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Original Research

CANadian CAnagliflozin REgistry: Patient-Reported Outcomes of Canagliflozin in the Treatment of Type 2 Diabetes Mellitus in Canadian Clinical Practice

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Key Messages

- Treatment with canagliflozin has been shown to be safe and effective in patients with type 2 diabetes, but little is reported on patient-reported outcomes.
- We provide a better understanding of the patient experience and patient satisfaction while on treatment with canagliflozin in a real-world Canadian setting.

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ABSTRACT

Objectives: To describe patient-reported outcomes (PROs) after initiation of treatment with canagliflozin (CANA) for type 2 diabetes mellitus (T2DM) in a real-world Canadian setting.
Methods: CANadian CAnagliflozin REgistry (CanCARE) is a prospective, observational, single-arm, real-world Canadian study of the effectiveness and safety of CANA for the treatment of T2DM in 527 subjects. PRO measures were collected in CanCARE using the Current Health Satisfaction Questionnaire (CHES-Q) at baseline and after 3, 6 and 12 months of CANA treatment to examine patient satisfaction regarding weight and overall health. Associations between changes in satisfaction with weight, systolic blood pressure (SBP) and glycated hemoglobin (A1C) levels were also investigated.
Results: Proportion of patients satisfied with their body weight and overall health increased from 22.1% and 26.9% at baseline to 32.4% and 49.2% after 12 months of CANA treatment, respectively. Satisfaction rates also increased on CHES-Q domains representing physical and emotional health. Correlations were found between improvement in satisfaction with body weight and weight loss ($r=-0.29$; $p<0.01$) and between improvements in satisfaction with overall health and weight loss ($r=-0.13$; $p=0.03$) and SBP ($r=-0.17$; $p<0.01$), but not with changes in A1C level.
Conclusions: Treatment with CANA is associated with improvements in satisfaction with body weight and overall health, which may be important drivers of patient self-management and hold the potential to positively influence long-term outcomes in T2DM.

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RÉSUMÉ

Objectifs : Décrire les résultats rapportés par les patients (RRP) après l'initiation d'un traitement à la canagliflozine (CANA) pour le diabète sucré de type 2 (DST2) dans un contexte canadien concret.
Méthodes : CANadian CAnagliflozin REgistry (CanCARE) est une étude canadienne prospective, observationnelle, à groupe unique, menée dans en situation réelle portant sur l'efficacité et l'innocuité du CANA pour le traitement du DST2 chez 527 sujets. Les mesures des RRP ont été recueillies dans l'étude CanCARE à l'aide du Questionnaire sur la Satisfaction de l'État de Santé Actuelle (Q-SESA) en début d'étude et après 3, 6 et 12 mois de traitement par la CANA afin d'examiner le niveau de satisfaction des patients quant à leur poids et leur état de santé général. Les associations entre les changements des niveaux de satisfaction à l'égard du poids, de la tension artérielle systolique (TAS) et des taux d'hémoglobine glyquée (A1C) ont également été étudiées.
Résultats : La proportion de patients satisfaits de leur poids corporel et de leur état de santé général est passée de 22.1 % et 26.9 % au début de l'étude à respectivement 32.4 % et 49.2 % après 12 mois de traitement à la CANA. Les niveaux de satisfaction ont également augmenté dans les registres du Q-SESA correspondant à la santé physique et émotionnelle. Des corrélations ont été observées entre l'amélioration de la satisfaction à l'égard du poids corporel et de la perte de poids (r=-0.29; $p<0.01$) et entre l'amélioration de la satisfaction à l'égard de la santé globale et de la perte de poids (r=-0.13; $p=0.03$) et de la TAS (r=-0.17; $p<0.01$), mais pas en regard des changements du taux d'A1C.
Conclusions : Le traitement par la CANA est associé à une amélioration du niveau de satisfaction à l'égard du poids corporel et de l'état de santé général, ce qui peut être un facteur incitatif important pour l'autogestion du patient et appuyant le potentiel d'influer positivement sur les conséquences à long terme du DST2.

Introduction

Diabetes mellitus is a chronic metabolic disease that affects all socioeconomic, age and sex groups (1). As of 2017, approximately 425 million adults worldwide were living with diabetes, and this trend is expected to increase; by 2045, this number will rise to 629 million (2). In Canada, as of 2015, approximately 3.5 million people have diabetes, with this figure expected to rise to 5 million (12.1% of the population) by 2025 (3). Of these, approximately 9 out of 10 will have type 2 diabetes mellitus (T2DM) (4). Diabetes is reported to be the seventh leading cause of death in Canada, with 1 in 10 Canadian adult deaths attributable to diabetes in 2008-2009 (3,5).

Patient-centred care is crucial in T2DM because patients are charged with a high degree of responsibility for their own disease management. Individual healthy behaviour choices, including medication adherence, diet and participation in exercise regimens drive treatment outcomes (6,7). The Diabetes Canada clinical practice guidelines note that the most effective behavioural interventions involve a patient-centred approach, shared decision-making, the development of problem-solving skills and the use of action plans directed toward patient-chosen goals; and treatment regimens and therapeutic targets in type 2 diabetes should be individualized (8). These recommendations reflect similar points in many position statements and treatment guidelines, and highlight the need for patient-centric care in T2DM. Patient-reported outcome (PRO) instruments are used to describe the impact of treatment on patient perceptions of their own health; importantly, this can influence their performance of self-care behaviours, including medication adherence and weight management via healthy eating and being active (9,10).

