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Schultes, Bernd ; Timper, Katharina ; Cavadini, Gionata ; Rüh, Josefine ; Gerber, Philipp A

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ORIGINAL ARTICLE

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Weight loss and treatment patterns in a real-world population of adults receiving liraglutide 3.0 mg for weight management in routine clinical practice in Switzerland (ADDRESS study)

Bernd Schultes MD[1] | Katharina Timper MD[2,3] | Gionata Cavadini PhD[4] | Josefine Rüh MSc[4] | Philipp A. Gerber MD[5]

[1]Metabolic Center St. Gallen, friendlyDocs Ltd, St. Gallen, Switzerland

[2]Endocrinology, Diabetes and Metabolism Clinic, University Hospital Basel, Basel, Switzerland

[3]Department of Biomedicine, University of Basel, Basel, Switzerland

[4]Novo Nordisk Pharma AG, Zurich, Switzerland

[5]Department of Endocrinology, Diabetology and Clinical Nutrition, University Hospital Zurich (USZ) and University of Zurich (UZH), Zurich, Switzerland

Correspondence
Philipp A. Gerber, Department of Endocrinology, Diabetology and Clinical Nutrition, University Hospital Zurich (USZ), 8091 Zurich, Switzerland.
Email: philipp.gerber@usz.ch

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Abstract

Aim: To assess weight loss associated with liraglutide 3.0 mg treatment in individuals with obesity (body mass index [BMI] ≥30 kg/m^2) or overweight (BMI > 27 to <30 kg/m^2) in a reimbursed, real-world setting in Switzerland.

Materials and Methods: ADDRESS was a non-comparative, multicentre, retrospective exposure cohort study in Switzerland, examining weight loss in individuals with obesity or overweight whose treatment was reimbursed (divided into BMI subgroups) or non-reimbursed. The primary outcomes were proportions of participants in the reimbursed cohort achieving predefined weight loss targets with liraglutide 3.0 mg at Week 16 (≥5% and ≥7% for the lower BMI [28 to <35 kg/m^2 with weight-related comorbidities] and higher BMI [≥35 kg/m^2] subgroups, respectively) and Month 10 (additional ≥5% from Week 16; per Swiss reimbursement criteria).

Results: The full analysis set comprised 258 individuals (195 reimbursed; 63 non-reimbursed). In the reimbursed cohort, 139 individuals (71.3%) achieved their weight loss targets at Week 16. Of individuals who met the Week-16 criteria, 43.2% attained an additional 5% weight loss at Month 10. In 162 individuals for whom data were recorded at Month 10, the mean (standard deviation) relative weight loss from baseline to Month 10 was −12.4% (6.4%).

Conclusions: Although reimbursement criteria may be difficult to achieve, particularly the additional weight loss of 5% from Week 16 to Month 10, a clinically relevant overall weight loss from baseline to Month 10 was shown in most individuals with obesity or overweight who received liraglutide 3.0 mg.

KEYWORDS
effectiveness, GLP-1, liraglutide, real-world evidence, weight control

Bernd Schultes and Katharina Timper are joint first authors.

1 | INTRODUCTION

According to the 2017 Swiss Health Survey, the prevalence of obesity in Switzerland, although lower than in other western European countries, has more than doubled in 25 years, from 5% in 1992 to 11% in 2017.[1] A further 31% of people in Switzerland were living with overweight in 2017 according to the same survey.[1] The prevalence of obesity and overweight appears to have stabilized over the past few years.[1]

An initial reduction in body weight of approximately 5% is often feasible with lifestyle changes alone and may help to improve health-related issues.[2] This weight loss is often not sustainable or may be followed by weight gains greater than the initial weight loss.[3] Lifestyle changes can be facilitated by pharmacological approaches.[4] According to the European Guidelines for Obesity Management in Adults, pharmacotherapy should be considered as part of a comprehensive disease management strategy and is recommended for adults with a body mass index (BMI) ≥30 kg/m^2 or a BMI ≥27 kg/m^2 with an obesity-related comorbidity.[5]

Glucagon-like peptide-1 (GLP-1) is an important hormonal signal of the gut–brain axis that plays a key role in prandial and postprandial processes, including satiation. The GLP-1 receptor agonist liraglutide 3.0 mg is approved in the United States (Food and Drug Administration),[6] Europe (European Medicines Agency),[7] the United Kingdom (Medicines and Healthcare Products Regulatory Agency),[8] Canada (Health Canada)[9] and Switzerland (Swissmedic)[10] as an adjunct therapy to diet and exercise for weight management.[10] Liraglutide is administered at a starting dose of 0.6 mg and is escalated in stepwise increments to a dose of 3.0 mg, injected once daily.[10]

In a 56-week randomized controlled trial, individuals demonstrated statistically significantly greater weight loss from baseline to Week 56 with liraglutide 3.0 mg (−8.0%) than with placebo (−2.6%). Furthermore, the proportions of individuals who achieved a weight loss of ≥5% and ≥10% were statistically significantly higher in the group receiving liraglutide 3.0 mg (63.2% and 33.1%, respectively) than in the placebo group (27.1% and 10.6%, respectively).[11]

Although liraglutide 3.0 mg has been shown to significantly support weight loss in clinical trials, evidence from real-world clinical practice in Switzerland is scarce. Although there is a lack of published real-world evidence as well as cost-effectiveness analyses, information provided in the evaluation and treatment guidance from the National Institute for Health and Care Excellence (NICE) in the United Kingdom suggests that liraglutide 3.0 mg, prescribed for up to 2 years, meets the prespecified cost-effectiveness criteria.[12] The NICE guidance recommends treatment with liraglutide 3.0 mg in individuals with a BMI of ≥35 kg/m^2 who have prediabetes (defined as fasting plasma glucose level of 5.5–6.9 mmol/L, or a glycated haemoglobin level of 42–47 mmol/mol) and have a high risk of cardiovascular disease (based on risk factors such as hypertension and dyslipidaemia).[8,12]

Because liraglutide 3.0 mg is reimbursed in Switzerland for individuals who meet strict reimbursement criteria, the Swiss Federal Office of Public Health (FOPH) requires evidence from clinical practice to evaluate whether treatment with liraglutide 3.0 mg and the existing reimbursement criteria can be considered effective, appropriate, and economically efficient in the Swiss care setting.

