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Pharmacological treatment of obesity in adults in Norway 2004–2022

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Abstract

Aims: To describe trends in the use of anti-obesity drugs in Norway during the period 2004–2022.

Materials and Methods: We assessed the annual utilization of any available drug indicated for obesity recorded in the nationwide Norwegian Prescribed Drug Register for adults (age 18–79 years) from 1 January 2004 to 31 December 2022. Prevalence was stratified by sex and age group (18–29 years and 10-year age groups thereafter). Additional analyses were performed in individuals initiating treatment with an antiobesity drug and on the cost of the anti-obesity drugs since 2017.

Results: The prevalence of anti-obesity drug use decreased from 2009, when sibutramine and rimonabant were withdrawn from the market, and increased again after the approval of bupropion-naltrexone in 2017 and liraglutide in 2018. The use of the peripheral-acting anti-obesity drug orlistat decreased from 2004. In 2022, 1.04% of the adult Norwegian population (72.8% women) filled at least one prescription of bupropion-naltrexone, 0.91% used liraglutide (Saxenda; 74.2% women), and semaglutide without reimbursement was used by 0.68% (76.7% women). The prevalence increased with age, peaking in the age group 50 to 59 years, and decreased in older age groups. From 2017 to 2022, 2.8% of the adult residents initiated treatment with an anti-obesity drug. The total sale of those drugs increased from 1.1 million euros in 2017 to 91.8 million euros in 2022.

Conclusions: The use of anti-obesity drugs in Norway has increased substantially in recent years, especially among women aged 40 to 59 years. Changes in availability and reimbursement have influenced the use of these drugs in recent years.

KEYWORDS

anti-obesity drug, obesity therapy, observational study, pharmaco-epidemiology

Prior presentation: Preliminary results from the study were presented in a short oral format at the European Association for the Study of Diabetes (EASD), Hamburg 2023, and at a national obesity conference in Norway (*Fedmeforskningsdagene* 2023, Tønsberg, Norway).

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1 | INTRODUCTION

Obesity is a chronic disease representing a major public health problem worldwide.^{1,2} It is associated with several medical conditions such as cardiovascular disease, diabetes, dyslipidaemia, osteoarthritis, and obstructive sleep apnoea.^{3,4} Obesity is caused by a combination of genetic predisposition, environmental drivers, excess calorie intake and a sedentary lifestyle. Worldwide, obesity is estimated to affect one in five women, one in seven men, and 13% of all children.⁵ In Norway, the prevalence of obesity has risen over the past few decades. The 2020 National Health Survey of Norwegian Adults aged 18 years and over found that 53% self-reported as being overweight or obese, with a higher proportion observed among men compared to women (59% and 47%, respectively). Women were found to be more likely to have attempted to lose weight.⁶ The highest rates of selfreported obesity were observed among those aged 35 to 64 years, and those with the lowest level of education.⁶

Treatment options for obesity include lifestyle interventions, pharmacological treatment, and bariatric surgery.^{7,8} According to current recommendations, pharmacological treatment should be prescribed as part of comprehensive management, thus far with the intent of lifelong use.⁹ In the last few years, several drugs have been approved for the treatment of obesity, with higher weight loss achieved in clinical trials with newer drugs.¹⁰ In Norway, orlistat (from 2003), bupropion-naltrexone (from 2017), liraglutide (from 2019) and semaglutide (from 2023) are currently approved for use as antiobesity treatment.

There were liberal reimbursement rules and wide availability of anti-obesity drugs in Norway throughout the study period. All doctors could apply for individual reimbursement under the Norwegian reimbursable prescription scheme for people with a body mass index (BMI) \geq 40 kg/m² or a BMI \geq 35 kg/m² and at least one weight-related complication. Little is known about current trends in the use of new anti-obesity drugs or how changes in indications and reimbursement have influenced the use of expensive drugs.

