



SHORT COMMUNICATION

Weight loss and persistence with liraglutide 3.0 mg by obesity class in the real-world effectiveness study in Canada

Sean Wharton¹  | Christiane L. Haase² | Elham Kamran¹ | Aiden Liu³ | Johanna Mancini⁴ | Drew Neish⁴ | Arash Pakseresht² | G Sarah Power⁵ | Rebecca A. G. Christensen¹ 

¹Wharton Medical Clinic, Burlington, Ontario, Canada

²Novo Nordisk A/S, Copenhagen, Denmark

³Novo Nordisk Canada Inc., Mississauga, Ontario, Canada

⁴IQVIA, Montreal, Quebec, Canada

⁵IQVIA, Mississauga, Ontario, Canada

Correspondence

Sean Wharton, Wharton Medical Clinic, 2951 Walkers Line, Main Floor, Burlington, ON, L7M 4Y1, Canada.
Email: wharton@whartonmedicalclinic.com

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Summary

Objective: Liraglutide 3.0 mg is associated with clinically significant weight loss in clinical trials, but real-world data are lacking. In this analysis, weight loss and persistence outcomes with liraglutide 3.0 mg were assessed across obesity classes, in a real-world clinical setting.

Methods: Secondary analysis of an observational, retrospective study of liraglutide 3.0 mg for weight management (as adjunct to diet and exercise) at six Wharton Medical Clinics in Canada. Patients were categorized by body mass index (BMI, kg/m²) into obesity class I (BMI 30–34.9); class II (BMI 35–39.9); and class III (BMI ≥40). Change in weight, categorical weight loss, time to maintenance dose (defined as the time to reach the full liraglutide 3.0 mg maintenance dose) and persistence were assessed for each class and for differences between classes.

Results: Of 308 patients, 70 (22.7%) had obesity class I, 83 (26.9%) obesity class II and 155 (50.3%) obesity class III. Similar percentage change in weight was observed between obesity classes (mean [standard deviation, SD]: −7.0% [6.0], −6.6% [6.0] and −6.1% [5.0], respectively; $p = .640$), and similar proportions achieved ≥5% weight loss (60.4%, 62.0% and 55.3%, respectively; $p = .717$) at 6 months. Mean time to maintenance dose (SD) was 64.2 (56.4) d, 76.4 (56.3) d and 71.4 (54.5) d for obesity classes I, II and III, respectively ($p = .509$). Persistence with medication was also similar between obesity classes ($p = .358$).

Conclusions: These findings suggest that real-world treatment with liraglutide 3.0 mg, regardless of obesity class, is associated with similar clinically significant weight loss, time to maintenance dose and medication persistence.

KEYWORDS

BMI, liraglutide, obesity class, persistence, weight loss

1 | INTRODUCTION

Increasing severity of obesity is associated with increasing risk of morbidity and mortality¹; however, weight loss of 5–10% of body weight is known to promote clinically relevant improvements in outcomes across obesity classes.^{2–10} Weight loss $\geq 5\%$ has been observed consistently in clinical trials of liraglutide 3.0 mg, regardless of baseline body mass index (BMI [kg/m^2]).^{11–13} In the SCALE Obesity and Prediabetes trial, 56-weeks' treatment with liraglutide 3.0 mg resulted in mean weight loss of 8.0% in 2487 patients,¹¹ independent of baseline BMI.

In the real-world clinical effectiveness study in Canada upon which this secondary analysis is based, this research team observed mean weight loss of 6.5% (7.3 kg) with liraglutide 3.0 mg for weight management over 6 months in 311 patients with overweight or obesity.¹⁴ Two further real-world studies have reported similar outcomes with liraglutide 3.0 mg. In the United Arab Emirates, median weight loss in 787 patients after ≥ 16 -week treatment was 6.4% (6.0 kg),¹⁵ and in Spain, mean weight loss in 100 patients over a median follow-up of 6.9 months was 7.7 kg¹⁶; however, these studies did not assess outcomes by obesity class.

This secondary analysis of the real-world clinical effectiveness study in Canada was undertaken to explore the hypothesis that liraglutide 3.0 mg is associated with similar weight loss and persistence, regardless of obesity class, in a real-world setting, in keeping with the evidence from clinical trials.