In Switzerland, the FOPH, who granted reimbursement for liraglutide 3.0 mg from 1 April 2020, has defined the relevant reimbursement criteria using relative weight loss targets specified by time point during treatment and by baseline BMI. Individuals are categorized as having either 'lower BMI' (28 to <35 kg/m^2) with weight-related comorbidities (prediabetes, type 2 diabetes [T2D], hypertension and/or dyslipidaemia) or 'higher BMI' (≥35 kg/m^2). The FOPH reimbursement targets at Week 16 were defined as weight loss of ≥5% in the lower BMI category and ≥7% in the higher BMI category. The target at Month 10 (conditional on meeting the Week-16 criterion), was defined as further weight loss of ≥5% from Week 16 for both groups.

A single-centre, real-world evidence study in Switzerland has investigated liraglutide 3.0 mg treatment in 54 adults with obesity or overweight in a reimbursed setting (treatment costs reimbursed via obligatory health insurance) and showed that 87% of individuals achieved a weight loss of ≥5% after 16 weeks.[13] The mean weight loss from baseline observed in the study was 12.4% after 10 months of treatment.[13]

The primary objective of the ADDRESS study was to further assess the weight loss associated with liraglutide 3.0 mg in individuals with obesity or overweight in a reimbursed, real-world setting in Switzerland, with the primary outcomes being the proportion of individuals meeting the FOPH criteria at Week 16 and Month 10.

2 | METHODS

2.1 | Study design and participants

ADDRESS was a non-comparative, multicentre, retrospective exposure cohort study in Switzerland, examining weight loss associated with liraglutide 3.0 mg in a real-world setting during routine clinical care in reimbursed and non-reimbursed individuals with obesity or overweight. The reimbursed cohort included only individuals who received liraglutide 3.0 mg through mandatory basic insurance starting from 1 April 2020 and comprised two subgroups: individuals with lower BMI and individuals with higher BMI, based on the FOPH criteria. Individuals were included in the non-reimbursed cohort if they received liraglutide 3.0 mg before 1 April 2020 through self-pay or additional private insurance. The non-reimbursed cohort had no subgroups and included individuals with a BMI of ≥28 kg/m^2, based on the BMI threshold for reimbursement set by the Swiss FOPH. The same BMI threshold was applied to the non-reimbursed cohort, to ensure that the baseline was consistent across groups.

All data were obtained through retrospective medical chart review from 14 different clinical practice sites. Relevant information was entered into electronic case report forms by the physicians or appropriately qualified and trained delegates from each study site.

The index date (i.e., the date of liraglutide 3.0 mg initiation) was used as the baseline time point for individuals. The end-of-study date was the date that the last available data point was obtained, with a cut-off of 31 March 2020 for the non-reimbursed cohort or 31 October 2021 for the reimbursed cohort. The end-of-study date was different between cohorts and was set for the non-reimbursed cohort as the final day before treatment was reimbursed.

The main evaluation time points were based on the reimbursement criteria defined by the FOPH at 16 weeks (with a window of ±4 weeks) and 10 months (with a window of ±2 months) after treatment initiation.

An overall retrospective data review period of approximately 38 months was available for the non-reimbursed cohort (from when liraglutide 3.0 mg was first available up to 31 March 2020, after which liraglutide 3.0 mg was reimbursed in Switzerland) and of up to 19 months for the reimbursed cohort (from 1 April 2020 as the first reimbursement date until 31 October 2021 as the cut-off date; Figure S1). Based on the review period of this study, the follow-up for individuals in the reimbursed cohort could range from 10 to 19 months. For the non-reimbursed cohort, patients were expected to have at least one follow-up visit within 12 months after treatment initiation, with a maximum follow-up of 38 months.

2.2 | Inclusion criteria

Eligible participants were aged 18–74 years (inclusive) at the time of treatment initiation and had to have been prescribed liraglutide 3.0 mg for weight management. Baseline weight measurement had to be recorded within 3 months before liraglutide 3.0 mg prescription/initiation and at least one weight assessment had to be recorded after liraglutide 3.0 mg prescription/initiation. For the reimbursed cohort, individuals had to meet the Swiss FOPH criteria with a BMI ≥35 kg/m^2 or a BMI of 28 to <35 kg/m^2 with additional weight-related comorbidities (prediabetes or T2D, arterial hypertension, dyslipidaemia), before receiving liraglutide 3.0 mg treatment. Individuals in the non-reimbursed cohort had to have a BMI ≥30 kg/m^2 or BMI ≥28 kg/m^2 with additional weight-related comorbidities (prediabetes or T2D, arterial hypertension, dyslipidaemia) before receiving liraglutide 3.0 mg treatment. Individuals were excluded if they were treated with any obesity medication for the 12 weeks before initiation of liraglutide 3.0 mg or had undergone bariatric surgery at any time before initiation of liraglutide 3.0 mg treatment. Full inclusion and exclusion criteria are reported in Table S1.