Canagliflozin (CANA) was the first oral selective inhibitor of sodium-glucose cotransporter 2 (SGLT2) approved in Canada. Pharmacologic inhibition of SGLT2 acts to decrease renal glucose reabsorption, resulting in lowered plasma glucose in individuals with elevated glucose concentrations. The increased urinary glucose and sodium excretion resulting from SGLT2 inhibition has secondary benefits of systolic blood pressure (SBP) and body weight reduction, as demonstrated in phase 3 trials of CANA in patients with T2DM both as monotherapy and in combination with other antihyperglycemic agents (11–16).

The CANadian CAnagliflozin REgistry (CanCARE) (17) is a prospective cohort study evaluating the efficacy and safety of CANA in a real-world practice setting in Canada that enrolled SGLT2 inhibitor–naïve adult patients with T2DM with suboptimally controlled glycated hemoglobin A1C (A1C) $\geq$7% on a stable antihyperglycemic agent regimen, with an estimated glomerular filtration rate $\geq$60 mL/min/1.73 m^2 and who were initiated on CANA as part of their usual treatment approach. CanCARE included measurements of PROs of health satisfaction to capture patient perspectives after initiation of treatment with CANA. We focused on health satisfaction because this concept has been shown to influence adherence to T2DM management behaviours, such as medication taking, making healthy food choices and increasing physical activity—behaviours that are imperative for optimal glycemic control over the longer term (18).

The objective of the current analyses is to describe the patient experience and satisfaction while on treatment with CANA in a real-world Canadian setting.

Methods

Study design and population

The results were obtained from patients enrolled in the CanCARE study who provided responses to the Current Health Satisfaction Questionnaire (CHES-Q) at the appropriate time points in the study. More details on patient population, inclusion/exclusion criteria, study design, efficacy and safety are detailed in the CanCARE publication of clinical efficacy and safety (17).

This study was conducted in accordance with the ethical principles from the Declaration of Helsinki and that are consistent with Good Clinical Practices. Additionally, each site received institutional review board approval, and CanCARE was registered in clinicaltrials.gov (identifier NCT02688075).

CHES-Q

To capture the patient experience during newly initiated CANA treatment, the CHES-Q was administered to each patient at baseline and again after 3, 6 and 12 months as an exploratory endpoint in CanCARE. CHES-Q provides a single, brief tool to evaluate satisfaction with many aspects of living with diabetes, especially as it relates to clinical outcomes, such as weight, blood glucose levels and blood pressure (6). The 14-item CHES-Q was designed and validated using best scientific practices (6), and then implemented in both randomized controlled trials and real-world studies to assess health satisfaction of patients with diabetes (6,7). Patients are asked to rate their level of agreement with each item on a 7-point Likert-style scale ranging from strongly disagree to strongly agree. The analysis presented herein focuses on items 1 and 13 of the CHES-Q ("I am satisfied with my current weight" and "I am satisfied with my current overall health," respectively). It also contains 2 psychological constructs measuring physical health satisfaction (comprised of 6 items addressing aspects of physical health, such as appetite, energy level, sleep and physical fitness) and emotional health satisfaction (comprised of 3 items addressing aspects of emotional health, such as social life, attitude toward diabetes and mood).

For each CHES-Q item, patients were considered satisfied if they replied that they agree or strongly agree with the given item, a conservative approach to rating satisfaction on a given item from the CHES-Q (6). Because of the symmetrical construction of the CHES-Q, we also defined an unsatisfied category for patients who replied that they disagree or strongly disagree. Patients were considered to be neutral on an item if they responded that they somewhat agreed, somewhat disagreed or neither agreed nor disagreed. Patients were considered satisfied within the domains of physical or emotional health if they were considered satisfied on at least one-half of the items comprising the construct within the CHES-Q (i.e. $\geq$2 of the 3 items in the emotional health construct, $\geq$3 of the 6 items in the physical health construct).

Weight change patterns

Based on a previous analysis using a clustering algorithm to define weight change patterns (10), we classified weight change patterns into the following 4 categories: loss-loss (pattern 1), consisting of patients who lost any weight from baseline to month 3 and lost any weight from month 3 to month 12; loss-gain (pattern 2), consisting of patients who lost any weight from baseline to month 3 and gained weight or did not change from month 3 to month 12; gain-loss (pattern 3), consisting of patients who gained any weight or did not change weight from baseline to month 3 and lost any weight from month 3 to month 12; and gain-gain (pattern 4), consisting of patients who gained any weight or did not change weight from baseline to month 3 and gained any weight or did not change weight from month 3 to month 12.

Statistical analysis

Where proportion of patients is reported, data are presented as a percentage of the total number of patients in the given category defined by their baseline responses minus the number of missing observations at that time point. For baseline demographic values of age, weight, A1C, body mass index (BMI), waist circumference and SBP, mean values and SDs were calculated for each time point using the subjects falling into the given category with no imputation of missing values.

