JAMA Network Open

Research Letter | Nutrition, Obesity, and Exercise

Discontinuation of Semaglutide Therapy for Obesity Management

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Introduction

Maintaining weight reduction achieved with semaglutide for obesity management (SOM) may require long-term treatment.[1,2] However, population-based evidence on clinical practice use patterns and discontinuation rates of SOM is limited.[3,4] We, therefore, aimed (1) to quantify the risk of SOM discontinuation among initiators in Denmark and (2) to examine baseline variables associated with SOM discontinuation.

Methods

We designed a registry-based,[5] nationwide cohort study of all first-time SOM users in Denmark between December 1, 2022, and November 1, 2024 (eMethods and eTable in Supplement 1). The study was reported to the Danish Data Protection Agency (record number 2022-0367531/3343) by Aarhus University. In Denmark, solely registry-based research studies are exempt from ethics committee approval and provision of informed consent by participants. We followed the STROBE reporting guidelines for cohort studies.

We included semaglutide-naive adults (aged ≥18 years) without diabetes. We observed the cohort and assessed early discontinuation by computing the 12-month cumulative incidence proportion (our main outcome) and examined discontinuation over time using 1 minus Kaplan-Meier curves. We defined discontinuation as the estimated end date of an SOM prescription coverage period that was followed by a prescription gap (grace period) of 60 or more days, accounting for suboptimal adherence or low dosing; 30-day and 90-day grace periods were examined in sensitivity analyses (eMethods and eFigure in Supplement 1).

We then examined the association between baseline characteristics and later discontinuation by performing an age- and sex-adjusted Poisson regression analysis with robust error variance to compute risk ratios (RRs) with 95% CIs (2-sided $\alpha = .05$). Finally, we described how many individuals reinitiated SOM within 3 months after end of the grace period, and how many filled other obesity management medications within 5 months after the discontinuation date. SAS statistical software version 9.4 (SAS Institute) was used for analyses.

Results

We identified 157 822 first-time SOM initiators between December 1, 2022, and November 1, 2024, comprising 108 551 women (69%) and 49 271 men (31%) (**Figure 1**). The median (IQR) age was 49 (39-58) years.

In total, 77 483 SOM initiators discontinued treatment within 12 months. The corresponding 12-month risk of discontinuation was 49%, using a grace period of 60 days. The risk was 58% and 45% when using 30-day and 90-day grace periods, respectively. The proportion of discontinuers increased from 13% (20 208 individuals) at 3 months to 27% (42 477 individuals) at 6 months and 39% (60 918 individuals) at 9 months (**Figure 2**).

+ Supplemental content

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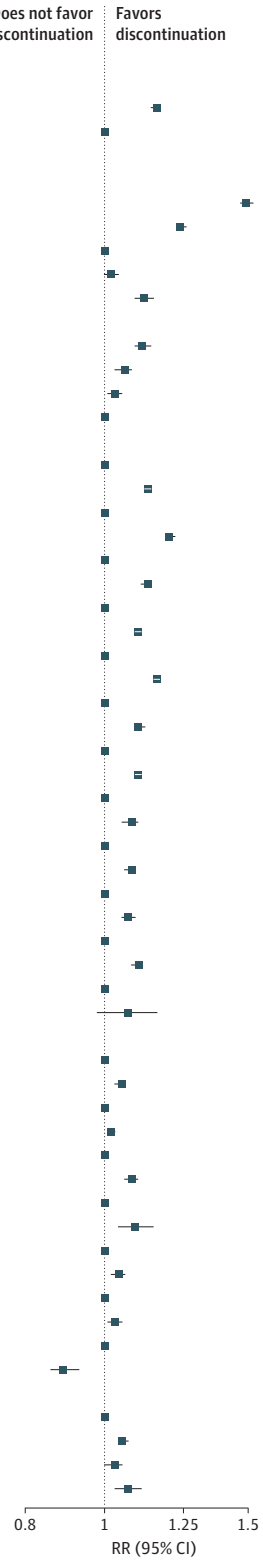
Figure 1. Forest Plot of Association Between Baseline Characteristics and Risk of Semaglutide Discontinuation for Obesity Management