The increasing number of individuals with obesity and the high cost of anti-obesity treatments represent a challenge for the healthcare economy. Drug utilization research is crucial for promoting costeffective healthcare and facilitating the judicious use of medications. Access to data on the shifting trends in anti-obesity drug use may support new guidelines and reimbursement regulations. We aimed to provide an update on trends in the use of anti-obesity drugs in Norway from 2004 to 2022 by sex and age.

2 | METHODS

2.1 | Data sources and population

The Norwegian Prescribed Drug Register (NorPD) includes all prescription drugs dispensed from all Norwegian pharmacies since 2004.¹¹ We identified all adult residents 18–79 years who filled at least one prescription of an anti-obesity drug from 2004 to the end of

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2022. In addition, we defined new users as those who had received their first dispensing of an anti-obesity drug between 1 January 2017 and 31 December 2022, and who had not received any anti-obesity drug in the period 1 January 2015 to 31 December 2016. Information on the Norwegian population size by sex and age was obtained from Statistics Norway.¹² Information on costs based on estimated pharmacy retail price was obtained from the Norwegian Drug Wholesales Statistics dataset (pharmacy sale price) and includes costs paid by the patients and/or the government through the reimbursement scheme.¹³

Approved drugs with an indication for weight loss during the study period 2004–2022 (Table 1) are listed below.

- Sibutramine, a norepinephrine and serotonin reuptake inhibitor that acts as an appetite suppressant (Anatomical Therapeutic Chemical [ATC] code: A08AA10), was approved by the European Medical Agency in 2002. Sibutramine was withdrawn from the market in 2010 because it was associated with an increased risk of cardiovascular events and strokes.
- Orlistat, a gastric and pancreatic lipase inhibitor (ATC code: A08AB01), has been used in Norway since 2003.
- Rimonabant (ATC code: A08AX01) led to a reduction in appetite and was approved in 2006 but withdrawn worldwide in 2008 due to serious psychiatric side effects.
- 4. Bupropion-naltrexone (ATC code: A08AA62), depot tablets (Mysimba) came onto the Norwegian market at the end of 2017. Bupropion is a weak dopamine and norepinephrine reuptake inhibitor and naltrexone is an opioid antagonist. It acts at the brain level controlling appetite and reward centres, but the mechanism of action has not been fully elucidated.
- 5. Liraglutide (ATC code: A10BJ02, Saxenda) is a glucagon-like peptide-1 receptor agonist (GLP-1RA) also used as a glucose-lowering drug and was approved for the treatment of obesity in 2019. The glucagon-like peptide-1 hormone is a physiological regulator of appetite and calorie intake. When we refer to liraglutide in this study, we mean only Saxenda.
- 6. Semaglutide (ATC code: A10BJ06, Ozempic), another GLP-1RA, is reimbursed for type 2 diabetes as a second-line medication after metformin. We included individuals using semaglutide outside the reimbursement clause in Norway, as it has been used off-label as an anti-obesity drug. It has been on the Norwegian market since 2018. Since January 2023, semaglutide has been marketed as an anti-obesity drug in Norway (Wegovy).

2.2 | Reimbursement regulations from 2017

There is universal healthcare access in Norway, it is funded by taxes and out-of-pocket payments (patient co-payments). The Norwegian Medicines Agency manages marketing authorization, classification, vigilance, pricing, and decisions on whether drugs should be eligible for general reimbursement (all patients fulfilling certain criteria are

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		5		Approved January 2023	%0	~300 euro ^d	

 TABLE 1
 Pharmacological options for obesity treatment in Norway 2004-2023.

^bOzempic is approved for type 2 diabetes, but it is used off-label without reimbursement for obesity. ^cPrice for 1 mg/weekly injection. ^dPrice for 2.4 mg/weekly.