2.3 | Outcomes

All outcomes were assessed in individuals who remained on treatment, and outcomes were considered available if data were recorded within 14 days of treatment discontinuation (i.e., stopping treatment with liraglutide 3.0 mg).

The primary outcomes for the reimbursed cohort were the proportions of participants with weight loss according to the FOPH criteria.

Secondary outcomes for the reimbursed cohort and exploratory outcomes for the non-reimbursed cohort included absolute and relative changes in body weight from baseline to Week 16, Month 10 and study end, from Week 16 to Month 10 and from baseline to study end after 10 months. Other secondary outcomes included duration of liraglutide 3.0 mg treatment in the period from baseline to end of study, treatment discontinuation throughout the study and presence of weight-related comorbidities at treatment initiation (prediabetes, T2D, hypertension and dyslipidaemia).

Exploratory outcomes included liraglutide dosing (starting dose, dose at each visit and maintenance dose) and reasons for treatment discontinuation.

Additionally, the proportions of individuals achieving weight loss of <5%, 5% to <10%, 10% to <15%, 15% to <20% and ≥20% were reported for all time points.

2.4 | Statistical analyses

All data are reported using descriptive statistics. All data were analysed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). All eligible individuals who signed an informed consent form (either study-specific or general consent for research) were included in the enrolled set. The full analysis set (FAS) comprised all eligible individuals receiving liraglutide 3.0 mg for whom data from weight assessments at baseline and Week 16 were available. Weight assessments were considered available if they occurred up to 14 days after treatment discontinuation. Women who became pregnant (enrolled set, $n = 2$; FAS, $n = 1$) and individuals who had undergone bariatric surgery during the study ($n = 0$) were excluded from further body weight and waist circumference analyses.

2.5 | Ethics

The ADDRESS study was conducted in accordance with the Declaration of Helsinki and the Guidelines for Good Pharmacoepidemiology Practices.[14,15] The protocol, patient information and informed consent forms, enrolment procedures and any other relevant documents were approved by an independent ethics committee (*Kantonale Ethikkommission Zürich*). Informed consent was requested from individuals at enrolment unless they had previously signed a general consent form for research.

3 | RESULTS

3.1 | Participant disposition and baseline characteristics

In total, 269 individuals were enrolled (reimbursed cohort, $n = 203$; non-reimbursed cohort, $n = 66$ [Figure S2]). The FAS comprised 258 individuals (reimbursed cohort, $n = 195$ [96.1% of enrolled individuals]; non-reimbursed cohort, $n = 63$ [95.5% of enrolled individuals]). The reimbursed cohort was further divided into lower BMI ($n = 77$) and higher BMI ($n = 118$) subgroups.

Most participants had recorded Week-16 and Month-10 visits: 84.7% in the reimbursed cohort (lower BMI subgroup, 86.3%; higher BMI subgroup, 83.7%) and 83.3% in the non-reimbursed cohort. In

total, 31 individuals were assigned by the investigator to either Week 16 or Month 10 despite the date of the relevant study visit falling outside of the predefined window (Week 16 ± 4 weeks or Month 10 ± 2 months): 11 in the lower BMI subgroup (seven at Week 16 only and four at Month 10 only) and 20 in the higher BMI subgroup (15 at Week 16 only, one at Month 10 only, four at both Week 16 and Month 10). Most data captured outside the predefined window were observed around the Week 16 window, where these were within 1 week or 2 weeks of the predefined window. At Month 10, fewer observations were made outside of the predefined window than at Week 16, and these ranged from a few days early, to several weeks after the window. Three individuals in the reimbursed cohort (two of lower BMI; one of higher BMI) had a Month-10 visit after the cut-off date (31 October 2021) and three individuals in the non-reimbursed cohort had a Month-10 visit after the cut-off date (31 March 2020).

The mean age at time of liraglutide initiation was similar in the two cohorts (Table 1). Most individuals had at least one relevant concurrent medical condition and were already receiving a concomitant medication at baseline (Table 1; Table S2). Two individuals who received medication listed in the exclusion criteria were included in the analysis because the disallowed medication (semaglutide) was started after Month 10 or after end of study after Month 10: one (reimbursed cohort, higher BMI subgroup) started it after stopping liraglutide 3.0 mg and the other (non-reimbursed cohort) started it after Month 10.

Relevant weight-related comorbidities, defined in the approved Swiss label (prediabetes, T2D, hypertension, and dyslipidaemia) were present at baseline in 135 individuals (69.2%) in the reimbursed cohort and 34 individuals (54.0%) in the non-reimbursed cohort, with dyslipidaemia reported most frequently (Table 1).

3.2 | Weight loss

In the reimbursed cohort, 139 individuals (71.3%) achieved target weight loss from baseline to Week 16, specifically, 66 (85.7%) in the lower BMI subgroup (target ≥5%) and 73 (61.9%) in the higher BMI subgroup (target ≥7%; Figure 1). Of these, 60 individuals (43.2%) achieved an additional weight loss of ≥5% at Month 10, while 67 (48.2%) did not; data for 12 individuals (8.6%) were missing (Figure 1). In the lower BMI group, 27 of 66 (40.9%) individuals and 33 of 73 (45.2%) individuals in the higher BMI group met the 10-month FOPH criteria (Figure 1). The corresponding proportions of individuals who achieved the weight loss target at Week 16 but not at Month 10 were similar in the two subgroups: 31 of 66 (47.0%) in the lower BMI subgroup and 36 of 73 (49.3%) in the higher BMI subgroup (Figure 1). Of the 195 individuals in the reimbursed cohort who started treatment, 60 (30.8%) achieved this required weight loss target for reimbursement at Month 10.

