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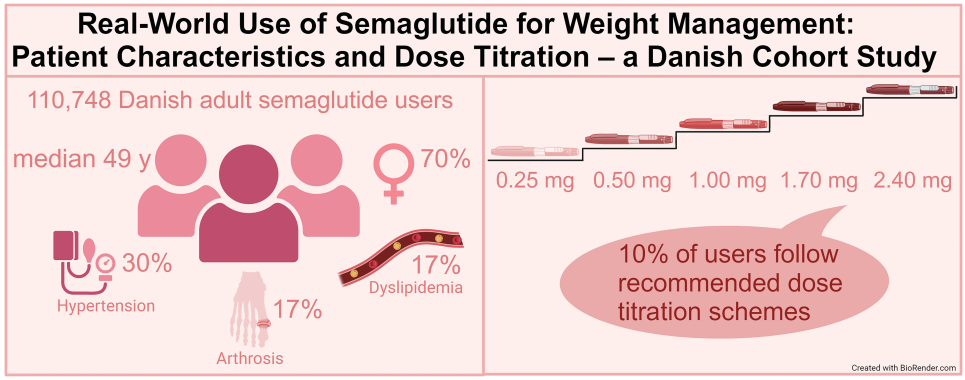

ARTICLE HIGHLIGHTS

- **Why did we undertake this study?**
  Real-world users of medicines are often different from participants in clinical trials and potentially have different use patterns from the dose regimens tested in the trials.
- **What is the specific question(s) we wanted to answer?**
  We investigated whether real-world user characteristics and dose titration patterns of semaglutide (Wegovy) differ from those tested in clinical trials.
- **What did we find?**
  Patient characteristics are largely comparable; however, titration patterns differ, with a substantial proportion of users not exceeding 1.0 mg rather than reaching the recommended target dose of 2.4 mg.
- **What are the implications of our findings?**
  The majority of real-world semaglutide users never reach the dosage evaluated in most clinical trials for weight management. The underlying reasons and consequences of this remain unknown.

Real-World Use of Semaglutide for Weight Management: Patient Characteristics and Dose Titration—A Danish Cohort Study

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BRIEF REPORT

OBJECTIVE

To determine patient characteristics and dose titration patterns of real-world semaglutide (Wegovy) users.

RESEARCH DESIGN AND METHODS

We used a population-based cohort study including Danish adults who filled semaglutide prescriptions from 12 December 2022 to 31 December 2023. Outcomes were patient characteristics, prescriber type, and dose titration patterns.

RESULTS

We identified 110,748 individuals (median age 49 years; 70% female) filling 773,708 prescriptions for semaglutide. General practitioners initiated treatment in 86%. Common comorbidities included hypertension (30%), dyslipidemia (17%), and arthrosis (17%). Only 13% reached the maximum dose of 2.4 mg by their fifth prescription, while 5.7% stopped after the first prescription. Few users (10%) followed recommended dose increases every 4 weeks. Overall, 25% filled at least one prescription of 2.4 mg, while 33–48% continued with the 1.0-mg dosage from the fourth prescription onward.

CONCLUSIONS

Real-world semaglutide users generally resembled trial participants, but few follow the dose titration schemes tested in premarket clinical trials.

On 4 June 2021, the U.S. Food and Drug Administration approved semaglutide (Wegovy) for chronic weight management in adults (1) based on documentation for on average 13% weight loss compared with placebo (2). More recently, semaglutide has also demonstrated a notable 20% decrease in risk of major cardiovascular events in patients with overweight or obesity with preexisting cardiovascular disease (3). Trials on the use of semaglutide have included adults with obesity with and without type 2 diabetes as well as patients with a history of cardiovascular disease (3–5). In all trials, semaglutide was initially administered at a dosage of 0.25 mg, with increments every 4 weeks until reaching 2.4 mg per week. Consequently, 2.4 mg is also the recommended target dose in current treatment guidelines.

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However, real-world users of medicines are often different from participants in clinical trials (6–8), and also potentially have different use patterns from the dose regimens tested in the trials (9). We therefore described patient characteristics and dose titration patterns of real-world semaglutide users in a nationwide cohort study.