2 | MATERIALS AND METHODS

2.1 | Primary analysis

The real-world clinical effectiveness study in Canada of liraglutide 3.0 mg (Saxenda[®]) for weight management was a retrospective, observational, single-arm, pre–post study. Using a database of de-identified electronic medical records (EMRs), a cohort was identified from six publicly funded Wharton Medical Clinics (WMCs) in Ontario, Canada, of patients who had initiated liraglutide 3.0 mg between 15 September 2015 and 30 September 2016, with a minimum 6-month follow-up period. The index date was defined as the date of liraglutide 3.0-mg initiation, estimated using a back-calculation based on the reported dose of liraglutide 3.0 mg at the first appointment where initiation was disclosed. Full details of the study design, including index date calculation and ethics approval, can be found in the primary manuscript.¹⁴

2.2 | Secondary analysis

For this post-hoc secondary analysis, the full cohort was divided by obesity class. Owing to a small sample size ($n = 3$), patients with overweight (BMI $< 30 \text{ kg}/\text{m}^2$) were excluded. Remaining patients were divided into obesity class I (BMI 30–34.9 kg/m^2); class II (BMI 35–39.9 kg/m^2); and class III (BMI $\geq 40 \text{ kg}/\text{m}^2$). Change in weight from baseline and categorical weight loss of $\geq 5\%$ and $> 10\%$ at 6 months

after index date were assessed for each obesity class. Time to maintenance dose (defined as the time between the index date of initiation and the date when the full liraglutide 3.0-mg maintenance dose was first reported), the maximum achieved dose of, and persistence with liraglutide 3.0 mg were also assessed; both median and mean values were reported to account for any skew in the data. The proportions of patients persistent at 4 and 6 months were also assessed. Potential differences between obesity classes were evaluated for each endpoint.

2.3 | Statistical analysis

For each obesity class, change in body weight from baseline was analyzed using a paired *t* test. A one-way analysis of variance was used to explore the association of liraglutide 3.0 mg with absolute and percentage change in weight, and mean maximum achieved dose, between obesity classes; an extended Fisher's exact test was used to compare categorical weight loss between classes and persistence at 4 and 6 months. Overall persistence and time to maintenance dose with liraglutide 3.0 mg between obesity classes were presented with Kaplan–Meier curves and formally tested with log-rank tests.

3 | RESULTS

3.1 | Patient disposition and baseline characteristics

In this analysis, 308 patients with obesity were included: 70 (22.7%) with obesity class I, 83 (26.9%) with obesity class II, and 155 (50.3%) with obesity class III. For patients with obesity classes I, II, and III, mean age (standard deviation, SD) was 53.0 (10.6) years, 47.8 (11.5) years, and 49.4 (12.0) years, and 87.1%, 88.0%, and 78.1% were female, respectively. Of those with obesity class I, 77.1% were normoglycemic, compared with 80.7% of those with obesity class II and 71.6% with obesity class III (Table 1).

3.2 | Change in weight from baseline

At 6 months, mean absolute change in weight from baseline (SD) was -6.2 (5.4) kg for patients with obesity class I; -6.7 (6.3) kg with class II; and -8.0 (6.5) kg with class III, $p < .001$ versus baseline for all (Figure 1A). Mean percentage change in weight (SD) was -7.0% (6.0), -6.6% (6.0), and -6.1% (5.0) in obesity classes I, II, and III, respectively. Between obesity classes, there were no differences in absolute ($p = .192$) or percentage ($p = .640$) change in weight at 6 months.

3.3 | Categorical weight loss

At 6 months, $\geq 5\%$ weight loss was achieved by 60.4% of patients with obesity class I, 62.0% with class II, and 55.3% with class III, while 37.5%,