Correlations between changes in patient satisfaction and clinical changes (i.e. body weight, SBP, A1C) were calculated using the change from baseline to month 12 in the appropriate measure and the change in their satisfaction level over the same time. Relative to baseline, a 1-point move on the Likert scale toward strongly agree was rated as 1 and a 1-point move toward strongly disagree was rated as −1 for the applicable CHES-Q item. Each point on the Likert scale was considered to be equidistant for the purposes of this analysis. The degree of correlation is reported as Pearson *r*.

Results

Demographics and baseline characteristics

A total of 538 patients were screened in CanCARE, of which 527 patients were enrolled at 28 Canadian sites and included in the final analysis set for effectiveness and safety. Eleven patients (2.0%) were excluded because they did not meet $\geq$1 of the eligibility criteria. The overall baseline demographic and disease characteristics were consistent with eligibility criteria and representative of the Canadian patient population with T2DM (17,19). As reported elsewhere, CANA treatment has been demonstrated to be safe and effective, with patients showing a mean reduction in A1C levels of 1.04% after 12 months of treatment. Additionally, mean body weight, waist circumference and BMI consistently decreased at 3, 6 and 12 months; and >80% of patients experienced weight loss, with approximately one-third of patients experiencing weight loss $\geq$5% after 12 months of treatment (17).

Baseline CHES-Q results for satisfaction with body weight were available for 511 patients, and satisfaction with overall health was available for 509 patients. At baseline, the proportions of patients classified as satisfied and unsatisfied on item 1 (I am satisfied with my current body weight) and item 13 (I am satisfied with my current overall health) are shown by demographic category in Table 1 (note that data on patients classified as neutral do not appear in the table).

A strong sex effect on baseline perceptions of weight was observed, with a higher proportion of women being dissatisfied than men (53.7% and 34.7%, respectively). A similar numerical difference was present for perception of overall health (24.9% of women were dissatisfied and 16.2% of men). Patients with shorter disease duration were also less likely to report being satisfied with their weight or health, and more likely to be unsatisfied. Baseline medication use did not seem to be a major factor in patient satisfaction; however, a very low proportion of patients taking metformin and a sulfonylurea at baseline reported being satisfied with their weight (6/68, 8.8%) relative to all other patients taking non-insulin antihyperglycemic agents (84/314, 26.8%). Additionally, as would be expected, mean baseline anthropomorphic characteristics such as weight, BMI and waist circumference differed with perceptions of both weight and health.

Improvements in patient satisfaction after initiation of CANA

Of the patients who completed the CHES-Q at baseline, additional CHES-Q data were obtained from 449 patients at 3 months, 404 patients at 6 months and 389 patients at 12 months. Weight satisfaction data were available for 324 patients, whereas overall health satisfaction data were available for 323 patients who completed 12 months of treatment. At baseline, 22.1% of patients overall reported being satisfied with their weight. This proportion increased to 31.2%, 37.1% and 32.4% after 3, 6 and 12 months of CANA treatment, respectively (Figure 1A). Similarly, for satisfaction with overall health, an increase from baseline (26.9% of patients were satisfied) through 3, 6 and 12 months of treatment was observed (44.0%, 51.2% and 49.2%, respectively) (Figure 1B).

Table 1
Baseline satisfaction with current body weight and current overall health by patient demographics