In individuals who achieved the weight loss target at Week 16 but not at Month 10, the mean (standard deviation [SD]) relative change in weight from baseline to Month 10 was −11.1% (5.0%), with

TABLE 1 Baseline demographics and clinical characteristics at liraglutide 3.0 mg initiation (full analysis set).

	Reimbursed cohort			Non-reimbursed cohort
	Lower BMI ($n = 77$)	Higher BMI ($n = 118$)	Total ($n = 195$)	Total ($n = 63$)
Age, years	46.4 (12.59)	46.5 (11.79)	46.5 (12.08)	48.7 (10.53)
Female, *n* (%)	59 (76.6)	90 (76.3)	149 (76.4)	49 (77.8)
Height, cm	167.74 (9.447)	166.44 (9.166)	166.95 (9.275)	165.86 (8.033)
Body weight, kg	89.29 (10.866)	109.02 (16.628)	101.23 (17.506)	96.72 (18.001)
BMI, kg/m^2	31.67 (1.807)	39.26 (4.243)	36.26 (5.098)	35.05 (5.347)
Waist circumference, cm	102.52 (13.261)	118.04 (11.777)	112.07 (14.434)	107.30 (12.545)
n	25	40	65	12
Any weight-related comorbidity[a]	62 (80.5)[b]	73 (61.9)	135 (69.2)	34 (54.0)
Prediabetes[c]	16 (20.8)	27 (22.9)	43 (22.1)	10 (15.9)
Type 2 diabetes	4 (5.2)	5 (4.2)	9 (4.6)	0
Hypertension[d]	25 (32.5)	42 (35.6)	67 (34.4)	13 (20.6)
Dyslipidaemia[e]	44 (57.1)	38 (32.2)	82 (42.1)	27 (42.9)
Any medical condition, *n* (%)	72 (93.5)	107 (90.7)	179 (91.8)	54 (85.7)
Any concomitant medication, *n* (%)	58 (75.3)	100 (84.7)	158 (81.0)	42 (66.7)

Note: All data are mean (SD) unless otherwise specified. Lower BMI: 28 to <35 kg/m^2; higher BMI: ≥35 kg/m^2.
Abbreviations: BMI, body mass index; SD, standard deviation.
[a]Weight-related comorbidities are reported based on the approved Swiss label and include prediabetes, type 2 diabetes, hypertension and dyslipidaemia.
[b]In the lower BMI subgroup, weight-related comorbidities were not reported for 15 individuals.
[c]Prediabetes includes impaired glucose tolerance and impaired fasting glucose.
[d]Hypertension includes hypertension and diastolic hypertension.
[e]Dyslipidaemia includes dyslipidaemia, hypercholesterolaemia, hyperlipidaemia and hypertriglyceridaemia.

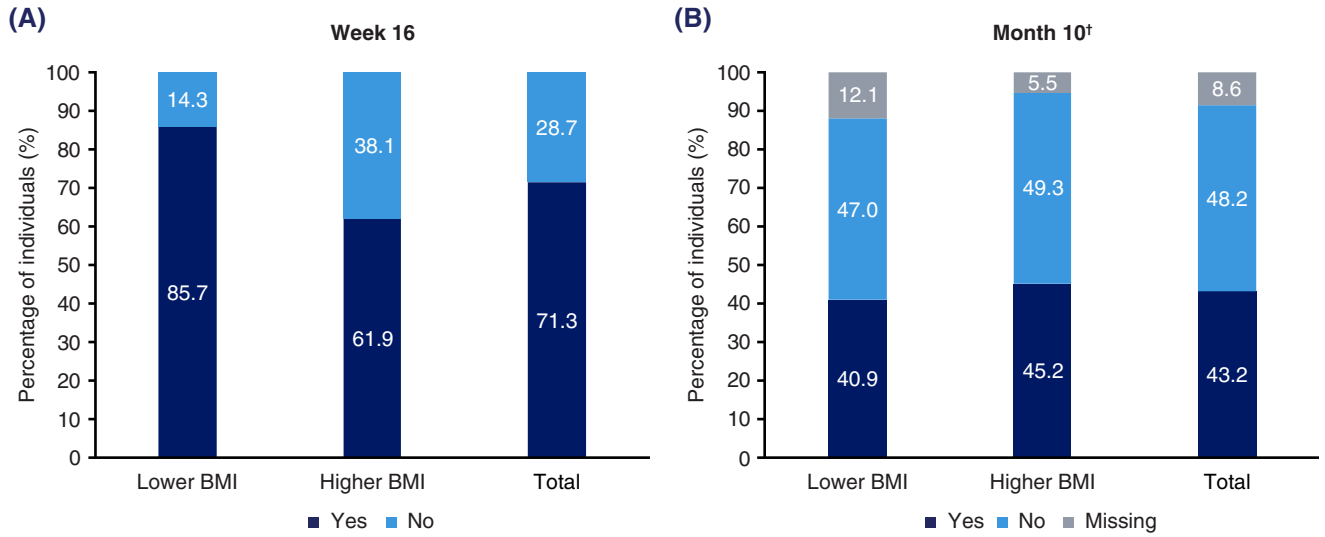

FIGURE 1 Proportion of individuals in the reimbursed cohort achieving the Swiss Federal Office of Public Health (FOPH) relative weight loss targets from baseline to Week 16 (A) and from Week 16 to Month 10 (B). 'Yes' denotes individuals who achieved the relevant FOPH relative weight loss target and 'no' denotes those who did not. Week 16: lower body mass index (BMI), $n = 77$; higher BMI, $n = 118$; total, $n = 195$. Month 10 (based on achieving weight loss from baseline to Week 16): lower BMI, $n = 66$; higher BMI, $n = 73$; total, $n = 139$. †Month 10 includes individuals who achieved the Week-16 weight loss target. Lower BMI, 28 to <35 kg/m^2; higher BMI, ≥35 kg/m^2.