Factors	Total, No. (%)	Discontinuers, No. (%)	Age- and sex-adjusted RR (95% CI)
Sociodemographic factors			
Sex			
Men	49 271 (31.2)	26 477 (53.7)	1.16 (1.14-1.17)
Women	108 551 (68.8)	51 006 (47.0)	1 [Reference]
Age			
Median (IQR)	49 (39-58)	NA	NA
18-29	15 442 (9.8)	10 005 (64.8)	1.49 (1.47-1.52)
30-44	44 818 (28.4)	24 304 (54.2)	1.24 (1.23-1.26)
45-59	68 302 (43.3)	29 804 (43.6)	1 [Reference]
60-69	21 873 (13.9)	9754 (44.6)	1.02 (1.00-1.04)
≥70	7387 (4.7)	3616 (49.0)	1.12 (1.09-1.15)
Average disposable annual income, DKK[a]			
≤240 000	14 340 (9.1)	7589 (52.9)	1.11 (1.09-1.14)
240 001-260 000	61 995 (39.4)	30 589 (49.3)	1.06 (1.03-1.08)
260 001-300 000	67 956 (43.2)	32 991 (48.5)	1.03 (1.01-1.05)
>300 000	13 017 (8.3)	6006 (46.1)	1 [Reference]
History of medication use			
No psychiatric medications	80 767 (51.2)	38 313 (47.4)	1 [Reference]
Psychiatric medications	77 055 (48.8)	39 170 (50.8)	1.13 (1.12-1.14)
No antipsychotics	142 262 (90.1)	68 409 (48.1)	1 [Reference]
Antipsychotics	15 560 (9.9)	9074 (58.3)	1.20 (1.19-1.22)
No anxiolytics	131 607 (83.4)	64 021 (48.7)	1 [Reference]
Anxiolytics	26 215 (16.6)	13 462 (51.4)	1.13 (1.11-1.14)
No hypnotics and sedatives	116 102 (73.6)	56 200 (48.4)	1 [Reference]
Hypnotics and sedatives	41 720 (26.4)	21 283 (51.0)	1.10 (1.09-1.11)
No antidepressants	102 106 (64.7)	48 302 (47.3)	1 [Reference]
Antidepressants	55 716 (35.3)	29 181 (52.4)	1.16 (1.15-1.17)
No gastrointestinal medications	58 330 (37.0)	28 020 (48.0)	1 [Reference]
Gastrointestinal medications	99 492 (63.0)	49 463 (49.7)	1.10 (1.09-1.12)
No antacids	73 505 (46.6)	35 466 (48.3)	1 [Reference]
Antacids	84 317 (53.4)	42 017 (49.8)	1.10 (1.09-1.11)
No antiemetics	150 484 (95.4)	73 691 (49.0)	1 [Reference]
Antiemetics	7338 (4.7)	3792 (51.7)	1.08 (1.05-1.10)
No laxatives	136 409 (86.4)	66 623 (48.8)	1 [Reference]
Laxatives	21 413 (13.6)	10 860 (50.7)	1.08 (1.06-1.09)
No antidiarrheals	142 054 (90.0)	69 593 (49.0)	1 [Reference]
Antidiarrheals	15 768 (10.0)	7886 (50.0)	1.07 (1.05-1.09)
No functional disorder drugs	128 759 (81.6)	62 618 (48.6)	1 [Reference]
Functional disorder drugs	29 063 (18.4)	14 865 (51.2)	1.10 (1.08-1.11)
No gallbladder and liver drugs	157 379 (99.7)	77 245 (49.1)	1 [Reference]
Gallbladder and liver drugs	443 (0.3)	238 (53.7)	1.07 (0.98-1.16)
Obesity-related complications and diseases			
No prediabetes	133 840 (84.8)	65 989 (49.3)	1 [Reference]
Prediabetes	23 982 (15.2)	11 494 (47.9)	1.05 (1.03-1.06)
No metabolic syndrome	79 473 (50.4)	39 424 (49.6)	1 [Reference]
Metabolic syndrome	78 349 (49.6)	38 059 (48.6)	1.02 (1.01-1.03)
No cardiovascular disease	147 163 (93.3)	72 202 (49.1)	1 [Reference]
Cardiovascular disease	10 659 (6.8)	5281 (49.5)	1.08 (1.06-1.10)
No chronic kidney disease	156 210 (99.0)	76 638 (49.1)	1 [Reference]
Chronic kidney disease	1612 (1.0)	846 (52.5)	1.09 (1.04-1.15)
No sleep apnea	145 969 (92.5)	71 511 (49.0)	1 [Reference]
Sleep apnea	11 853 (7.5)	5972 (50.4)	1.04 (1.02-1.06)
No osteoarthritis (knee)	143 517 (90.9)	70 859 (49.4)	1 [Reference]
Osteoarthritis (knee)	14 305 (9.1)	6624 (46.3)	1.03 (1.01-1.05)
No previous bariatric surgery	153 777 (97.4)	75 823 (49.3)	1 [Reference]
Previous bariatric surgery	4045 (2.6)	1661 (41.1)	0.89 (0.86-0.93)
Charlson comorbidity index scores			
0	125 224 (79.4)	61 575 (49.2)	1 [Reference]
1	19 331 (12.3)	9649 (49.9)	1.05 (1.04-1.07)
2	9516 (6.0)	4427 (46.5)	1.03 (1.00-1.05)
≥3	3751 (2.4)	1832 (48.8)	1.07 (1.03-1.11)



