV Inhibitors (Trajenta, Onglyza, Januvia)	GLP-1 Agonists (Trulicity, Victoza, Ozempic)
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Select from the following choices:	☐	☐	☐	☐	☐
------------------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

What medications were you taking for your diabetes? (Continued)				
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	SGLT2 Inhibitors (Jardiance, Invokana, Forxiga)	Repaglinide	TZDs: pioglitazone, rosiglitazone	Insulin
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Select from the following choices:	☐	☐	☐	☐
------------------------------------	--------------------------	--------------------------	--------------------------	--------------------------

Rank from 1-4 (as 1-most important and 4-least important). What were the contributing factors in putting your type 2 diabetes in remission?				
	Change in diet	Change in exercise	Support from health care team	Family support

1 (most important)	☐	☐	☐	☐
2	☐	☐	☐	☐
3	☐	☐	☐	☐
4 (least important)	☐	☐	☐	☐

If there were other contributing factors in the above question, please indicate the contributing factors here

If you changed your diet, what kind of diet was it?

- ☐ Low-carbohydrate diet
- ☐ Very-low carbohydrate diet or Ketogenic diet
- ☐ Low-calorie diet
- ☐ Low-calorie diet using meal replacement products
- ☐ Mediterranean diet
- ☐ others

Please describe "Other":

Rank from 1-4 (1-most important and 4-least important). What factors made it difficult to achieve type 2 diabetes remission?

	Maintaining dietary changes	Maintaining physical activity changes	External stressors	Lack of support from health care team	Give up medication
1 (most important)	☐	☐	☐	☐	☐
2	☐	☐	☐	☐	☐
3	☐	☐	☐	☐	☐
4 (least important)	☐	☐	☐	☐	☐

If there were other factors to the above question, please indicate them here.

If you selected Lack of Support from Health Care Team as 1 or 2, please also indicate which health care professionals (pharmacist, physician, dietitian, etc)

When did you achieve diabetes remission? (please put an approximate date, month/year)

Have you used any glucose medication since then?

- ☐ Yes
☐ No

How are you currently maintaining remission?

How would you describe your current diet while maintaining remission?

- ☐ Very-low carbohydrate diet or Ketogenic diet
☐ Low-calorie diet
☐ Low-calorie diet using meal replacement products
☐ Mediterranean diet
☐ Others

Please describe "Other":

What methods do you use to monitor your blood glucose?

- ☐ finger prick devices (e.g. One Touch, Accu-chek, Contour)
☐ continuous glucose monitoring sensors (e.g. FreeStyle Libre, Dexcon)
☐ regular laboratory exams
☐ I do not monitor my blood glucose

For how long have you been using any of the methods cited above?

- ☐ 3 months or less
☐ 3-6 months
☐ one year
☐ more than 1 year
☐ I don't use any of the methods

If you don't use any of the methods above, or if you use them and think they are challenging, what are the main concerns?

- ☐ too expensive
☐ uncomfortable and invasive
☐ the app and technology is difficult to understand
☐ difficulty in finding them for purchase
☐ they are not helpful to monitor my glucose
☐ I have no challenges

What is your strategy when your HbA1C or blood sugar trends up?

Which members of your health care team did you contact regarding remission?

Select from the following choices:

Doctor ☐ Pharmacist ☐ Dietitian ☐ Nurse ☐ Naturopath ☐ Other ☐ None ☐

If you selected any health care professionals from above, please describe the conversations you had with them

Rank from 1-6 (1-most important and 6-least important). What health professional was mostly involved in your remission process: pharmacist, physician, dietitian, health-coach, nurse, chiropractor

	Pharmacist	Physician	Dietitian	Nurse	Chiropractor	Health-coach
1 (most important)	☐	☐	☐	☐	☐	☐
2	☐	☐	☐	☐	☐	☐
3	☐	☐	☐	☐	☐	☐
4	☐	☐	☐	☐	☐	☐
5	☐	☐	☐	☐	☐	☐
6 (least important)	☐	☐	☐	☐	☐	☐

Appendix 3. How are you currently maintaining remission?