TABLE 2 Relative change in body weight (full analysis set).

	Reimbursed cohort			Non-reimbursed cohort
	Lower BMI ($n = 77$)	Higher BMI ($n = 118$)	Total ($n = 195$)	Total ($n = 63$)
From baseline to Week 16				
n[a]	77	118	195	63
Change, %	−8.68 (3.848)	−8.36 (4.284)	−8.49 (4.110)	−7.09 (4.358)
From Week 16 to Month 10				
n[a]	64	98	162	43
Change, %	−3.90 (3.992)	−3.53 (5.099)	−3.67 (4.683)	−2.94 (4.830)
From baseline to Month 10				
n[a]	64	98	162	43
Change, %	−12.50 (5.512)	−12.31 (6.884)	−12.39 (6.360)	−9.64 (6.484)
From baseline to EOS				
n[a]	77	118	195	63
Change, %	−11.56 (5.662)	−10.92 (7.187)	−11.17 (6.619)	−9.09 (6.335)
From baseline to EOS after Month 10				
n[a]	6	9	15	6
Change, %	−9.05 (5.350)	−13.85 (7.433)	−11.93 (6.909)	−6.83 (4.518)

Note: All change data are mean (SD). Lower BMI, 28 to <35 kg/m^2; higher BMI, ≥35 kg/m^2.
Abbreviations: BMI, body mass index; EOS, end of study; SD, standard deviation.
[a]Individuals for whom there were data.

similar weight loss between the lower BMI and higher BMI subgroups: −11.5% (4.3%) and −10.8% (5.6%), respectively (Figure S3). Of note, most of the relative weight loss in these participants was achieved within the first 16 weeks: mean (SD) relative change in weight from baseline to Week 16 and from Week 16 to Month 10 was −10.0% (3.6%) and −1.3% (3.3%), respectively.

For individuals who maintained (i.e., did not discontinue) treatment until Week-16 data were recorded, the mean (SD) relative change in body weight from baseline to Week 16 was −8.5% (4.1%) in the total reimbursed cohort, −8.7% (3.8%) in the lower BMI subgroup and −8.4% (4.3%) in the higher BMI subgroup (Table 2; Figure 2). The mean (SD) relative change in body weight from Week 16 to Month 10 was −3.7% (4.7%) in the reimbursed cohort, −3.9% (4.0%) in the lower BMI subgroup and −3.5% (5.1%) in the higher BMI subgroup. The mean (SD) relative change in body weight from baseline to Month 10 was −12.4% (6.4%) in the reimbursed cohort,