RESEARCH DESIGN AND METHODS

Semaglutide (Wegovy) entered the Danish market in December 2022 for weight management in individuals with a BMI $\geq$27 kg/m^2 and one or more adiposity-related comorbidities or with a BMI $\geq$30 kg/m^2. The cost of semaglutide is not publicly reimbursed but is covered, in part by, some private health insurances.

Study Population

We identified all Danish adults who filled semaglutide (Wegovy) prescriptions from 12 December 2022 to 31 December 2023 using the Danish National Prescription Registry (10) (Supplementary Table 1). Individuals were included on the date of filling the first prescription for semaglutide and followed until 30 April 2024 (end of data availability).

Analysis

First, to describe patients at the time of treatment initiation, we performed a detailed characterization in terms of age, sex, adiposity-related comorbidities, comedications, glycated hemoglobin, hospital contacts, and type of prescriber initiating treatment.

Second, we described dose titration patterns of semaglutide for all individuals redeeming their first prescription before 31 May 2023 (i.e., ensuring at least 11 months of data availability up to 30 April 2024). Prescription number (first, second, etc.) was plotted against dose and displayed using a Sankey diagram. If a person filled more than one dose on the same day, the one with the highest strength was used. If an individual did not fill any prescription for semaglutide within a 3-month period, they were classified as stopped (discontinued). Individuals were censored upon death, migration, and end of study period. We performed supplementary analyses without the time constraint of 31 May as well as restricting to *1*) individuals who had redeemed a prescription for any glucose-lowering drug used in diabetes before their first semaglutide prescription, *2*) individuals who had semaglutide initiated by their general practitioner, and *3*) individuals with and without prior use of liraglutide (Saxenda) and semaglutide (Ozempic) and without a marker of type 2 diabetes. Finally, we also determined sex differences in dose titration patterns of semaglutide.

Approvals and Ethics

According to Danish law, studies based solely on register data do not require approval from an ethics review board (11). The data underlying this study are available from the Danish Health Data Authority. Restrictions apply to the availability of these data, which were used under license for this study.

RESULTS

We identified 110,748 adult Danish individuals who initiated semaglutide (Wegovy) treatment during 2022–2023. These individuals filled a total of 773,708 prescriptions with a median of 8 prescriptions (interquartile range [IQR] 5–10).

Users of semaglutide (Table 1) were most often women (70%) and had a median age of 49 years (IQR 40–57 years). A large proportion (20%) had previously used either liraglutide for weight management (Saxenda; 11%) or semaglutide (Ozempic; 10%) without a marker of type 2 diabetes (indicative of Ozempic off-label use). Semaglutide was primarily initiated by general practitioners (86%). The most common obesity-related comorbidities among semaglutide users were hypertension (30%), dyslipidemia (17%), and arthrosis (17%), whereas only 7.7% had established atherosclerotic cardiovascular disease. Of those with an available HbA_{1c} measurement within 1 year prior to semaglutide initiation (76%), 24% were in the prediabetes range, and about 4% of our population had diagnosed/treated