Clinical characteristics	Baseline weight satisfaction				Baseline overall health satisfaction			
	Number of patients	Unsatisfied	Neutral	Satisfied	Number of patients	Unsatisfied	Neutral	Satisfied
Weight, kg	508	100.1±21.9	86.9±16.7	75.9±13.8	506	99.4±22.7	90.1±20.5	83.4±17.3
BMI, kg/m^2	506	36.1±6.4	30.6±4.7	27.1±3.5	504	35.2±6.6	32.4±6.4	29.3±5.0
Waist circumference, cm	497	114.9±15.3	104.4±12.0	98.0±11.6	495	113.7±15.5	107.8±14.4	102.4±13.9
Age, years	511	59.1±10.2	62.5±10.7	61.6±11.3	509	59.8±11.3	60.3±10.4	62.6±10.6
Systolic BP, mmHg	508	131.5±12.1	130.6±13.1	129.7±13.3	506	131.8±11.8	130.5±13.1	130.6±12.8
Satisfaction by demographics								
All patients	511	216 (42.3)	182 (35.6)	113 (22.1)	509	100 (19.6)	272 (53.4)	137 (26.9)
Sex								
Male	308	107 (34.7)	118 (38.3)	83 (26.9)	308	50 (16.2)	154 (50.0)	104 (33.8)
Female	203	109 (53.7)	64 (31.5)	30 (14.8)	201	50 (24.9)	118 (58.7)	33 (16.4)
Duration of diabetes, years								
0 to <5	149	81 (54.4)	40 (26.8)	28 (18.8)	148	41 (27.7)	73 (49.3)	34 (23.0)
5 to <10	151	70 (46.4)	43 (28.5)	38 (25.2)	151	31 (20.5)	76 (50.3)	44 (29.1)
≥10	211	65 (30.8)	99 (46.9)	47 (22.3)	210	28 (13.3)	123 (58.6)	59 (28.1)
A1C, %								
Mean A1C	495	8.42±1.33	8.51±1.28	8.43±1.30	493	8.64±1.31	8.50±1.28	8.24±1.00
<7	1	0 (0.0)	0 (0)	1 (100.0)	1	0 (0.0)	1 (100.0)	0 (0.0)
7 to <7.5	94	42 (44.7)	32 (34.0)	20 (21.3)	93	17 (18.3)	48 (51.6)	28 (30.1)
7.5 to <8.5	211	86 (40.8)	74 (35.1)	51 (24.2)	210	38 (18.1)	110 (52.4)	62 (29.5)
≥8.5	189	78 (41.3)	71 (37.6)	40 (21.2)	189	39 (20.6)	106 (56.1)	44 (23.3)
Baseline AHA medications								
None	10	5 (50.0)	3 (30.0)	2 (20.0)	10	2 (20.0)	6 (60.0)	2 (20.0)
Met only	98	43 (43.9)	29 (29.6)	26 (26.5)	97	26 (26.8)	41 (42.3)	30 (30.9)
Met+DPP4	84	37 (44.0)	24 (28.6)	23 (27.4)	84	12 (14.3)	45 (53.6)	27 (32.1)
Met+SU	68	37 (54.4)	25 (36.8)	6 (8.8)	67	16 (23.9)	36 (53.7)	15 (22.4)
Met+DPP4+SU	68	16 (23.5)	32 (47.1)	20 (29.4)	68	10 (14.7)	36 (52.9)	22 (32.4)
Other noninsulin AHA	54	27 (50.0)	14 (25.9)	13 (24.1)	54	10 (18.5)	30 (55.6)	14 (25.9)
Insulin ± other AHA	129	51 (39.5)	55 (42.6)	23 (17.8)	129	24 (18.6)	78 (60.5)	27 (20.9)

A1C, Glycated hemoglobin; *AHA,* antihyperglycemic medication; *BMI,* body mass index; *BP,* blood pressure; *DPP4,* DPP-4 inhibitor; *Met,* metformin; *SU,* sulfonylurea.
Note: Values are mean ± SD, n (%), or as otherwise indicated.

Satisfaction rates with respect to physical and emotional health also increased over the course of the study. The proportion of patients satisfied with physical health rose from 35.2% at baseline to 51.5% after 12 months of treatment (n=324) (Figure 1C). Similarly, the proportion of patients who reported emotional health satisfaction increased from 56.4% at baseline to 67.3% after 12 months of treatment (n=323) (Figure 1D).