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eligible to receive reimbursement). For pharmaceuticals or indications not eligible for general reimbursement, the Norwegian Health Economics Administration can grant reimbursement for individual patients after an application from the treating physician.¹⁴

Anti-obesity drugs have approved indications for obesity (BMI \geq 30 kg/m²) or overweight (BMI 27.0–29.9 kg/m²) plus at least one weight-related comorbid condition or risk factor. However, the reimbursement rules are stricter. From 2017 to 2020 anti-obesity drugs were reimbursed for individuals with BMI \geq 40 kg/m² or BMI \geq 35 kg/m² with comorbidities, such as hypertension, type 2 diabetes, and obstructive sleep apnoea. The barrier for reimbursement for those with a BMI between 35 and 40 kg/m² was lowered in 2020 when the list of eligible comorbid conditions was increased to 29 conditions.

The reimbursement regulation in Norway required bupropionnaltrexone as the first treatment choice due to lower cost (if there were no contraindications). Pharmacological treatment should be interrupted if the patient has not lost ≥5% weight after 16 weeks.¹⁵ Most patients with obesity are treated at the primary care level. All physicians in Norway were able to prescribe these drugs until February 2023 (detailed information is provided in the Supplementary Methods: Reimbursement regulations).

2.3 | Statistical analysis

We describe the annual prevalence (%) trends in the use of anti-obesity drugs stratified by age and sex in the adult Norwegian population and present the total number and the incidence per 100 000 individuals for the new users of anti-obesity drugs from 2017. We explore trends in the reimbursement options, with prevalent users stratified by type of reimbursement: either reimbursable prescription or out-of-pocket payments from the patients (without reimbursement). The total cost per calendar year is reported in million euros. We used STATA version 17 for the analysis and figures (StataCorp LP, College Station, TX, USA).

2.4 | Ethics approval

Permission to conduct this descriptive study was not required from the Regional Committee for Medical Research Ethics.

3 | RESULTS

The prevalence of anti-obesity drug use in Norway from 2004 to 2022 is shown in Figure 1. There was a decreasing trend in use during the first years, followed by a rapid growth after 2017 when the new drugs came onto the market. The prevalence of all the anti-obesity drugs during the whole study period was higher among women (Supplemental Table S1 and Figure S1). Sibutramine was widely prescribed until 2009, when it reached 1.2% prevalent users among women and 0.27% among men, but was removed from the market in

2010. Rimonabant peaked in its second year on the market (2007), reaching a use prevalence of 0.22% among women and 0.07% among men, and was removed from the market in 2008. The use of the peripheral-acting anti-obesity drug orlistat decreased throughout the entire study period. From 2010 to 2017, orlistat was the only anti-obesity drug on the Norwegian (and European) market and had a use prevalence of 0.4% to 0.15%.

In 2017, 265 individuals filled a prescription of bupropion-naltrexone (0.007% of the adult population) compared to 42 808 individuals (1.04% of the population) in 2022. The drug was predominantly used by women (72.8% of all users in 2022; Supplemental Figure S2). During 2018, 2019 and 2020, the prevalence was highest among women aged 40 to 49 years (Figure 2 and Supplemental Figure S2). However, since 2021, the age group 50 to 59 years had the highest prevalence (2.44% in 2022). Among men, the prevalence has consistently been highest in the age group 50 to 59 years, with a top of 0.56% users in 2022. In 2022, 67.7% of all bupropion-naltrexone users received reimbursement (78.6% among men and 63.5% among women; Supplemental Figure S3 and Table S2).

Liraglutide, with obesity indication (Saxenda), was used by 616 people in 2019 and 37 475 (0.91.% of the population) in 2022 (73.5% women; Figure 1 and Supplemental Figure S4). Like bupropion-naltrexone, liraglutide had a higher prevalence of users in the age groups 40 to 49 years and 50 to 59 years (Figure 2 and Supplemental Figure S4). Reimbursement was granted to 8.9% of users in 2019 and 83.2% in 2022 (Supplemental Figure S3 and Table S2).

In 2022, there were 27 983 users of semaglutide (0.68% of the population) without a type 2 diabetes indication (76% women; Figure 1 and Supplemental Figure S5).