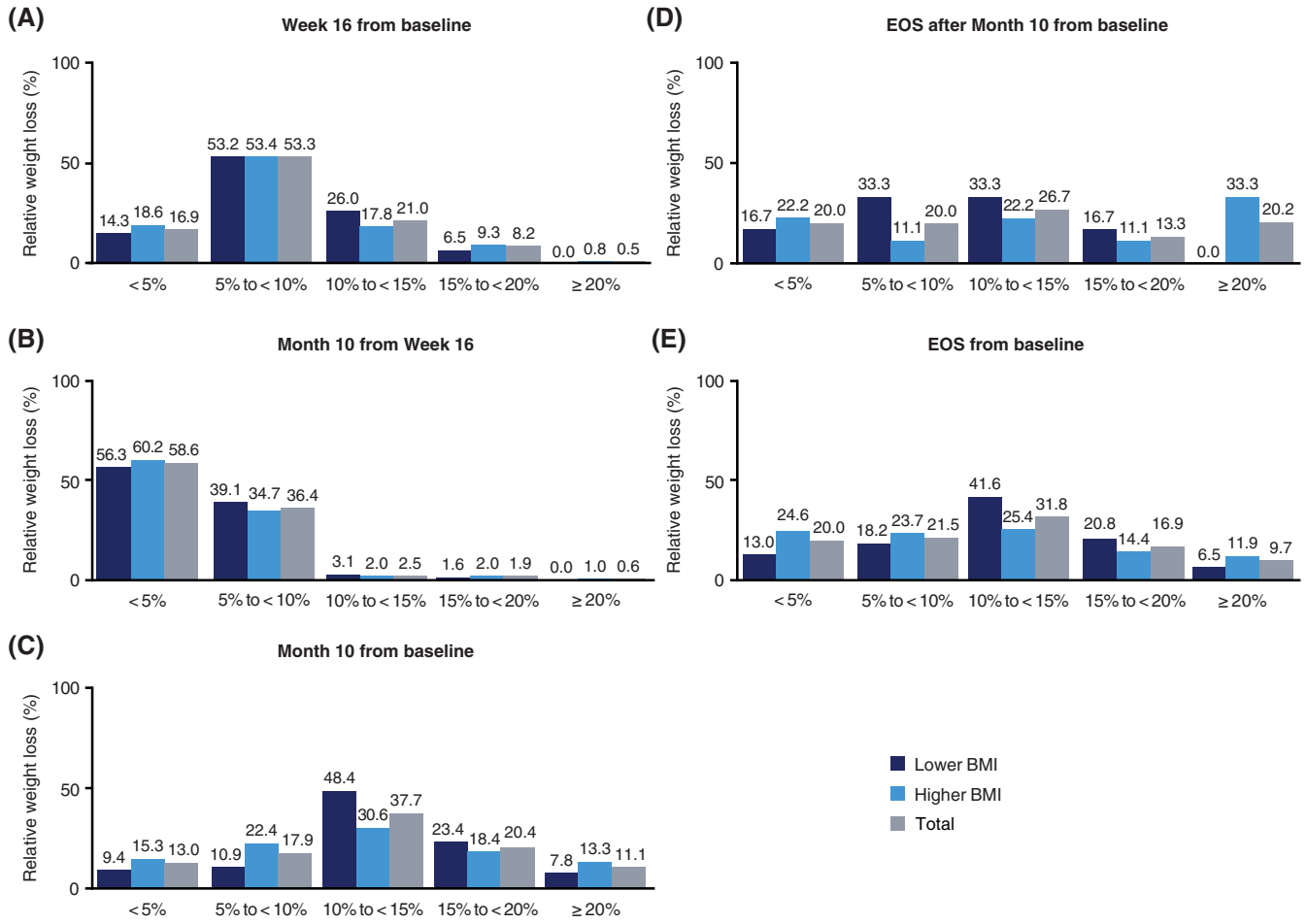

FIGURE 2 Proportion of individuals in the reimbursed cohort in weight loss categories for (A) baseline to Week 16, (B) Week 16 to Month 10, (C) baseline to Month 10, (D) baseline to end of study (EOS) after Month 10 and (E) baseline to EOS. Week 16 and EOS: lower body mass index (BMI), $n = 77$; higher BMI, $n = 118$; total, $n = 195$. Month 10 (from baseline and from Week 16): lower BMI, $n = 64$; higher BMI, $n = 98$; total, $n = 162$. EOS after Month 10: lower BMI, $n = 6$; higher BMI, $n = 9$; total, $n = 15$. Lower BMI, 28 to <35 kg/m^2; higher BMI, ≥35 kg/m^2.

−12.5% (5.5%) in the lower BMI subgroup and −12.3% (6.9%) in the higher BMI subgroup (Table 2). The mean relative changes in body weight for all time points are shown in Table 2. The proportions of individuals achieving weight loss categories of <5%, 5% to <10%, 10% to <15%, 15% to <20% and ≥20% are shown in Figure 2. The proportions of individuals achieving the cumulative weight loss categories of <5%, ≥5%, ≥10%, ≥15% and ≥20% are shown in Table S4.

In the non-reimbursed cohort, the mean (SD) relative change in body weight from baseline to Week 16, from Week 16 to Month 10 and from baseline to Month 10 was −7.1% (4.4%), −2.9% (4.8%) and −9.6% (6.5%), respectively (Figure S4).

Absolute weight loss and change in weight at all time points for both cohorts are shown in Table S5.

3.3 | Treatment duration, dose and discontinuation

The mean (SD) duration of liraglutide treatment during the period from baseline to end of study was 372 (120.0) days for the reimbursed cohort and 382 (194.4) days for the non-reimbursed cohort (Table 3). Liraglutide dosing, duration of treatment and time on maximum dose are shown in Table 3. In the reimbursed cohort, 93.3% of individuals reached the liraglutide 3.0-mg dose; the mean time to reach this dose was 41.5 days. In the non-reimbursed cohort, 69.8% of individuals reached the liraglutide 3.0-mg dose, and the mean time to reach it was 54.2 days.

Overall, seven individuals (3.4%) in the reimbursed cohort and four individuals (6.1%) in the non-reimbursed cohort discontinued treatment during the period from baseline to Week 16 (Table S6). From Week 16 to Month 10, a further 32 individuals (15.8%) in the reimbursed cohort and 19 individuals (28.8%) in non-reimbursed cohort discontinued treatment (Table S6). From Month 10 to end of study, 54 individuals (26.6%) and 19 (28.8%) individuals in the reimbursed and non-reimbursed cohorts, respectively, discontinued treatment (Table S6). A post hoc analysis of participants in the reimbursed cohort who discontinued treatment owing to lack of effectiveness at or after Month 10 showed that overall mean weight loss from baseline to Month 10 was −6.0% ($n = 32$ for the FAS), with basically all the weight loss happening during baseline to Week 16 (−5.9%) and none thereafter (−0.1% between Week 16 and Month 10). Only one

TABLE 3 Liraglutide treatment exposure and dose (full analysis set).