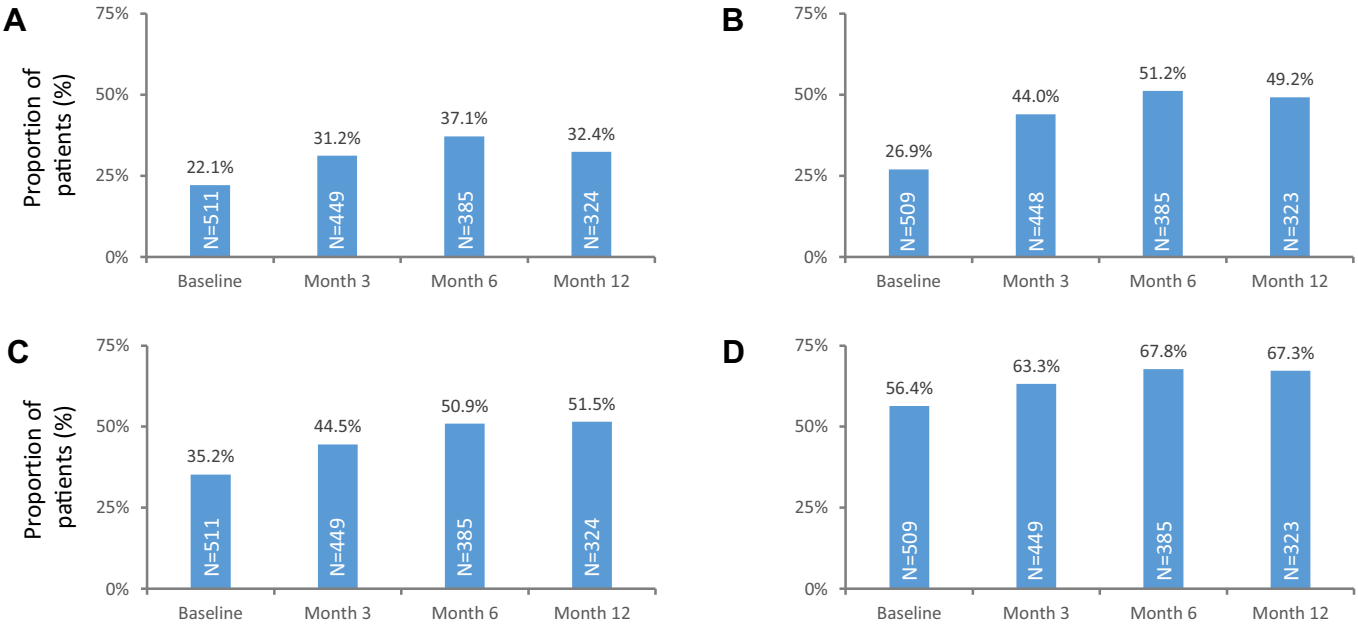

Figure 1. Patient satisfaction rates over time during 12 months of treatment with canagliflozin. (A) Percentage of patients who responded agree or strongly agree to CHES-Q item 1 (I am satisfied with my current body weight) from baseline through 12 months of treatment with canagliflozin. (B) Percentage of patients who responded agree or strongly agree to CHES-Q item 13 (I am satisfied with my current overall health) from baseline through 12 months of treatment with canagliflozin. (C) Percentage of patients who responded agree or strongly agree to at least 3 of the 6 items comprising the Physical Health Satisfaction construct of the CHES-Q. (D) Percentage of patients who responded agree or strongly agree to at least 2 of the 3 items comprising the Emotional Health Satisfaction construct of the CHES-Q. *CHES-Q,* Current Health Satisfaction Questionnaire.

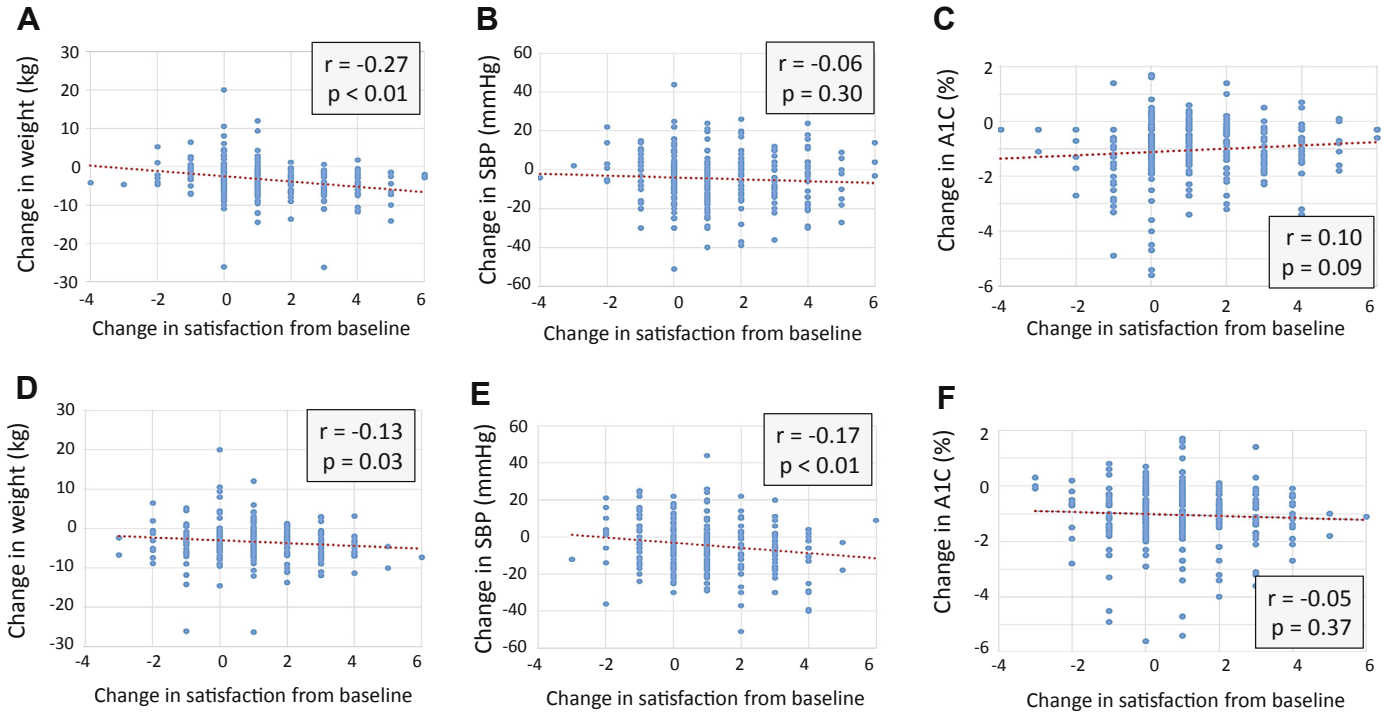

Figure 2. Correlations between change from baseline to month 12 in patient satisfaction with weight (A–C) and overall health (D–F) with changes in weight, SBP and A1C levels. (A) A statistically significant correlation was found between weight loss and improvement in patient satisfaction with weight (Pearson $r=-0.27$; $p<0.01$). (B and C) No statistically significant correlations were found between changes in patient satisfaction with their body weight and either change in SBP (B) ($p=0.30$) or change in A1C (C) ($p=0.09$). (D and E) Statistically significant correlations were found between improvement in patient satisfaction with overall health and both weight loss (D) (Pearson $r=-0.13$; $p=0.03$) and lowered SBP (E) ($r=-0.17$; $p<0.01$). (F) No statistically significant correlation was found between change in patient satisfaction with overall health and change in A1C ($p=0.37$). *A1C*, glycated hemoglobin; *SBP*, systolic blood pressure.