Points represent age- and sex-adjusted risk ratios (RRs), with their corresponding 95% CIs as lines. Age is modeled as a cubic spline. Medications and comorbidities are based on the definitions and codes provided in the eTable in Supplement 1. NA indicates not applicable.

[a] Average disposable annual income in the municipality of residence, in Danish Kroner (DKK; 1 DKK = $0.155 US as of July 20, 2026).

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Risk of discontinuation was 41% or higher across all strata of baseline characteristics, suggesting that no user subgroup had a distinctly lower risk of stopping SOM (Figure 1). On a relative scale, risk of discontinuation was increased for young users (for age 18-29 years vs 45-59 years, RR, 1.49; 95% CI, 1.47-1.52) and for men compared with women (RR, 1.16; 95% CI, 1.14-1.17). We also observed a slightly higher risk of discontinuation for persons living in a low-income vs high-income municipality (RR, 1.11; 95% CI, 1.09-1.14), as well as for persons who previously used gastrointestinal (RR, 1.10; 95% CI, 1.09-1.12) or psychiatric (RR, 1.13; 95% CI, 1.12-1.14) medications (Figure 1). SOM discontinuation was also slightly higher among persons with metabolic syndrome (RR, 1.02; 95% CI, 1.01-1.03), prediabetes (RR, 1.05; 95% CI, 1.03-1.06), preexisting cardiovascular disease (RR, 1.08; 95% CI, 1.06-1.10), kidney disease (RR, 1.09; 95% CI, 1.04-1.15), and higher Charlson Comorbidity Index scores (Figure 1). One of 4 discontinuers reinitiated SOM, and relatively few filled a prescription for liraglutide for obesity management (1088 individuals [1.4%]) or tirzepatide (563 individuals [0.7%]), which entered the Danish market on October 30, 2024, after discontinuation.

Discussion

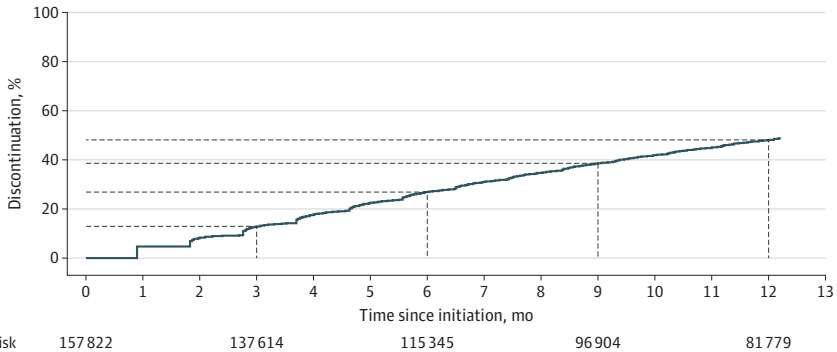
In this nationwide cohort of persons initiating SOM in Denmark, approximately half discontinued treatment within 12 months. Discontinuation was associated with younger age, male sex, socioeconomic disadvantage, higher comorbidity burden, and prior gastrointestinal or psychiatric treatment, suggesting the roles of financial barriers and increased susceptibility to adverse effects.