Participant ID	Maintaining remission
1	stick to the carnivore way of life
2	Dinner : plate method: 1/2 plate veggies. 1/4 plate good carbs 1/4 plate protein plus dairy chose n fruit choice inside. Secondly MOVEMENT ACTIVITY! Line dancing 1x week dragonboating 2x week longer walk 1 yr min) 1x week
3	Diet and exercise
4	Ketovore diet is number one. I've maintained the same level of activity as I have for years. Walking and yoga several times per day, Ukrainian Dance 3x/week, and soccer 2x/week.
5	Paying attention to the foods I am eating
6	Trying keep my diet and doing exercise
7	So far I've had 3 years of diet based remission
8	carnivore diet, intermittent fasting, exercise
9	Diet. Trying to ensure my fat intake (specifically saturated fats) are as low as possible.
10	Maintain diet changes, increase physical activity, manage stress
11	Self-discipline on eating habits; regular and vigorous exercise. (I am an avid cyclist plus I walk my German Shepherd dog several times a day.) I monitor my weight daily!
12	By genuinely wanting to live a healthy life for my children and myself
13	Low carb, 1 or 2 meals per day
14	Following specific way of eating. Low carb high protein no sugar. Also exercise every day.
15	Avoiding sugar and watching carb intake
16	Diet, minimal exercise.
17	Yes
18	Trying to eat healthy. Staying away from processed food. Finding it difficult to maintain activity due to shoulder/arm pain.
19	Diet and exercise.
20	Yes as per January 2024 hbA1c of 5.8.
21	Maintaining regular healthy diet and approx 2 hours walking daily.

Unedited answer

Appendix 4. What is your biggest challenge to eating healthy?

Participant ID	Challenge to eating healthy
1	I never eat out, and when we have guests for dinner I have already eaten
2	Actually that! Eating healthier. Veggies. I need to consume more!!
3	emotionally binge eating, salty sweet snacks.
4	Carb addiction and societal pressures.
5	When I get busy I have no set schedule and if there is snacks I will snack all day. I struggle with sugar.
6	Increase veggies in my diet
7	The time it takes to meal prep combined with the cost of food and finding ingredients with no added sugar.
8	Social events, sometimes a restaurant
9	I used to eat lots of junk food and lots of cheese. The challenge was stopping those
10	busy schedules
11	eating healthy is expensive
12	maintenance
13	addiction to sweets/carbs
14	Ensuring I get to the grocery store to have fresh produce available
15	time
16	Occasional cravings
17	Cost of food
18	Bread. Chips and sometimes cookies or sweets. I like a glass of wine or 2 but usually only have wine on Sundays as I have the family over for dinner
19	I like my carbs
20	the time it takes to prepare whole food. 2nd is difficulty eating outside of home.
21	Time

Unedited answer

Appendix 5. Supplementary figures

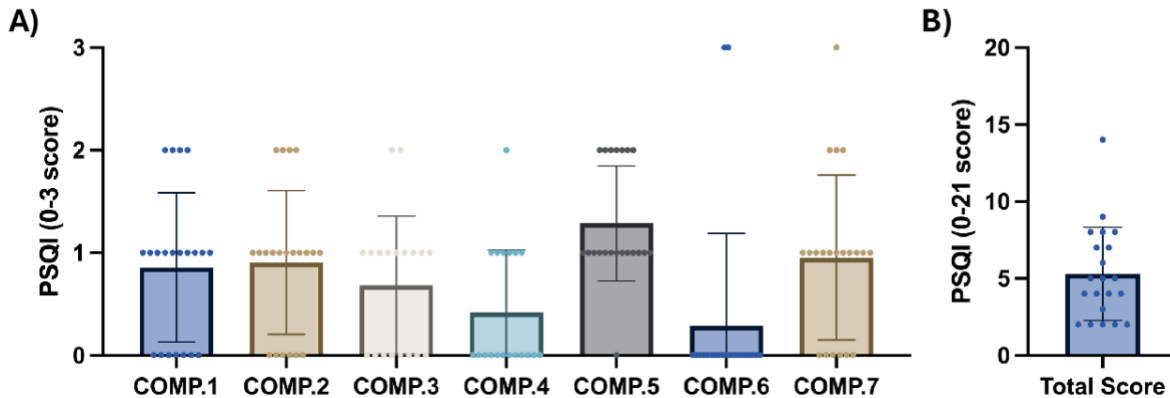


Figure S1. Sleep quality assessed with the Pittsburgh Sleep Quality Index

Results are presented as mean $\pm$ SD; A) 7 components of the PSQI ranging from 0 to 3; B) Global sleep quality score ranging from 0 to 21, where a higher score indicates a worse sleep quality; COMP.1= Subjective sleep quality; COMP.2= Sleep latency; COMP.3= Sleep duration; COMP.4= Sleep efficiency; COMP.5= Sleep disturbance; COMP.6= Sleep medication.