Associations of patient satisfaction with changes in weight, SBP and A1C

As expected, there was a statistically significant negative correlation between change in weight satisfaction and change in weight from baseline to month 12 ($r=-0.27$, $p<0.01$) (Figure 2A). No significant correlations between weight satisfaction and change in either SBP ($p=0.30$) (Figure 2B) or A1C level ($p=0.09$) (Figure 2C) were observed.

Associations between changes in weight, SBP and A1C levels from baseline to month 12 and satisfaction with overall health were also investigated. There were significant correlations between overall health satisfaction and changes in both body weight ($r=-0.13$, $p=0.03$) (Figure 2D) and SBP ($r=-0.17$, $p<0.01$) (Figure 2E). However, there was no statistically significantly correlation between overall health satisfaction and the change in A1C levels ($p=0.37$) (Figure 2F).

Weight change patterns

Mean weight change at months 3, 6 and 12 are depicted for all 4 patterns in Figure 3. Notably, 82% of patients lost weight in the first 3 months of CANA treatment (patterns 1 and 2), and 67.7% of those patients continued to lose weight throughout the 12 months of treatment (pattern 1). A higher proportion of patients from patterns 1 and 2 (67.9% and 63.9%, respectively) were satisfied with their overall health after 12 months of treatment relative to those in patterns 3 and 4 (44.7% and 26.7%, respectively; data not shown). Because of the low sample size in pattern 4 ($n=15$, <5% of total patients), no reliable analysis could be conducted on group differences in satisfaction with weight or health.

Discussion

CanCARE is a prospective evaluation of CANA's effectiveness and safety in the treatment of T2DM when prescribed in a real-world Canadian clinical practice setting (17). The current exploratory analysis of PROs from CanCARE demonstrates that CANA is associated with improvements in satisfaction with body weight and overall health. Satisfaction with health and weight have been previously associated with more consistent and persistent positive health behaviours (e.g. medication taking, increased physical activity, healthy eating) (20). These health behaviours are of particular importance for patients with diabetes because self-care behaviour, which largely lies beyond the control of physicians, is a highly important factor in T2DM management and a driver of long-term outcomes (8).

Several key points regarding perceptions of weight and overall health among patients with T2DM who were followed for 1 year after initiating CANA in the CanCARE study must be highlighted. At baseline, a higher proportion of patients were unsatisfied with their body weight (42.3%) compared with their overall health (19.6%), a difference that was far less apparent when looking at the proportion of patients who reported being satisfied with their weight and health (22.1% and 26.9%, respectively) (Table 1). As expected, patients who had higher mean body weight, BMI and waist circumference at baseline were less satisfied with their weight. The same trend was also present for satisfaction with overall health, albeit to a lesser extent. This may reflect weight as a more salient concept for patients than overall health, given it is easy to monitor and more readily apparent in the daily lives of patients compared with clinical measures, such as blood pressure or A1C level, which may in turn reflect a need for further patient education about T2DM and disease management goals. Changes in weight and patient