Overall, between 2017 and 2022, 2.8% of the adult population (114 070 individuals, 73% women) were new users of an anti-obesity drug in Norway (Figure 3). Bupropion-naltrexone was the drug most frequently prescribed to new users, increasing from 5 per 100 000 individuals in 2017 to 707 per 100 000 in 2022 (Supplemental Table S3).

Figure 4 shows the development in total sales of anti-obesity drugs in the period 2017 to 2022 in million euros for the pharmacy retail price. The total sales trends increased exponentially from 2020, with liraglutide being the drug with the highest total cost followed by semaglutide and bupropion-naltrexone.

4 | DISCUSSION

In this nationwide study in Norway, we found that the use of antiobesity drugs increased noticeably in adults in the years 2019–2022, at the same time as pharmacological treatment options were diversified. More women than men used anti-obesity drugs. In both sexes, the drug use peaked in the age group 40 to 59 years. Our findings show that bupropion-naltrexone was the most prescribed initial antiobesity drug from 2017 to 2022, probably due to reimbursement rules. The increase in use is probably attributable to the new and more

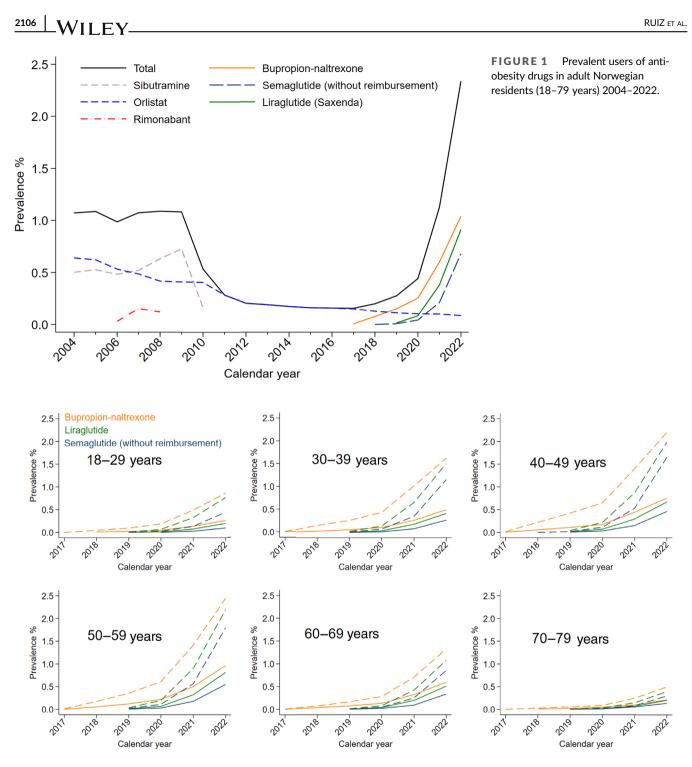


FIGURE 2 Prevalent users of anti-obesity drugs by drug type (orange: bupropion-naltrexone; green: liraglutide (Saxenda) and dark blue: semaglutide Ozempic, without reimbursement), by age group and sex (women: dashed line; men: solid line) in Norway 2017–2022.

effective drugs which have a greater effect on weight loss than the older preparations.

4.1 | Comparison with other studies

There are few studies on trends in anti-obesity drugs use with upto-date data. Our results are consistent with previous studies from the United States showing increased use of the new agents.¹⁶⁻¹⁸ We found a disproportionate use of anti-obesity drugs among women, resembling studies from the United States.¹⁶⁻¹⁸ Despite higher rates of obesity among men in Norway, an intriguing trend has emerged showing a much higher usage of anti-obesity drugs among women. Drugs might be more appealing to women because societal expectations and standards may affect women differently from men. Women may have higher weight loss goals and different health-seeking

FIGURE 3 New users of anti-obesity drugs in adult Norwegian residents 2017–2022. A new user was defined as a person who had received their first dispense of an anti-obesity drug between 1 January 2017 and 31 December 2022, and who had not received any anti-obesity drug in the period 1 January 2015 to 31 December 2016.