SOM is expensive (approximately €2200 to €3700 [$2500 US to $4200 US] per year in Denmark depending on doses up to 2.4 mg) and is not currently reimbursed, creating a considerable economic burden for patients. Gastrointestinal adverse effects are common,[6] and preexisting gastrointestinal conditions may increase susceptibility. Prior psychiatric medication use may reflect lower adherence to medications in general[7] or increased vulnerability to mental adverse effects, although recent evidence suggests neutral or slightly beneficial population-level mental health effects of SOM.[8]

Notably, 1 in 4 discontinuers appeared to reinitiate therapy within 3 months, and estimated discontinuation decreased slightly with a longer grace period. These findings may reflect frequent temporary treatment interruptions or self-adjusted dosing[9] below guideline-recommended levels.

Strengths of this study include a large nationwide sample of all individuals initiating SOM in a universal health care system with high-quality, population-based registries. Limitations include lack of exact anthropometric data (eg, body mass index) in the registries, and absence of individual-level

Figure 2. 1 Minus Kaplan-Meier Curve Showing Cumulative Risk of Semaglutide Discontinuation for Obesity Management Within 3, 6, 9, and 12 Months of Initiation



Dashed lines represent the key time points reported in the Results.

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information on income, insurance coverage, and out-of-pocket payments. Also, data on weight loss after initiation were unavailable. Finally, our findings may not be fully generalizable to other countries.

ARTICLE INFORMATION

Accepted for Publication: July 4, 2026.

Published: August 28, 2026. doi:10.1001/jamanetworkopen.2026.31371

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Author Contributions: Ms Mailhac and Dr Pedersen had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Mailhac, Petersen, Sørensen, Thomsen.

Acquisition, analysis, or interpretation of data: Mailhac, Pedersen, Pottegård, Sørensen, Thomsen.

Drafting of the manuscript: Mailhac.

Critical review of the manuscript for important intellectual content: All authors.

Statistical analysis: Mailhac, Pedersen.

Administrative, technical, or material support: Pottegård, Sørensen.

Supervision: Petersen, Pottegård, Sørensen, Thomsen.

Conflict of Interest Disclosures: Ms Mailhac reported that the Department of Clinical Epidemiology, Aarhus University and Aarhus University Hospital, receives funding for other studies from the Danish Medicines Agency and companies in the form of research grants to (and administered by) Aarhus University; none of these studies have any relation to the present study. Dr Pottegård reported receiving grants from AbbVie, Alcon, Almirall, Astellas, AstraZeneca, Boehringer-Ingelheim, Bristol Meyers Squibb, LEO Pharma, Novo Nordisk, Pfizer, and Servier outside the submitted work. Dr Sørensen reported that the Department of Clinical Epidemiology, Aarhus University, receives funding for other studies in the form of institutional research grants to (and administered by) Aarhus University; none of these studies have any relation to the present study. Dr Sørensen reported receiving personal fees from the University of Oslo, the Norwegian Research Council, the Independent Research Fund Denmark, the European Research Council, and EpidStrategies. Dr Thomsen reported receiving fees for presentations on epidemiological research for pharmaceutical companies, including AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, Novo Nordisk, and Sanofi (with or without financial compensation to institution or self, no permanent affiliation to any company) outside the submitted work and reported that the Department of Clinical Epidemiology, Aarhus University and Aarhus University Hospital, receives funding for other studies from the Danish Medicines Agency and companies in the form of research grants to (and administered by) Aarhus University; none of these studies have any relation to the present study. No other disclosures were reported.

Data Sharing Statement: See Supplement 2.

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SUPPLEMENT 1.

eMethods. Supplemental materials and methods
eTable. Codes used in this study
eFigure. Schematic illustration of the rationale for enrolment and end-of-follow-up dates (A), as well as for the definition and identification of drug coverage time and discontinuers (B and C)
eReferences

SUPPLEMENT 2.

Data Sharing Statement

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