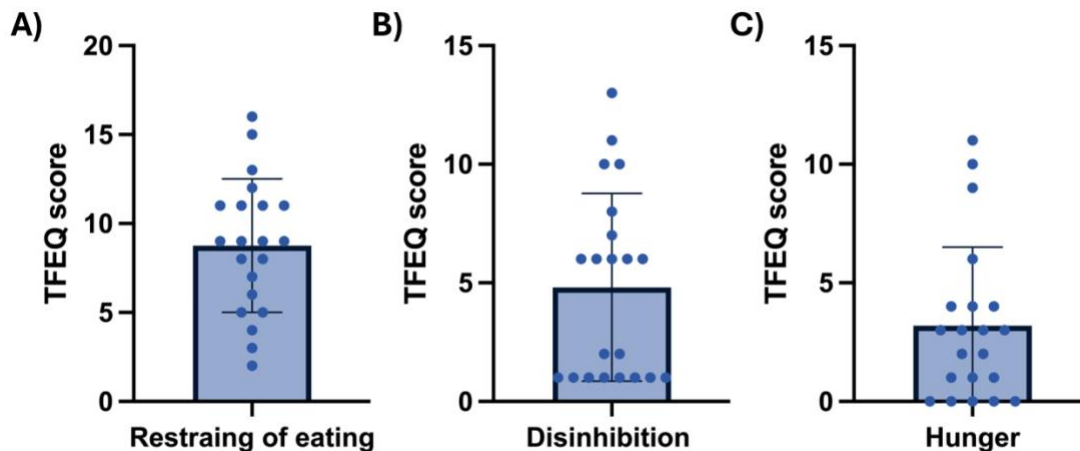


Figure S2. Three factors eating questionnaire components.

Data are presented as mean $\pm$ SD; A) Cognitive restraint of eating; B) disinhibition; C) Hunger

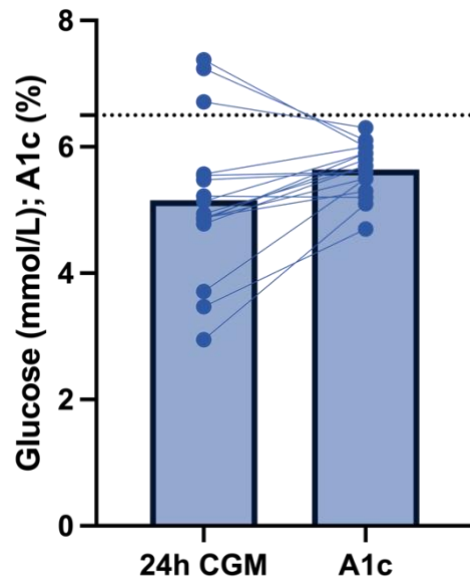


Figure S3. 24h CGM glucose average in relations to A1c

Data are presented as mean and individuals data point; dotted line represent the 6.5 % threshold for T2D remission.