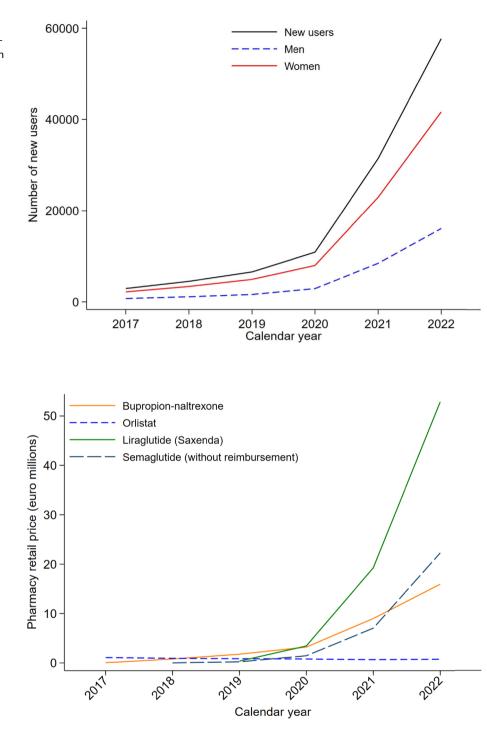


FIGURE 4 Cost of anti-obesity drugs in Norway 2017 to 2022 in million euro (all age groups).

behaviours from men. Women are more likely to be diagnosed with obesity and ask for treatment, including behavioural and pharmacological interventions, and bariatric surgery.¹⁹ Men tend to underperceive their weight,²⁰ and being overweight perhaps has less stigma for men than for women. Another explanation could be a different distribution of non-traditional factors such as stress, depression, and socio-economic status.²¹

Pharmacotherapy choice is heavily dependent on reimbursement options.²² There have been generous reimbursement rules and availability in Norway during the study period. In some patient groups, there is a great demand from the patients themselves, including a willingness to self-pay, partly driven by social media. $^{\rm 23}$

In Norway, four drugs were approved for the treatment of obesity in 2023 as a supplement to dietary regulation and exercise. If the treatment is effective, these medications must be maintained for a long time.²⁴ Long-term weight loss has only been documented after surgical treatment in people with morbid obesity.²⁵ The GLP-1RAs (liraglutide and semaglutide) are to date the most effective available drug group for obesity treatment.²⁶

4.2 | Public health perspectives

Obesity is an increasing health and social problem in Norway, as it is in the rest of the world. Obesity and anti-obesity treatment represent an economic burden on individuals and healthcare systems.²⁷ As obesity is a chronic disease that occurs more often in individuals with low education levels and income, to promote social equity, treatment for obesity, including drugs, should be available equitably and at a reasonable cost. To prevent obesity at the societal level, both populationfocused and individual-focused interventions are necessary. Primary prevention programmes early in life should be a priority (a costeffective strategy). Obesity should be managed as a chronic disease, using long-term plans and follow-ups with regular appointments. Pharmacological treatment could be considered in patients who do not reach their treatment goal with intensive lifestyle treatment alone as part of disease management. It can help patients to maintain compliance and prevent the development of obesity comorbidities (such as cardiovascular diseases and diabetes). Anti-obesity drugs should be closely monitored, and treatment should be discontinued in nonresponders²⁸ (currently a weight reduction lower of 5% body weight after 16 weeks).

4.3 | Strengths and limitations

The main strength of the study is its capture of complete use of antiobesity drugs for the entire adult population in Norway from 2004 to 2022, including the last period from 2017 when novel anti-obesity drugs were introduced. Only information about drugs dispensed and purchased by individuals is entered into the NorPD, with primary noncompliance not being an issue.²⁹ This gives us more precise information about the real use of anti-obesity drugs than information only about what has been prescribed.