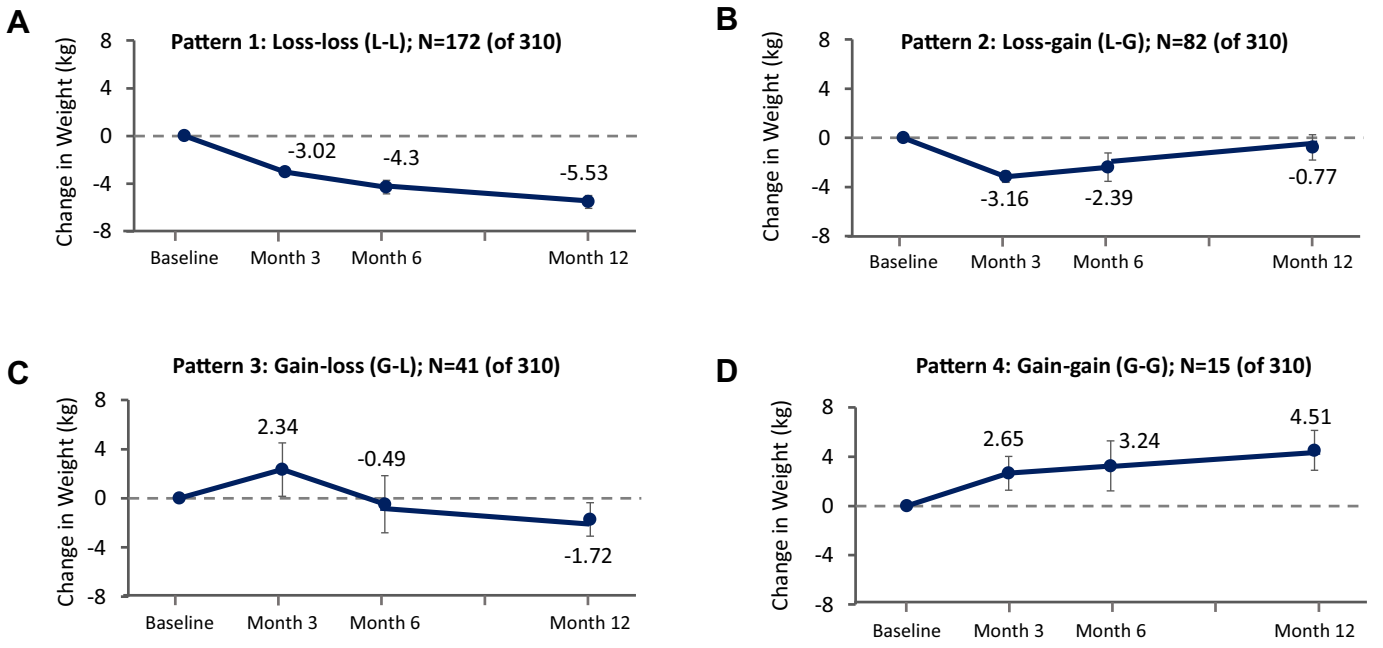

Figure 3. Patterns in weight change from baseline to month 12. Patients were classified into 4 patterns, with their mean weight change shown for each time point: weight loss at both 3 and 12 months (loss-loss) (A); weight loss in the first 3 months followed by weight gain (loss-gain) (B); weight gain in the first 3 months followed by weight loss (gain-loss) (C) and weight gain at both 3 and 12 months (gain-gain) (D).

perception of weight are known to be important factors in the performance of self-care behaviours in patients with T2DM (10). Together, these results suggest weight is one of the most relevant aspects of overall health perceptions in people living with T2DM.

Sex had an important influence on baseline satisfaction, with more women than men being unsatisfied with their weight (53.7% vs 34.7%) and more men being satisfied with their overall health (33.8% vs 16.4%). Patients with a longer history of diabetes (≥10 years) were much less likely to be unsatisfied with their current health (13.3%) and weight (30.8%) than those with durations of <5 years (27.7% and 54.4%, respectively). This difference may reflect that patients with a longer disease course who are least satisfied with their health may not have been sufficiently healthy to enter the trial; it may also partially reflect a degree of complacency in patients about their diabetes that develops over time living with the disease or with age, a loss of urgency (or clinical inertia) from physicians treating their disease or a combination of these factors.

In CanCARE, the proportion of patients satisfied with their body weight increased after initiation of CANA treatment. Additionally, 59.4% of patients who were unsatisfied with their body weight at baseline, and who completed the study, reported satisfaction improvements after 12 months of treatment (data not shown). The data reported in Figure 1 reflect the CHES-Q scores of all participants for whom there are scores at each time point, regardless of whether they completed the study. The data were remarkably similar when looking only at participants who completed the study (the proportion of subjects satisfied with weight at each of the 4 time points was 17.4%, 29.4%, 35.1%, and 31.9%; the same proportions satisfied with health were 25.0%, 46.0%, 51.4%, and 49.3%, respectively).

Satisfaction with overall health has been demonstrated to be a predictor of long-term treatment outcomes in many chronic conditions, including low back pain, chronic obstructive pulmonary disease, cardiovascular disease, cancer and diabetes (21–26). Poor health satisfaction has been associated with depression, anxiety, stress, reduced energy and physical activity levels and impaired social functioning (21,27). Satisfaction with overall health is, therefore, an important indicator for patients with diabetes. In CanCARE, treatment with CANA was associated with higher satisfaction with overall health, emotional health and physical health. Taken together, these positive outcomes may serve as additional predictors of long-term success in the treatment and goal achievement for metabolic parameters among these patients.

While investigating associations between patient satisfaction and several key clinical measures, we observed a statistically significant relationship between weight change and change in patient satisfaction with body weight, such that larger weight loss was associated with a higher increase in satisfaction with body weight. There was no association between satisfaction and either SBP or A1C level (Figures 2B, 2C). These results indicate a direct relationship between weight loss and patient satisfaction with weight, as might be expected. On the other hand, we found little contribution of other health factors, such as A1C levels or SBP to satisfaction with weight. In contrast, changes in satisfaction with overall health were linked to changes in SBP and weight. Interestingly, there was no association between A1C levels and satisfaction with overall health. This unexpected finding that glycemic control does not seem to influence PROs relating to overall health, health-related quality of life or depressive symptoms in patients with T2DM is corroborated by published literature (28). This result implies that change in A1C levels may not influence patient perceptions of their own health, and that antihyperglycemic medications providing benefits beyond glycemic control (e.g. weight loss, blood pressure lowering) may improve health-related quality of life and patient perceptions of their own health to a greater extent than medications that do not offer these added benefits. It may also demonstrate a need for additional patient education regarding the importance of glycemic control and its measurement. The linear regression used to analyze the association between patient satisfaction and clinical measures assumes that each response to a given Likert-style item in the CHES-Q is equidistant from the adjacent response (e.g. the distance between the responses of disagree and slightly disagree is equal to that between agree and strongly agree), and this assumption may not have aligned with the perceptions of the patient.