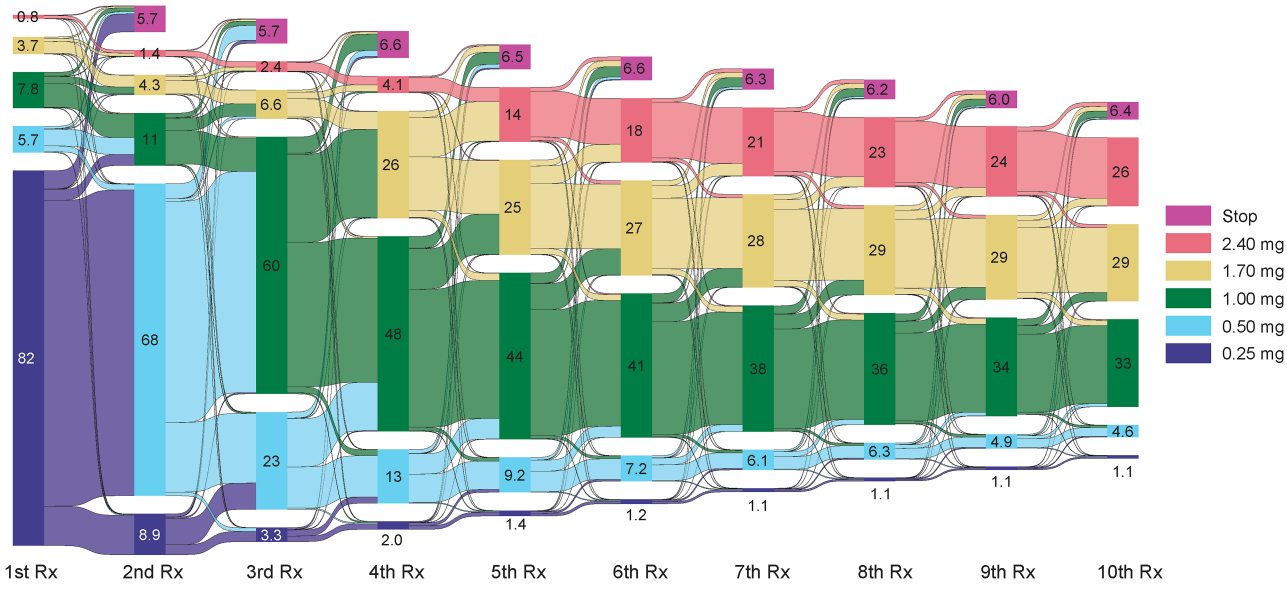

Figure 1—Sankey diagram showing dose titration of semaglutide from first prescription (Rx) until the tenth prescription for users redeeming semaglutide before 31 May 2023 (i.e., ensuring at least 11 months follow-up). The number in each column indicates the relative percentages of individuals using the given dose for the given prescription number.

Table 1—Patient characteristics of new users of semaglutide (Wegovy) during the period December 2022 to 31 December 2023

Characteristic	Overall (*n* = 110,748)
Age at initiation, years, median (IQR)	49 (40–57)
Female sex, *n* (%)	77,993 (70)
Past-year use of liraglutide (Saxenda) or semaglutide (Ozempic) without type 2 diabetes, *n* (%)*	22,165 (20)
Comorbidities, *n* (%)†	
Hypertension	32,948 (30)
Arthrosis	18,410 (17)
Dyslipidemia	18,825 (17)
Chronic lung disease	11,785 (11)
Asthma	9,895 (8.9)
Markers of smoking	12,345 (11)
Sleep apnea	9,611 (8.7)
Atherosclerotic cardiovascular disease	8,493 (7.7)
Ischemic heart disease	2,416 (2.2)
Markers of alcohol overuse	6,887 (6.2)
Type 2 diabetes	3,749 (3.4)
Polycystic ovary syndrome	2,527 (2.3)
Eye disease	1,743 (1.6)
Renal disease	1,295 (1.2)
Heart failure	1,201 (1.1)
Neurological disease	967 (0.87)
Nonalcoholic fatty liver disease	827 (0.75)
Type 1 diabetes	803 (0.73)
Number of comorbidities, *n* (%)†	
0	29,897 (27)
1	33,153 (30)
2	21,276 (19)
3	12,775 (12)
4+	13,647 (12)
Comedication, *n* (%)*	
Medication for chronic lung disease	11,154 (10)
Antiplatelets	5,852 (5.3)
Anticoagulants	3,679 (3.3)
Antihyperglycemic drugs (excluding glucagon-like peptide 1 agonists)	3,423 (3.1)
HbA_{1c} within a year prior to semaglutide initiation, *n* (%)‡	81,972 (76)
HbA_{1c} <39	55,631 (52)
HbA_{1c} between 39 and 47	25,729 (24)
HbA_{1c} ≥48	607 (0.57)
Hospital contacts (in or outpatient), median (IQR)§	3 (1–7)
Prescriber type, *n* (%)	
General practitioner	94,698 (86)
Hospital physician	1,700 (1.5)
Primary care (other specialty/unknown)	12,667 (11)

*Drug use is based on the definitions defined in Supplementary Table 1. †Comorbidities are based on the definitions defined in Supplementary Table 2. ‡Excluding patients taking antihyperglycemic drugs (excluding glucagon-like 1 peptide 1 agonists). §Hospital contacts refers to all in- and outpatient hospital visits 2 years before a Wegovy prescription.

diabetes. Of note, 27% had no registered adiposity-related comorbidities.