TABLE 1 Baseline characteristics and adherence to diet and exercise program

	Obesity class I BMI 30–34.9	Obesity class II BMI 35–39.9	Obesity class III BMI ≥40
N	70	83	155
Age, years	53.0 (10.6)	47.8 (11.5)	49.4 (12.0)
Female, n (%)	61 (87.1)	73 (88.0)	121 (78.1)
Ethnicity, White, n (%)	50 (71.4)	63 (75.9)	125 (80.6)
Missing, n (%)	10 (14.3)	3 (3.6)	9 (5.8)
BMI, kg/m ²	32.9 (1.5)	37.2 (1.5)	46.3 (5.6)
Weight, kg	90.9 (11.1)	103.7 (11.6)	132.1 (24.9)
HbA _{1c} , % ^a	5.9 (1.3)	5.8 (0.7)	5.9 (0.7)
Systolic blood pressure, mmHg	121.6 (9.8)	124.5 (9.3)	131.3 (11.3)
Diabetes ^b			
None, n (%)	54 (77.1)	67 (80.7)	111 (71.6)
Prediabetes, n (%)	10 (14.3)	14 (16.9)	36 (23.2)
Type 2 diabetes, n (%)	6 (8.6)	2 (2.4)	8 (5.2)
Adherence to exercise program ^c			
None, n (%)	4 (5.7)	13 (15.7)	23 (14.8)
Some, n (%)	20 (28.6)	17 (20.5)	41 (26.5)
Meeting or exceeding, n (%)	23 (32.9)	32 (38.6)	48 (31.0)
Missing, n (%)	23 (32.9)	21 (25.3)	43 (27.7)
Adherence to diet ^{c,d}			
Never, n (%)	2 (2.9)	5 (6.0)	8 (5.2)
Sometimes, n (%)	11 (15.7)	14 (16.9)	15 (9.7)
Always, n (%)	19 (27.1)	18 (21.7)	38 (24.5)
Missing, n (%)	38 (54.3)	46 (55.4)	94 (60.6)

Note: Data are mean (standard deviation), unless otherwise stated.

Abbreviations: ATC, anatomical therapeutic chemical code; A10, drugs used in diabetes; HbA_{1c}, glycated hemoglobin; BMI, body mass index (kg/m²); WMC, Wharton Medical Clinic.

^aBaseline HbA_{1c} data were missing for 46.4% of the secondary analysis cohort.

^bA patient was determined to have type 2 diabetes if taking any prescription with ATC code A10 with start date prior to their index date, had fasting plasma glucose >7 mmol/L at least two times in the year prior to their index date or HbA_{1c} > 6.5% in the year prior to their index date.

^cAdherence to exercise program and to diet was based on personalized recommendations made by physicians at WMCs and was patient-reported, taken from visit immediately prior to index date.

^dFor adherence to diet: “never,” always exceeding calorie deficit; “sometimes,” patient reports meeting or being under caloric prescription some of the time but not always; “always,” patient reports always meeting or being under the prescribed caloric restriction.

32.0%, and 24.3% achieved >10% weight loss, respectively (Figure 1B). There were no differences between obesity classes in the percentage of patients achieving ≥5% weight loss ($p = .717$) or >10% weight loss ($p = .228$).

3.4 | Time to maintenance dose of liraglutide 3.0 mg

Mean (SD) time to maintenance dose for patients with obesity class I, II, and III was 64.2 (56.4) days, 76.4 (56.3) days and 71.4 (54.5) days, respectively (Table 2). There were no differences in time to maintenance dose between obesity classes ($p = .509$). The mean (SD) maximum achieved dose of liraglutide 3.0 mg during the study period was 2.7 (0.6) mg for those with obesity class I, 2.8 (0.5) mg with

obesity class II, and 2.7 (0.7) mg with obesity class III, with no difference between classes ($p = .645$) (Table 2).

3.5 | Persistence with liraglutide 3.0 mg

Persistence with liraglutide 3.0 mg, reported as mean (SD), was 6.7 (4.0) months for patients with obesity class I, 6.0 (3.5) months with class II, and 6.3 (4.5) months with class III (Table 2); persistence was similar between classes ($p = .358$). At 4 and 6 months, the percentages of patients who remained on liraglutide 3.0 mg were, respectively, 71.4% and 57.1% (obesity class I), 68.7% and 51.8% (obesity class II), and 65.8% and 53.4% (obesity class III). There were no differences between obesity classes in persistence at 4 months ($p = .687$) or 6 months ($p = .800$).