	Reimbursed cohort			Non-reimbursed cohort
	Lower BMI ($n = 77$)	Higher BMI ($n = 118$)	Total ($n = 195$)	Total ($n = 63$)
Duration of liraglutide treatment				
Total duration, days	377.2 (108.17)	368.1 (127.45)	371.7 (120.00)	382.1 (194.38)
1–112 days, *n* (%)	1 (1.3)	4 (3.4)	5 (2.6)	2 (3.2)
113–280 days, *n* (%)	13 (16.9)	19 (16.1)	32 (16.4)	17 (27.0)
≥281 days, *n* (%)	63 (81.8)	95 (80.5)	158 (81.0)	44 (69.8)
Maximum dose reached, *n* (%)				
0.6 mg	0	0	0	0
1.2 mg	0	0	0	6 (9.5)
1.8 mg	0	0	0	8 (12.7)
2.1 mg	0	0	0	1 (1.6)
2.4 mg	4 (5.2)	9 (7.6)	13 (6.7)	4 (6.3)
3.0 mg	73 (94.8)	109 (92.4)	182 (93.3)	43 (68.3)
3.6 mg	0	0	0	1 (1.6)[a]
Calculated dose, mg, median	3.0	3.0	3.0	3.0
Time on maximum dose, days	307.4 (129.32)	304.4 (147.59)	305.6 (140.32)	301.8 (213.04)
Liraglutide 3.0 mg dose achieved, *n* (%)	73 (94.8)	109 (92.4)	182 (93.3)	44 (69.8)
Duration receiving liraglutide 3.0 mg, days	314.8 (126.20)	312.9 (145.33)	313.6 (137.62)	308.2 (161.35)
Time to reach liraglutide 3.0 mg dose, days	43.1 (41.53)	40.4 (40.04)	41.5 (40.55)	54.2 (55.44)

Note: All data are mean (SD) unless otherwise specified. Lower BMI: 28 to <35 kg/m^2; higher BMI: ≥35 kg/m^2.
Abbreviations: BMI, body mass index; SD, standard deviation.
[a]Liraglutide 3.6 mg is not an approved dose and is included here as reported in the electronic case report forms.

of these 32 participants fulfilled the weight loss requirements mandated by the FOPH. Among the 30 FAS participants for whom data were available, a weight loss from baseline to Month 10 of ≥5% and ≥10% was achieved by 20 and four individuals. Reasons for discontinuation are shown in Table S6.

4 | DISCUSSION

The primary objective of the ADDRESS study was to assess the weight loss associated with liraglutide 3.0 mg treatment in individuals living with obesity or overweight in a reimbursed, real-world setting in Switzerland, with the primary outcomes being the proportions of individuals meeting the FOPH criteria at Week 16 and Month 10. More than 70% of individuals in the reimbursed cohort met the FOPH criterion at Week 16, of whom <50% met the FOPH criterion at Month 10, which is lower than may have been expected. Nonetheless, the results reported here show that most of the individuals with obesity or overweight who received liraglutide 3.0 mg achieved clinically relevant weight loss of ≥5% from baseline to Month 10 (87.0% of reimbursed individuals and 79.1% of non-reimbursed individuals), consistent with results from another real-world study.[13]

In the ADDRESS study, for the reimbursed cohort, the mean relative reduction in body weight from baseline to Week 16 was −8.5% and from baseline to Month 10 it was −12.4%. These findings on mean relative reduction in body weight are consistent with those from another real-world study[13] and an early-responders analysis[16]; these show promising results in addition to those reported in a series of large, phase 3 randomized controlled trials, in which an average reduction in body weight of approximately 8% was found after 12 months of liraglutide 3.0 mg treatment,[11,17–20] with the caveat that these clinical studies[11,17–20] included all individuals, whereas this study and the other publications mainly focused on good responders.[13,16] The reason for including only good responders in the present analysis is that non-responders would not be reimbursed to continue treatment after Week 16.

The relative weight loss targets at 16 weeks (≥5% and ≥7% for individuals with lower BMI and higher BMI, respectively) were achieved by a higher proportion of individuals in the lower compared to the higher BMI subgroup (85.7% vs. 61.9%). Although individuals in the higher BMI subgroup may achieve a higher absolute weight loss (in kg), these findings indicate that a higher relative weight loss target (≥7%) in individuals with higher BMI may be more difficult to achieve than a lower relative weight loss target (≥5%) in individuals with lower BMI. Therefore, having a higher threshold for those with higher BMI should be reviewed. Although <50% of individuals achieved an additional weight loss of ≥5% between Week 16 and Month 10, it should be noted that among those who had not achieved the target at Month 10, the mean relative weight loss from baseline to Month 10 was 11.1%, indicating that substantial weight loss still occurred during this

period even though the reimbursement target was not met. This is notable because a weight loss of ≥10% has the potential to yield positive health benefits.[21] Owing to the restrictive relative weight loss target from Week 16 to Month 10 that is stipulated by the FOPH for reimbursement at the time of this study, physicians might resort to mitigating strategies, such as slowing dose uptitration to avoid excessive weight loss during the first 16 weeks. This potential influence of strict regulatory guidance on clinical decision-making (such as dose adjustments) is undesirable and may be detrimental to individuals seeking treatment, suggesting that target definitions regarding subsequent weight loss after the initial 16 weeks of treatment should be avoided.

Weight loss does not follow a linear function over time and is highly individual; therefore, very good responders may lose most weight early on during treatment and subsequently experience weight loss at a lower rate, potentially putting them at a disadvantage when considering the specific predefined sequential weight loss criteria. To avoid bias in measuring treatment success, it could be argued that weight loss at any time point should be measured from baseline, and not from a previous time point during treatment. In line with our findings, the FOPH reimbursement criteria have been revised to require individuals to meet a cumulative weight loss from baseline to Month 10, not to Week 16; the revised criteria were implemented on 1 June 2023.

The data reported in this study show that >90% of the reimbursed cohort reached the target dose of liraglutide 3.0 mg compared with <70% of the non-reimbursed cohort. The mean time to reach the liraglutide 3.0-mg dose was lower in the reimbursed cohort than in the non-reimbursed cohort (41.5 days vs. 54.2 days). The lower dose and the slower uptitration in the non-reimbursed cohort may be explained by cost concerns, considering that many individuals were paying for the treatment themselves. The mean duration of liraglutide treatment during the period from baseline to end of study was just over 1 year in both groups. It should be noted that many individuals were still receiving liraglutide 3.0 mg at the cut-off date, so treatment duration was longer for those individuals.