When restricting to those with at least 11 months follow-up (i.e., initiating treatment before 31 May 2023), a total of 62,824 individuals initiated semaglutide, with a median of 10 redeemed prescriptions (IQR 5–10). The trajectories for these individuals are shown in Fig. 1. The majority (82%) started treatment with a 0.25-mg semaglutide dose (Fig. 1). By the second prescription, 68% titrated up to 0.5 mg, and, by the third, 60% reached a dosage of 1 mg. Thereafter, a smaller percentage titrated to 1.7 mg and 2.4 mg from the fourth prescription onward, while a substantial proportion (33–48%) continued with the 1-mg dosage of semaglutide. Only 13% reached 2.4 mg at their fifth prescription. Nearly 5.7% stopped treatment after the first prescription, and 25% had stopped after their fifth prescription. Overall, 10% followed the treatment guidelines of increasing the dose every 4 weeks. Only 52% had at least one prescription of 1.7 mg semaglutide, and 25% had at least one prescription of 2.4 mg semaglutide. The time between prescriptions was highly consistent with a median time of 28 days (IQR 25–31 days). Similar dose titration patterns were found when not restricting to initiators prior to 31 May or when specifying for individuals with a previous prescription of any glucose-lowering drug, or if the initiation was specified to general practitioner (data not shown). Nevertheless, most adults with prior use of liraglutide (Saxenda) or semaglutide (Ozempic) without a marker of type 2 diabetes initiated semaglutide (Wegovy) at a higher dose than 0.25 mg compared with those without such use (Supplementary Figs. 1 and 2). Finally, males reached higher doses faster than females, with 17% of males redeeming 2.4 mg of semaglutide at their fifth prescription compared with 9.7% of females (Supplementary Figs. 3 and 4).

CONCLUSIONS

We describe patient characteristics and dose titration patterns of semaglutide in the entire Danish adult population. Most users were middle-aged women, with one-fifth previously using liraglutide (Saxenda) or semaglutide (Ozempic). Semaglutide treatment was overwhelmingly initiated by general practitioners. Only 10% of users escalated their doses in accordance with guidelines, and a considerable proportion never exceeded dosages above 1 mg semaglutide.

A key strength of this study is its use of national registries, enabling a comprehensive analysis of user characteristics and dose titrations of semaglutide while eliminating selection biases. One constraint lies in our inability to directly assess practical drug application. Nevertheless, the consistent redemption of prescriptions suggests adherence to physician guidance. Anthropometric measures such as body weight or BMI would have been of interest in regard to study comparison as well as evaluating adherence to treatment guidelines, but, unfortunately, these data are not available on a population level in the

Danish health registries. Moreover, our data set spans only a single year, because of limited market availability.

In the Semaglutide Treatment Effect in People with Obesity (STEP) program trials, which investigated the efficacy of semaglutide in people without diabetes, the mean age ranged from 46 to 55 years (2,4,12,13), 70–80% were females (2,4,12,13), and comorbidities such as hypertension and dyslipidemia ranged between 36 and 38%, sleep apnea 12–18%, arthrosis 12–18% (2,4,12,13), and prediabetes 45–51% (2,4). Thus, obesity-related comorbidities appeared to be somewhat (10–20 percentage points) more frequent in patients from the trials compared with the real-world users included in our study, although a lack of clinical detail in our registries (e.g., blood pressure measurements, primary care diagnoses) could explain part of the differences.

The real-world utilization pattern deviated substantially from the trials, where the majority of patients reached the target dose of 2.4 mg (2,4,5,12,13). The use of lower dosages of semaglutide in the real-world setting could be due to side effects, but, whereas almost 6% discontinued treatment already after the first dose of 0.25 mg in our study, discontinuation of treatment because of side effects was reported in 6–7% of participants after 68 weeks of treatment in the trials (twice as frequent as in the placebo arm) (4,12), with only minor differences in discontinuation rates between the 1.0- and 2.4-mg dosages (5.0% and 6.2%, respectively) (5). This suggests that, in the real-world setting, other factors such as the higher cost of the drug as the dosage increases (in Denmark, the drug price increases for dosages above 1.0 mg) or patients achieving their desired weight loss at lower dosages may also influence the dose escalation of semaglutide. Importantly, an early phase 2 trial demonstrated a clear dose-response relationship, with higher doses of semaglutide leading to markedly larger weight losses without limiting side effects (14), which is also supported by pharmacokinetic studies (15). Thus, the use of lower-than-recommended dosages of semaglutide in the real-world setting could be associated with suboptimal treatment effect and, subsequently, more modest health benefits. Considering the considerable uptake of semaglutide, this should be investigated further.