Appendix 6. Continuous glucose monitoring outcomes

Variables	24h	Diurnal	Nocturnal
Data availability (days)	13.2 ± 2.0	NA	NA
Average glucose (mmol/L)	5.2 ± 1.2	5.3 ± 1.2	4.8 ± 1.1
SD	1.00 ± 0.37	1.00 ± 0.40	0.71 ± 0.27
CV (%)	19.0 ± 4.4	18.6 ± 4.6	15.0 ± 4.4
eA1c (%)	4.88 ± 0.73	NA	NA
Min glucose (mmol/L)	2.7 ± 0.6	2.9 ± 0.8	3.1 ± 0.8
Max glucose (mmol/L)	9.1 ± 2.7	9.0 ± 2.6	7.3 ± 2.3
MAGE	2.45 ± 1.09	2.5 ± 1.1	1.7 ± 0.84
Time in range (3.9-10 mmol/L; %)	81.3 ± 27.2	82.6 ± 25.9	77.7 ± 32.6
Time in tight range (3.9-7.8 mmol/L; %)	76.4 ± 26.2	76.6 ± 25.7	76.0 ± 31.8
Time below range (< 3.9 mmol/L; %)	17.5 ± 27.8	15.9 ± 26.6	22.2 ± 32.7
Time below range (lvl.1: 3.0-3.9 mmol/L; %)	11.8 ± 17.9	11.8 ± 19.4	11.8 ± 15.7
Time below range (lvl.2: < 3.0 mmol/L; %)	5.7 ± 13.9	4.1 ± 11.3	10.4 ± 23.5
Time above range (> 10.0 mmol/L; %)	1.2 ± 2.9	1.6 ± 3.8	0.2 ± 0.4
Time above range (lvl.1: > 10.0-13.9 mmol/L; %)	1.2 ± 2.9	1.5 ± 3.8	0.2 ± 0.4
Time above range (lvl.2: > 13.9 mmol/L; %)	0.01 ± 0.4	0.01 ± 0.05	0.0 ± 0.0

Data are presented as mean ± SD; n=17; SD= standard deviation; CV= coefficient of variation; MAGE= mean amplitude of glycemic excursions; lvl= level; NA= not applicable.

Appendix 7. Interview Guide



a place of mind
THE UNIVERSITY OF BRITISH COLUMBIA



Title: Putting Type 2 Diabetes into Remission: Developing a person-centered, interdisciplinary nutrition intervention

Interview Guide

Hello NAME, my name is [Name of interviewer] and I am a member of the research team carrying out the T2D Remission cohort study.

Everything we will talk about is confidential and will be de-identified. This means that your identifying information, such as your name and places which could be used to identify you, have been removed from the transcripts, and only [Redacted] (the PI of this study) and [Redacted] (a postdoctoral scholar conducting the research), [Redacted] (Collaborating Professor) and students/staff from University of Manitoba will be able to look at the content of the interview for the purposes of analysis. Feel free to interrupt me with questions if you have any. You can stop the interview or withdraw completely at any time without giving any reason.

Zoom is the leader in modern enterprise video communications, with an easy, reliable cloud platform for video and audio conferencing, collaboration, chat, and webinars. Zoom allows for video, audio, and screen sharing between participant and research team. UBC's Zoom license has a Canadian hosting services, the Cloud recording is now active and will be stored on-line until it is moved to a UBC secure drive. You can protect your identity and increase your protection of personal information by not using your actual name in Zoom. You can do this by: using only a nickname or a substitute name when logging into the Zoom meeting link. You will receive an automatic notification when recording is enabled. The recordings will be moved from the server and stored in UBC's secure drive in a UBC configured computer accessed only by individual password from the researchers ([Redacted]) which is located in [Redacted] with limited access by coded card. The following Zoom security measures will be used • Meeting links will not be shared on social media or public outlets • Personal Meetings ID (PMI) will not be used and there will be no hosting of public events • Manage Screen Sharing - there will be no screen sharing and that function will be disabled • Lock the meeting – the meeting will be locked and it will be a one-on-one meeting only • The video will be on due to protocol requirements.

We will record this meeting so that I can go back to what we will have talked about. Do you consent to this recording? [participant answers yes or no] Thank you. Please make yourself comfortable as this will be a very informal conversation with duration of 30-60 minutes. If you are comfortable with this, the following interview will be done through this Zoom video call. Shall we start?

First of all, I would like to be clear about what the term diabetes remission means. No worries if you have never heard of it as it is rather recent and still not 100% defined by health organizations. That's why there is also another term such as reversal, which means an A1c below 6.5% with no glucose lowering medications except for metformin. But, for the sake of our study, we are going to use the definition given by the American Diabetes Association that diabetes remission means having an A1c lower than 6.5% and using no glucose control medications for at least 3 months. Do you have any questions you would like to ask about this?

Description: Type 2 Diabetes Remission Cohort; Study Number: [H22-00478]
Version 4 June 6, 2023



Okay, so now I will start with our conversation. Feel free to add any information you would like to..

- a) To start things off can you discuss how you knew you were in diabetes remission?