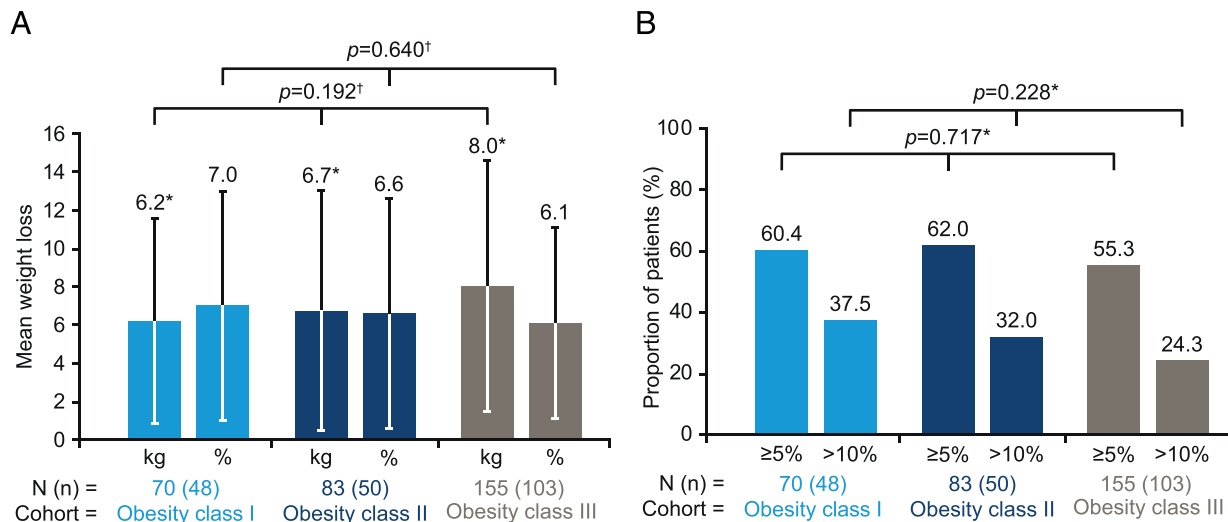


FIGURE 1 Weight loss outcomes. A, Change in weight (kg) from baseline to 6 months. Data are mean (SD). *Paired *t* test, $p < .001$ versus baseline. †Based on one-way ANOVA test comparing three obesity classes. ANOVA, analysis of variance; N, number of patients with measurement at baseline; n, number of individuals with a weight measurement at 6 months; SD, standard deviation. B, Percentage of patients achieving $\geq 5\%$ and $>10\%$ weight loss at 6 months. *Based on extended Fisher's exact test comparing three obesity classes. N, number of patients with a weight measurement at baseline; n, number of individuals with a weight measurement at 6 months

TABLE 2 Time to maintenance dose, persistence, and achieved dose of liraglutide 3.0 mg

	Obesity class I BMI 30–34.9 (n = 70)	Obesity class II BMI 35–39.9 (n = 83)	Obesity class III BMI ≥ 40 (n = 155)	<i>p</i> value for difference between obesity classes
Time to maintenance dose, days				
Mean (SD)	64.2 (56.4)	76.4 (56.3)	71.4 (54.5)	0.509 ^a
Median (IQR)	47.0 (35.0–63.0)	56.5 (42.0–98.0)	49.0 (34.5–88.0)	
Persistence, months				
Mean (SD)	6.7 (4.0)	6.0 (3.5)	6.3 (4.5)	0.358 ^a
Median (IQR)	6.7 (3.2–9.4)	6.2 (3.0–8.7)	6.5 (2.3–9.1)	
Persistence, % of patients				
At 4 months	71.4	68.7	65.8	0.687 ^b
At 6 months	57.1	51.8	53.4	0.800 ^b
Maximum achieved dose, mg				
Mean (SD)	2.7 (0.6)	2.8 (0.5)	2.7 (0.7)	0.645 ^c
Median (IQR)	3.0 (2.4–3.0)	3.0 (3.0–3.0)	3.0 (3.0–3.0)	

Abbreviations: ANOVA, analysis of variance; BMI, body mass index (kg/m^2); IQR, inter-quartile range; N, number of patients; SD, standard deviation.

^aBased on log-rank test comparing three obesity classes.

^bBased on extended Fisher's exact test comparing three obesity classes.

^cBased on one-way ANOVA test comparing three classes.

4 | DISCUSSION

In this secondary analysis, patients treated with liraglutide 3.0 mg as an adjunct to diet and exercise over 6 months achieved clinically significant weight loss, regardless of obesity class, with similar time to maintenance dose and medication persistence.