Although ADDRESS was not designed or powered to compare the non-reimbursed and reimbursed cohorts, results suggest that weight loss during the study was lower in the non-reimbursed cohort than in the reimbursed cohort. Differences between cohorts in the maximum dose reached, potentially influenced by treatment costs, may have contributed to differences in observed weight loss between cohorts. Another factor that may have influenced relative weight loss in the two cohorts is how the Swiss label guidance (treatment should be discontinued if a weight loss of ≥5% is not achieved after 12 weeks of liraglutide at the 3.0-mg dose) is applied in the different reimbursement settings. How relevant criteria were applied in the non-reimbursed setting is unknown, and non-responders may have continued treatment.

Few individuals discontinued treatment up to Week 16. Discontinuation was higher from Week 16 to Month 10 and from Month 10 to end of study post Month 10 than from baseline to Week 16, possibly driven by the sequential weight loss target as part of the reimbursement criteria. It is important to note that weight stabilization may be (mis)perceived as loss of effectiveness by many individuals, which may contribute to the decision to stop treatment. Indeed, it could be argued that weight maintenance in general should be seen as a success in a scenario when otherwise weight regain would be expected. Individuals should be informed that weight maintenance is also part of the disease management strategy.

4.1 | Limitations

This study has some limitations. All analyses in this study were descriptive, precluding the interpretation of any observed potential differences between the two cohorts, the two BMI subgroups, or baseline and follow-up. Owing to the retrospective nature of the study, it was not feasible to obtain data precisely at Week 16 or Month 10. Consequently, there was no strict window of time allowed for classifying measurements during these time points. Furthermore, the lack of effectiveness that was recorded in electronic case report forms did not have a clear definition to distinguish between reimbursement conditions versus the interpretations of individuals and physicians. Weight measures at each time point were only included for individuals who continued treatment until the indicated time points. Finally, the potential effects of age or demographic characteristics were not investigated here and could be investigated in future studies.

5 | CONCLUSIONS

In this real-world study in Switzerland, most individuals with obesity or overweight who received liraglutide 3.0 mg achieved clinically relevant weight loss. Overall, more than two-thirds of individuals in the reimbursed cohort achieved the FOPH Week-16 weight loss target, of whom fewer than half achieved the FOPH further weight loss target by Month 10. Among individuals who did not achieve the Month 10 FOPH criterion, the mean relative change in weight from baseline to Month 10 was −11.1%, indicating meaningful reductions in body weight. To measure treatment and weight loss successes in a non-discriminating manner (e.g., not stopping reimbursement), it is important that weight loss at any given time point is measured using weight at baseline as a reference, because weight loss is highly individual and does not occur linearly over time, that is, early treatment responders may not meet the target weight loss after 10 months, owing to early treatment success. This issue is now adequately addressed in the revised Swiss reimbursement criteria.

AUTHOR CONTRIBUTIONS

All authors contributed to the acquisition, analysis or interpretation of study data and participated in preparing the manuscript, with the support of medical writing services. All authors agreed with the results and conclusions of the study and approved the submitted version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

Bernd Schultes reports receiving consulting fees from Abbott, Boehringer Ingelheim, Lilly and Novo Nordisk, other fees from Abbott, Lilly, Novo Nordisk and Sanofi, and an unrestricted research grant from Novo Nordisk. Katharina Timper reports receiving research grants from Fondation Machaon (Geneva), the Goldschmidt-Jacobson Foundation (Basel), the Gottfried and Julia Bangerter-Rhyner Foundation, the Novartis Foundation for Medical-Biological Research, Novo Nordisk, the Olga Mayenfisch Foundation, the propatient Research Foundation of University Hospital Basel, the Swiss Diabetes Association, the Swiss National Science Foundation, the Swiss Society of Endocrinology and Diabetology, and University Hospital Basel, the University of Basel. Katharina Timper also reports receiving fees from Novo Nordisk, receiving support for attending meetings and/or for travel from Novo Nordisk, participation on data safety monitoring boards or advisory boards for Novo Nordisk, and being a member of the committee of the Swiss Association for the Study of Obesity. Gionata Cavadini and Josefine Rüh are employees of Novo Nordisk and hold shares. Philipp A. Gerber reports receiving grants from the Dr Angela Reiffer Foundation, the Iten-Kohaut Foundation, the Swiss National Science Foundation, the Uniscientia Foundation and the Vontobel Foundation, consulting fees from Amgen, Boehringer Ingelheim, Lilly, Novo Nordisk and Sanofi, fees from Amgen, Lilly and Novo Nordisk, and support for attending meetings and/or for travel from Novo Nordisk. Philipp A. Gerber also reports participation on data safety monitoring boards or advisory boards for Amgen, Lilly and Novo Nordisk, and being a member of the committee of the Swiss Society of Endocrinology and Diabetology.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.15403.

DATA AVAILABILITY STATEMENT

Data will be shared with bona fide researchers submitting a research proposal approved by the independent review board. Individual participant data will be shared in data sets in a de-identified and anonymized format. Data will be made available after research completion. Information about data access request proposals can be found at novonordisk-trials.com.

ORCID

Bernd Schultes https://orcid.org/0000-0002-5301-1163
Katharina Timper https://orcid.org/0000-0002-4988-6338
Gionata Cavadini https://orcid.org/0009-0000-5102-3534
Philipp A. Gerber https://orcid.org/0000-0002-2476-7076

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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