Probe for family doctor, specialist, other health care professionals

- b) When did you first notice that your blood sugar had stabilized? How long did it take you to achieve remission?
- c) What have you done to learn and inform yourself about living in remission?

Probe for websites, doctors, friends, family, other people who also achieved remission.

- d) Did you ever share information found on your own with your health care team?

If yes, can you describe the types of information you shared and your reasons for sharing?

If no, can you discuss the reasons for not sharing the information?

- e) What actions have you taken, if any, to facilitate your diabetes remission?
- f) What inspired you to take these actions?
- g) Has your quality of life changed since achieving remission? How? Can you please tell me more about this?

Each action described by the participants (e.g., diet, exercise, etc.) should be investigated thoroughly by asking ad-hoc questions.

Probe for different domains (e.g., psychological, social, physical, spiritual, economical)

- h) What were the challenges have you faced to achieve remission?

Probe for each challenge described by study participants.

- i) Have you ever struggled to maintain remission? If yes, please describe the struggles.
- j) What did you do to get back on track?
- k) Did you use different methods to get through barriers or did you switch to a different method?
- l) What contributed to your success in putting diabetes into remission?
- m) Currently, how do you feel about your ability to continue in remission?
 - How do you plan to continue staying on track with your diet and exercise habits? (Only if diet or exercise were chosen as a strategy)
 - Do you feel like you have tools and support to do so?
 - If not, what supports do you wish were available to you? Why? How could these help you? Why/How?

Probe for specific tools/resources

Probe for different support systems

- You mentioned _____ as a support for you. Can you describe how they support you?

Ok so we are going to switch gears and talk a little bit more about your eating and exercise habits.

Description: Type 2 Diabetes Remission Cohort; Study Number: [H22-00478]

Version 4 June 6, 2023



n) Can you describe the diet you followed that contributed to you achieving remission?

Probe for keto, low carb, etc.

- How did you manage portion sizes and cravings?
- Did the diet impact your regular life and routines?
- Did you make any changes to the diet overtime?
- Did you face any adverse effect while following your diet? (Hypoglycemia, nutrient malabsorption, gastrointestinal issues etc.)
- Was the diet recommended by the healthcare team? / Did you receive any support or guidance in following the diet?

o) How would you describe your current eating habits?

How are they similar or different than the eating habits you had in the past?

Will you stick to this eating habit? If yes/ no. Why?

- p) What do you think are the biggest challenges of your diet and keeping on track?
- q) How about exercise, how did it contribute to your remission process and how does it contribute nowadays?

Tell me a bit of how you maintain your exercise levels?

- Have your eating habits had to alter because of your exercise routine while in remission? If so, how. Why?
- What type of exercise did you mostly do? (HIIT, resistance training etc.) Did you receive any support from health care team?
- Can you tell me how often do you exercised and what time you used to exercise most often? (Before a meal, after a meal, in the morning, in the evening, etc.)
- r) In terms of the diet and exercise changes you just described, can you discuss why you either chose or chose not to consult your health care team before making those changes.

Ok great, now just to expand on the topic of health care teams:

- s) Did any healthcare professional help you through your diabetes remission journey? How?
- t) Can you please describe [healthcare professional] helped you through the remission journey? (Ask this question for each healthcare professional mentioned by the participant)

Were you recommended to see a dietitian?

If yes, who provided the recommendation, and did you end up speaking with one?

If you did speak with one what was your motivation to see them?

If you chose not to speak with one what were the reasons why?



- u) Was there anything you wished your healthcare team had done to help you achieve and maintain remission?
- v) What role do you think healthcare professionals and the healthcare system play in supporting your future and the future of other patients?
- w) Thinking about the future, how do you feel about staying in remission?
 - How would you describe your confidence to maintain remission in the future?
 - How is your remission status being monitored and how often?
 - Did you make a plan with your healthcare team to manage any potential challenges or setbacks in the future?
 - Can you describe what your hopes and fears are related to your future and remission?

Okay (Insert name) this has been an informative discussion. Before I let you go:

- x) Do you have any other information you would like to add about your remission process?
- y) Do you have any other questions for me?

I appreciate your collaboration. Thank you!