In the original analysis from this research team, mean weight loss was 6.5% at 6 months.¹⁴ In this analysis exclusively assessing patients with obesity, weight loss of 7.0%, 6.6%, and 6.1% was observed for patients with obesity class I, II, and III, respectively, with no differences between obesity classes in absolute, percentage, or categorical

weight loss; this was in keeping with post-hoc analyses of the SCALE Obesity and Prediabetes trial data. After 56-week treatment with liraglutide 3.0 mg, there were no differences in mean weight loss between patients with a BMI 27 to $35 \text{ kg}/\text{m}^2$ or $\geq 35 \text{ kg}/\text{m}^2$ (8.2% vs. 7.9%, $p = .26$)¹² or between those with a BMI < 50 and $\geq 50 \text{ kg}/\text{m}^2$ (8.0% vs. 7.8%, $p = .16$).¹³

Mean persistence on liraglutide 3.0 mg was 6.3 months across all patients ($n = 311$) in the primary analysis,¹⁷ similar to the 6.7 months for patients with obesity class I, 6.0 months with obesity class II, and 6.3 months with obesity class III. This is the first analysis to evaluate time to maintenance dose and persistence between obesity classes

for any anti-obesity medication (AOM); no significant differences were observed for either ($p = .509$ and $p = .358$, respectively).

The mean time to maintenance dose was much longer than the per-label recommendation of 28 days among patients in all classes,¹⁸ potentially owing to pragmatism with real-world use. Challenges of treatment tolerability or expense may have been mitigated with longer titration regimens; equally, titration may have been slowed or stopped if clinically relevant weight loss was observed at lower doses. This may explain why some patients never reached the full maintenance dose. These results indicate that this effect is not more pronounced in particular obesity classes.

A key strength of this real-world study was the use of EMR data from six WMCs, permitting longitudinal follow-up of a large cohort representative of patients prescribed AOMs in real-world clinical practice. A limitation was the estimation of the index date of liraglutide 3.0-mg initiation using a back-calculation based on the dose reported at the first appointment, where initiation was disclosed. Consequently, not all dates of liraglutide 3.0-mg initiation are exact; dates of discontinuation may also be inexact, for example, owing to late reporting of discontinuation or patients lost to follow-up.

In a real-world setting, regardless of obesity class, similar clinically relevant weight loss, time to maintenance dose, and persistence were observed during treatment with liraglutide 3.0 mg for weight management, as an adjunct to diet and exercise. These findings may help support clinicians to make evidence-based treatment decisions when selecting and initiating weight loss medications for patients across the clinical spectrum of obesity and suggest that the use of liraglutide 3.0 mg may support weight loss regardless of baseline obesity class.

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- S.W.: owner and medical director of the Wharton Medical Clinic (WMC) and internal medicine specialist at Hamilton Health Sciences. He has previously received funding in the forms of grants for research from CIHR and Mitacs and also received funding in the past from Novo Nordisk, Bausch Health, Eli Lilly, Janssen and AstraZeneca for advisory work.
- C.L.H.: employee of Novo Nordisk A/S, Copenhagen, Denmark.
- E.K.: research coordinator at WMC and a member of this working group.
- A.L.: employee of Novo Nordisk Canada Inc.
- J.M.: employee of IQVIA Solutions Canada Inc., responsible for the study (management, analysis and dissemination).
- D.N.: employee of IQVIA Solutions Canada Inc., responsible for the study (management, analysis and dissemination).
- A.P.: employee of Novo Nordisk A/S, Copenhagen, Denmark.

- G.S.P.: employee of IQVIA Solutions Canada Inc., responsible for the study (management, analysis and dissemination).
- R.A.G.C. was an employee of WMC at the time of this study and is a member of this working group.

AUTHOR'S CONTRIBUTIONS

S.W. and R.A.G.C. were responsible for the conception and design of the study, acquisition, and interpretation of the data and review of the manuscript. A.P. and C.L.H. were responsible for the conception and design of the study, interpretation of the data, and review of the manuscript. E.K. and A.L. were responsible for the interpretation of the data, and review of the manuscript. J.M. was responsible for the conception and design of the study, interpretation of the data, and development and review of the manuscript. D.N. was responsible for the analysis and interpretation of the data, and development and review of the manuscript. G.S.P. was responsible for the conception and design of the study, analysis and interpretation of the data, and development and review of the manuscript.

ORCID

Sean Wharton  <https://orcid.org/0000-0003-0111-1530>

Rebecca A. G. Christensen  <https://orcid.org/0000-0001-5212-8688>

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