Study limitations include the fact that we were not able to study the duration of the pharmacological treatment in the current dataset. In addition, individuals with obesity may also have diabetes and receive a GLP-1RA with that indication. The use of dispensed antiobesity drugs is a proxy for obesity, but we did not have information on BMI, hence some individuals may have used these drugs for cosmetic weight loss. However, we believe that reimbursement could be a proxy for obesity severity, meaning that those with a BMI < 35 kg/m² did not receive reimbursement for the anti-obesity drugs. From the available data, we were not able to determine if the antiobesity drugs were prescribed by a general practitioner or by a specialist in obesity.

4.4 | Implications for research and practice

Anti-obesity drugs have historically been associated with many adverse effects.^{30,31} Examples from the past include adverse cardio-vascular effects after the use of sibutramine³² and neuropsychiatric side effects, with an increased risk of suicide associated with

rimonabant use.³³ Data on safety outcomes from randomized trials may be not representative of real-world use. Adverse events after the use of GLP-1RAs have been reported.^{34,35} Long-term safety studies for the new agents are needed, with post-marketing surveillance when many individuals are treated.³³ For instance, the lack of data on cardiovascular outcomes after bupropion-naltrexone treatment indicates that this drug combination should be used with caution in patients with cardiovascular disease. Data from trials showed a good safety profile after exclusion of participants with risk of side effects.³⁶

The newer anti-obesity drugs may be able to reduce the need for bariatric surgery, reducing late complications from surgery. Some of the disadvantages of these drugs are unsatisfactory weight reduction, the need for lifelong treatment, side effects and high cost.

Future cohort studies with longitudinal data are needed to examine clinical outcomes and treatment duration of anti-obesity drugs. Treatment with semaglutide 2.4 mg was approved by the US Food and Drug Administration in 2021 and has had marketing authorization in Europe (Denmark, United Kingdom, Germany, and Norway) since 2022. From 1 February 2023, reimbursement for liraglutide was heavily restricted in Norway, and only orlistat and bupropionnaltrexone will be reimbursed for obesity treatment. The same strict reimbursement restrictions apply for semaglutide (Wegovy), available in Norway since January 2023. Several anti-obesity drugs in development have not yet been given final approval by the regulatory authority in Europe, including tirzepatide.³⁷ Collaboration between healthcare providers and policymakers is essential to reduce the burden of obesity and to address effective and safe treatment and preventive measures.

In this nationwide study, we found an increased use of antiobesity drugs, especially among middle-aged women. Changes in availability and reimbursement have influenced the use of these drugs in recent years.

AUTHOR CONTRIBUTIONS

Author contributions were as follows: Kari Furu and Paz Lopez-Doriga Ruiz: study conception and design; Kari Furu and Øystein Karlstad: data collection; Paz Lopez-Doriga Ruiz: analysis of data; Paz Lopez-Doriga Ruiz: writing the first draft of the manuscript; all authors: revising and finalizing the manuscript.

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We would like to thank the NorPD for making the data material available. No specific funding was obtained for this study.

CONFLICT OF INTEREST STATEMENT

Kari Furu, Øystein Karlstad, and Paz Lopez-Doriga Ruiz report participation in research projects funded by pharmaceutical companies (one on diabetes drug), all regulator-mandated Phase IV studies (PASS) unrelated to the submitted work, with all funds paid to their institution (no personal fees). Elisabeth Qvigstad and Kari Anne Sveen perform contract studies, for which all funds are paid to their institution (Oslo University Hospital) and have received renumeration for lectures and consulting from Novo Nordisk, Sanofi, Lilly, AstraZeneca and Boehringer Ingelheim. Kjersti Nøkleby, Kristina Slåtsve, Hanne Gulseth and Haakon E. Meyer report no conflict of interest.

PEER REVIEW

The peer review history for this article is available at https://www. webofscience.com/api/gateway/wos/peer-review/10.1111/dom. 15515.

DATA AVAILABILITY STATEMENT

Restrictions apply to the availability of these data, applications for data from the Norwegian Prescribed Drug Register (NorPD) must be sent via Helsedata.no.

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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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