Appendix 8. Term of Use (EQ-5D-5L)

Friday, July 25, 2025 at 10:25:11 AM Pacific Daylight Time

Subject: Terms of Use Non-Commercial for the registration ID: 46609
Date: Monday, January 17, 2022 at 12:36:21 PM Pacific Standard Time
From: EuroQol - Registration
To: [REDACTED]
CC: registration@euroqol.org

[CAUTION: Non-UBC Email]



Dear Dr. [REDACTED]

Thank you for your registration.

The study / project titled "Putting Type 2 Diabetes into Remission: Developing a patient-centred, interdisciplinary nutrition intervention for delivery in urban and rural community pharmacies".you registered fulfills the conditions for you to use the requested version(s) free of charge.

Below you find our Terms of Use Non-Commercial. We will provide you with the requested versions free of charge once we have received your agreement with our Terms of Use. You can indicate your agreement by pressing the green "Agree" button below. If you do not agree, please press "Disagree".

If you have any questions please contact us by sending an email to userinformationservice@euroqol.org.

Thank you in advance.

Kind regards,

1 of 6

These Terms of Use of the **STICHTING EUROQOL RESEARCH FOUNDATION**, also trading as **EUROQOL RESEARCH FOUNDATION**, a registered charity incorporated under the laws of The Netherlands, having its registered office in Rotterdam, and its principal place of business in (3068 AV) Rotterdam at the Marten Meesweg 107, The Netherlands (hereinafter '**EuroQol**') should be accepted for the use of the EQ-5D in a Non-Commercial study or ROM/PROMS project, including registries (hereinafter '**Study**' or '**ROM/PROMs Project**').

By registering the Study or ROM/PROMs Project at the EuroQol website (<https://euroqol.org/>) and explicitly confirming acceptance of these Terms of Use by clicking the box "Accept" or by accepting the Terms by e-mail, the registered natural person or legal registered person becomes a User ('**User**').

Article 1. Approved use

1. User is allowed to use the requested EQ-5D version on paper to be filled out by pen(cil) (hereinafter '**EQ-5D Paper version**') and/or as ready-to-use surveys to collect EQ-5D data electronically on supported Electronic Data Capture (EDC) platforms (hereinafter '**EQ-5D module**') for the Study or ROM/PROMs Project registered on EuroQol's website. Note: For use of EQ-5D on unsupported EDC platforms, for which currently no EQ-5D module is available, a license agreement will be drawn up and a screenshot review fee will be charged.
2. Considering that the Study or ROM/PROMs Project is non-commercial, EuroQol grants permission to use the full version (*descriptive system, Visual Analogue Scale and copyright statement*) of the EQ-5D Paper version and/or the EQ-5D module free of charge for the duration of the Study or ROM/PROMs Project: Putting Type 2 Diabetes into Remission: Developing a patient-centred, interdisciplinary nutrition intervention for delivery in urban and rural community pharmacies with registration ID 46609.
3. In order to request use of the EQ-5D Paper version and/or the EQ-5D module in a new study/project a new registration should be made on the website of EuroQol.
4. Separate permission is required if the Study or ROM/PROMs Project is funded by a pharmaceutical company, medical device manufacturer or other profit-making stakeholder.
5. Separate permission is required when the intention is to charge a fee for third party access to collected EQ-5D data in the Study or ROM/PROMs Project.
6. The permission to use the EQ-5D Paper version and/or the EQ-5D module is restricted to:
 - A maximum of 5,000 unique respondents when used in a Study or

- Registry;
 - A maximum of 100,000 unique respondents when used in a ROM/PROMs Project;
 - 5 years from the date of acceptance of the Terms of Use when used in a ROM/PROMs project or Registry.
7. Upon acceptance of these Terms of Use, EuroQol will make the requested available EQ-5D Paper version(s) and/or EQ-5D module(s) accessible to User by means of a portal. The link and password will be sent by registration@euroqol.org to User through an automatically generated e-mail.
 8. The provided EQ-5D Paper version and/or EQ-5D module may not be distributed to third parties other than clinical sites without prior approval of EuroQol. Distribution includes, but is not limited to, making available on the internet and/or providing the versions to third parties other than respondents or clinical sites.
 9. The provided EQ-5D Paper version may **only** be provided to respondents **on paper** to be **filled out with a pen(cil)**.
 10. The provided EQ-5D Paper version and/or EQ-5D module version may **only be used in accordance with the written instructions** of EuroQol as set out in the corresponding user guide (<https://euroqol.org/publications/user-guides/>). For the proper use of the EQ-5D module a separate guide will be issued, together with the EQ-5D module.
 11. Implementation of the provided EQ-5D Paper version into an online survey, app or an electronic device is not allowed.
 12. Implementation of the provided EQ-5D module onto other (EDC) platform(s) than for which it is developed, is not allowed.