In prior studies, the temporal pattern of change in body weight has been shown to influence performance of diabetes self-care behaviours and help provide a more complete picture of the individual treatment experience (10). We observed that patients who lost weight in the first 3 months were more likely to be satisfied with their overall health and weight after 12 months of treatment relative to patients who gained weight in the first 3 months. However, the limited number of patients falling into some groups prevented conducting any meaningful statistical analyses on these observed differences.

One potential limitation of this prospective, observational registry is the open-label study design, which may have introduced a selection bias related to the inclusion of patients who would most likely benefit from the CANA treatment. However, validated satisfaction instruments that measure patient perceptions, such as the CHES-Q, would not be expected to be influenced significantly. Weight loss in the study may be confounded by external factors, such as changes in diet or exercise regimens, which were not collected in CanCARE. However, the magnitude of weight loss in our study was similar to that observed in the CANA's phase 3 clinical trial program (11–16). Similarly, satisfaction with current body weight or overall health may have been influenced by psychological or social factors, variables that were not captured in this study. Some of these scores in our observational study may be influenced by concomitant medication changes or other unmeasured variables. Another limitation is the dropout rate observed in the study (26%), which may have included a high number of unsatisfied patients. Given that a substantial percentage of patients (42.3%) reported being unsatisfied with weight at baseline, a floor effect could have potentially limited decreases in patient satisfaction with body weight. However, as shown in Figure 2, some patients reported decreased satisfaction with their weight over time on CANA treatment, which suggests that such a limitation was unlikely to impact overall findings. Additionally, the potential for a floor effect on satisfaction with overall health was far lower because only 19.6% of patients reported being unsatisfied at baseline. Baseline satisfaction also did not seem to strongly influence completion rates (data not shown): the proportion of patients who completed the study and were unsatisfied, neutral and satisfied with their weight at baseline was 81.5%, 70.3% and 74.3%, respectively. With respect to baseline satisfaction with overall health, these percentages were 73.0%, 76.8% and 75.9%, respectively. The lack of a control group represents another limitation of the study; however, the findings from this study supplement the growing body of evidence on significant real-world outcomes with CANA.

Conclusions

This analysis of PROs from CanCARE, a prospective, observational study in a real-world, Canadian context, demonstrates that treatment with CANA is associated with improved patient satisfaction with weight and overall health, and satisfaction with physical and emotional health. These results parallel the sustained, clinically meaningful improvements in cardiometabolic parameters reported for the CanCARE study (17). Improvements in satisfaction with body weight and overall health have the potential to drive positive health behaviours, improve overall health outcomes and predict long-term success in diabetes management.

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Author Disclosures

VW served as an investigator and received grant support from Janssen Inc during the conduct of the study; is involved in clinical trials for Eli Lilly, Locemia, BMS, AstraZeneca, Janssen, Merck, Novo Nordisk and Sanofi and is on the advisory boards for Eli Lilly, Merck, AstraZeneca, Novo Nordisk, Janssen and Sanofi. AB served as an investigator and received grant support from Janssen Inc during the conduct of the study and received personal fees for speaking CME development, advisory boards and grants for clinical trials from AstraZeneca, Bristol-Myers Squibb Company, Novartis AG, Pfizer, Bayer AG, Eli Lilly and Company, Boehringer Ingelheim Pharmaceuticals, Inc., Sanofi, Valeant and Pharmaceuticals International Inc. MC served as an investigator and received grant support from Janssen Inc during the conduct of the study; received personal fees for speaking and CME development from Novo Nordisk and received personal fees from Eli Lilly, Sanofi, AstraZeneca, Boehringer Ingelheim and Abbott. LN served as an investigator and received grants from Janssen Inc during the conduct of the study; received research fees from Novo Nordisk and Sanofi and received consulting and/or speaking fees from Janssen, Abbott, AstraZeneca, Bristol-Myers Squibb Company, Novartis AG, Pfizer Inc, Bayer AG, Eli Lilly and Company, Boehringer Ingelheim Pharmaceuticals Inc., Sanofi, Valeant Pharmaceuticals International Inc and Merck. MAT received grants from Janssen Inc and served as an investigator during the conduct of the study and is involved in clinical trials for Eli Lilly, AstraZeneca, Novo Nordisk and Sanofi. FC received grants from Janssen Inc during the conduct of the study and received grants from Janssen Pharmaceuticals. ST is a current employee of Janssen Global Services LLC. NG, JBR and DS are current employees of Janssen Inc. HSB served as an investigator and received grant support from Janssen Inc during the conduct of the study and has received research support or personal fees from Abbott, Astra Zeneca, Bayer, Boehringer Ingelheim Inc, Eli Lilly, Janssen, Merck, Novo Nordisk, Sanofi, Pfizer, Takeda and Valeant Pharmaceuticals International Inc.

Author Contributions

AB, MC, HSB, VW, NG, ST, and JBR were involved with the study concept, design, protocol, statistical analysis plan development and review. FC was involved with statistical analysis plan development and review. AB, MC, HSB, VW, NG, ST, FC, MAT, LN, JBR and DS were involved in interpreting the data and drafting the manuscript. All authors were involved in reviewing the manuscript and approved the final draft of the manuscript for submission.

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