In conclusion, the characteristics of real-world semaglutide users are close to those of trial participants. However, few follow the dose titration schemes tested in premarket clinical trials, with the majority using lower dosages and/or slower dose escalation than what has been investigated in most clinical trials.

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Author Contributions. L.L., A.M., C.D., K.N.B.-M., and A.P. were involved in the conception, design, and conduct of the study and the interpretation of the results. M.T.E. contributed to the analysis and interpretation. All authors edited, reviewed, and approved the final version of the manuscript. L.L. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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References

1. U.S. Food and Drug Administration. FDA approves new drug treatment for chronic weight management, first since 2014. Accessed 11 March 2024. Available from https://www.fda.gov/news-events/press-announcements/fda-approves-new-drug-treatment-chronic-weight-management-first-2014
2. Garvey WT, Batterham RL, Bhatta M, et al.; STEP 5 Study Group. Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. Nat Med 2022;28:2083–2091
3. Lincoff AM, Brown-Frandsen K, Colhoun HM, et al.; SELECT Trial Investigators. Semaglutide and cardiovascular outcomes in obesity without diabetes. N Engl J Med 2023;389:2221–2232
4. Wilding JPH, Batterham RL, Calanna S, et al.; STEP 1 Study Group. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med 2021;384:989–1002
5. Davies M, Færch L, Jeppesen OK, et al.; STEP 2 Study Group. Semaglutide 2·4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial. Lancet 2021;397:971–984
6. Van Spall HGC, Toren A, Kiss A, Fowler RA. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: a systematic sampling review. JAMA 2007;297:1233–1240
7. He J, Morales DR, Guthrie B. Exclusion rates in randomized controlled trials of treatments for physical conditions: a systematic review. Trials 2020;21:228
8. Knudsen JS, Thomsen RW, Pottegård A, Knop FK, Sørensen HT. Differences between randomized clinical trial patients and real-world initiators of the glucagon-like peptide 1 receptor agonist liraglutide. Diabetes Care 2018;41:e133–e135
9. Haase CL, Serratore Achenbach MG, Lucrezi G, Jeswani N, Maurer S, Egermann U. Use of liraglutide 3.0 mg for weight management in a real-world setting in Switzerland. Obes Facts 2021;14:568–576
10. Pottegård A, Schmidt SAJ, Wallach-Kildemoes H, Sørensen HT, Hallas J, Schmidt M. Data resource profile: the Danish National Prescription Registry. Int J Epidemiol 2017;46:798–798f
11. Thygesen LC, Daasnes C, Thaulow I, Brønnum-Hansen H. Introduction to Danish (nationwide) registers on health and social issues: structure, access, legislation, and archiving. Scand J Public Health 2011;39(7_suppl):12–16
12. Wadden TA, Bailey TS, Billings LK, et al.; STEP 3 Investigators. Effect of subcutaneous semaglutide vs placebo as an adjunct to intensive behavioral therapy on body weight in adults with overweight or obesity: the STEP 3 randomized clinical trial. JAMA 2021;325:1403–1413
13. Rubino D, Abrahamsson N, Davies M, et al.; STEP 4 Investigators. Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity: the STEP 4 randomized clinical trial. JAMA 2021;325:1414–1425
14. O'Neil PM, Birkenfeld AL, McGowan B, et al. Efficacy and safety of semaglutide compared with liraglutide and placebo for weight loss in patients with obesity: a randomised, double-blind, placebo and active controlled, dose-ranging, phase 2 trial. Lancet 2018;392:637–649
15. Overgaard RV, Delff PH, Petri KCC, Anderson TW, Flint A, Ingwersen SH. Population pharmacokinetics of semaglutide for type 2 diabetes. Diabetes Ther 2019;10:649–662