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8. The User of the EQ-5D module is responsible for the correct representation of EQ-5D in the Study or ROM/PROMs Project. The EQ-5D should be represented as shown in the demo pages that can be found on the EuroQol website: <https://euroqol.org/eq5d-instruments/sample-demo/>).
9. The User of the EQ-5D module is responsible for any license required for the use of the EDC platform if applicable.
10. Upon agreeing to the Terms of Use, User automatically transfers and assigns in advance irrevocably all Intellectual Property Rights in, or in connection with any modification, alteration, amendment or any (new) translation of the version, flowchart, legend, dictionary or manual, which transfer EuroQol hereby accepts. User warrants that the intellectual property rights shall be assigned and transferred to EuroQol Group without any encumbrance pursuant to this Article. In addition, any moral rights shall to the best of User's knowledge be waived.
11. The provided EQ-5D Paper version and/or EQ-5D module **may not be reproduced in a publication or on the internet without written permission.**

Article 3. Study or ROM/PROMs Project data

1. User is proprietor with regard to all personal and other data which is collected in connection with the use of the requested version.
2. EuroQol shall not request nor receive any collected data from User. Therefore, User will be solely responsible with regard to the compliance with all applicable laws and regulations in respect of

the protection of the collected (personal) data.

Article 4. Liability

1. User is solely responsible for the use of the EQ-5D Paper version and/or EQ-5D module and the data resulting from such use.
2. For the avoidance of any doubt, EuroQol is not liable towards User for any damage resulting from the use of the EQ-5D Paper version and/or EQ-5D module in the Study or ROM/PROMs Project, except in case of gross negligence or willful misconduct by EuroQol.
3. User shall indemnify EuroQol and hold EuroQol harmless against any and all damages, claims, liabilities, costs and expenses, which may arise out of or are related to the (mis)use and/or reproduction of the content of the EQ-5D Paper version and/or EQ5D module provided by EuroQol to User, except in case of gross negligence or willful misconduct by EuroQol.

Article 5. Miscellaneous

1. In case of questions regarding data analysis, User is requested to send an e-mail to userinformationservice@euroqol.org. Please refer to the ID number and Study title.
2. Frequently asked questions relating to the EQ-5D are answered on EuroQol's website (<https://euroqol.org/support/faqs/>).

Article 6. Governing law

These Terms of Use shall be governed by, and construed in accordance with, the laws of the Netherlands.

Article 7 - Dispute Resolution and Governing Law

a) Vested outside the EU

1. If User is vested outside the EU, any dispute arising out of or in connection with these Terms of Use, including any question regarding its existence, validity or termination, shall be referred to and finally resolved by arbitration conducted in accordance with the International Chamber of Commerce Rules for Arbitration ("ICC Rules") for the time being in force, which rules are deemed to be incorporated by reference.
2. The number of arbiters shall be one (1) and shall be appointed by the Court of Arbitration. In principle, the arbiter shall not have the nationality of either of the parties. The place of arbitration shall be Rotterdam. The arbitral procedure shall be conducted in the English language. The arbitral court shall decide in accordance

with the rules of law.

3. Notwithstanding the foregoing, nothing shall affect either party's right to seek an immediate remedy of an injunction, specific performance or similar court order to enforce the defaulting party's obligations.
4. These Terms of Use shall be governed by and construed in accordance with the laws of the Netherlands.

b) Vested in the EU

1. If User is vested in the EU these Terms of Use shall be governed by, and construed in accordance with, the laws of the Netherlands.
2. All disputes arising out or in connection with these Terms of Use shall be finally settled by the competent court in Rotterdam, the Netherlands.

Agree

Disagree

Best regards,

Bernhard Slaap
Executive Director
EuroQol Research Foundation



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