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# Effects from treating moderate- to high-risk obesity patients with anti-obesity medication from a societal perspective

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**Obesity is a global health concern with new medication treatment options. So far, research on how programs with newer anti-obesity medication (AOM) for the moderate- to high-risk population can mitigate the prevalence of obesity and reduce the economic burden of society is limited. We aimed to assess such impacts of AOM and lifestyle intervention with the GLP-1 receptor agonist semaglutide on patients with different obesity classes, i.e. risks (and no diabetes), based on clinical trial data. We estimated the treatment effect on prevalence, medical and indirect costs using the population-attributable fraction approach and various data sources. We modified prevalence data from the Austrian Health Interview Survey 2019 ($n$ = 15,461) using data about proportional weight reductions after the treatment with semaglutide as an adjunct to lifestyle intervention. In a life-cycle model, we compared the costs of obesity classes. Treating 50% of patients with obesity class II and III (excl. diabetes patients, including patients not responding to the treatment) over 68 weeks, reduced the prevalence from 4% to 2.74% (95% CI 2.739–2.743) and from 1.45% to 0.97% (95% CI 0.969–0.997), respectively. This resulted in a reduction of 12.9% (€ – 108.7 million) of expenses related to obesity class II and III per year. Over the life cycle, a reduction in obesity class reduced costs by about 40% per patient. The newer AOM can aid in reducing moderate- and high-risk obesity rates and bring economic and health benefits to society, given that AOM are available and affordable for the respective populations.**

**Keywords** Moderate-risk obesity, High-risk obesity, Semaglutide, Prevalence, Costs

The increasing rates of obesity put a high economic burden on societies[1]. In the past, only a limited number of patients with obesity have taken anti-obesity medications due to uncertainties regarding their safety and effectiveness[2]. Diet, behavioural and exercise interventions, moreover, have turned out to be of limited effect especially for people with higher risk obesity[3]. In 2021, the glucagon-like peptide 1 receptor (GLP-1) agonist semaglutide has been offered as a new anti-obesity medication treatment option—followed by tirzepatide in 2022—and the demand for AOM has been rising since then[4].

Initially, GLP-1 agonists were intended solely for the treatment of diabetes, as they facilitate glucose-dependent insulin secretion and inhibit glucagon secretion. However, it became apparent that they also led to weight loss in many patients. GLP-1 agonists can increase the feeling of satiety through receptors in the area postrema of the brain as well as by reducing gastric and intestinal motility, which also accounts for most of its unwanted side effects[5]. Semaglutide in particular has a half-life of approximately seven days and thus needs to be administered only once weekly[6]. The weight loss with semaglutide lasts longer than former AOM and adverse events are mainly transient gastrointestinal disorders and cholelithiasis and rarely, but notably, acute pancreatitis[7]. Hence, we have selected semaglutide as an instance of AOM to examine how a moderate- and high-risk-population AOM treatment program can mitigate risk exposure and impact health care expenditure as an adjunct to a lifestyle intervention program.

While previous studies have primarily focused on cost-effectiveness or individual health care expenditures within the context of AOM[8–10] in the present study, we examined how a moderate- to high-risk population AOM treatment program with semaglutide including lifestyle intervention can reduce the prevalence of obesity and reduce the economic burden on societies.

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We estimated the effects of three treatment scenarios and their impacts on direct medical and indirect costs based on a prevalence approach to measure the public health impact of exposures in populations. The underlying AOM effect for our scenarios is derived from a double-blind clinical trial study by Wilding et al.[7] assessing the effect of a once-weekly injection of semaglutide (2.4 mg) as an adjunct to a lifestyle intervention over the period of 68 weeks (excluding patients with diabetes, including patients not responding to the treatment). We define the three scenarios as "50%-II & 50%-III", "20%-I & 50%-II & 50%-III", and "20%-II & 50%-III", which differ in the proportion of the population with different degrees of obesity, i.e. risks, who receive the treatment. This choice tries to represent a range of possible real-world realisations, taking into account that not all patients are eligible, will receive reimbursement, will opt for a pharmaceutical therapy (e.g. vs. bariatric surgery) or will adhere to the therapy over the longer term.

## Methods

### Prevalence and treatment scenarios

We drew the prevalence data of overweight and obesity in the Austrian adult population from the Austrian Health Interview Survey[11]. The sample consisted of 14,606 Austrian adults and was weighted with respect to sex, age groups, education, nationality, and income groups by Statistics Austria to represent the Austrian population[12]. We calculated the body mass index (BMI) in kg/m$^2$ with the self-reported data on body weight and height. Because self-reported data usually lead to an underestimation of the actual prevalence of obesity[13], we adjusted BMI values by correcting factors according to an Austrian validity study on self-reported body weight and height[14]. In 2019, which is the year with the most recent data, 14.1% of the Austrian adult population fall into obesity class I (BMI 30–34.9), another 4% into obesity class II (BMI 35–39.9) and 1.4% into obesity class III (BMI ≥ 40). The proportion of persons with excess body weight increases steadily with age up to 79 years; the respective distribution of BMI categories by age group for men and women are shown in the figures S-1 and S-2 in the appendix.

We modified the prevalence by using data from Wilding et al.[7] about proportional weight reductions after the treatment with semaglutide as an adjunct to lifestyle intervention (see Fig. 1) and by applying them to the data from the Austrian Health Interview Survey (described above). Wilding et al.[7] provide evidence that the semaglutide treatment together with a lifestyle intervention program is associated with sustained, clinically relevant reduction in body weight. Figure 1 illustrates the observed percentages of participants who experienced body weight reductions from baseline to week 68 (excluding those who discontinued the treatment).

First, we restricted the sample of the Austrian Health Interview Survey to individuals without diabetes and individuals above the age of 20 and below 74 years. Secondly, we assigned uniformly distributed random variates spanning the interval zero to one to all observations of our sample. In the third step, we used these to assign proportional weight reductions: 7.6% receive a weight-reduction below 5%, 17.6% receive a weight-reduction between 5% and 10%, 20% receive a weight-reduction between 10% and 15%, 20% receive a weight-reduction between 15% and 20% and 34.8% receive a weight-reduction between 20% and 25%. We are assuming that the weight loss achieved after the 68-week treatment will persist, which could be accomplished with further treatment[15]. Because there is no evidence that treatment effects differ by subgroups[16], we have not considered patient characteristics in our model.

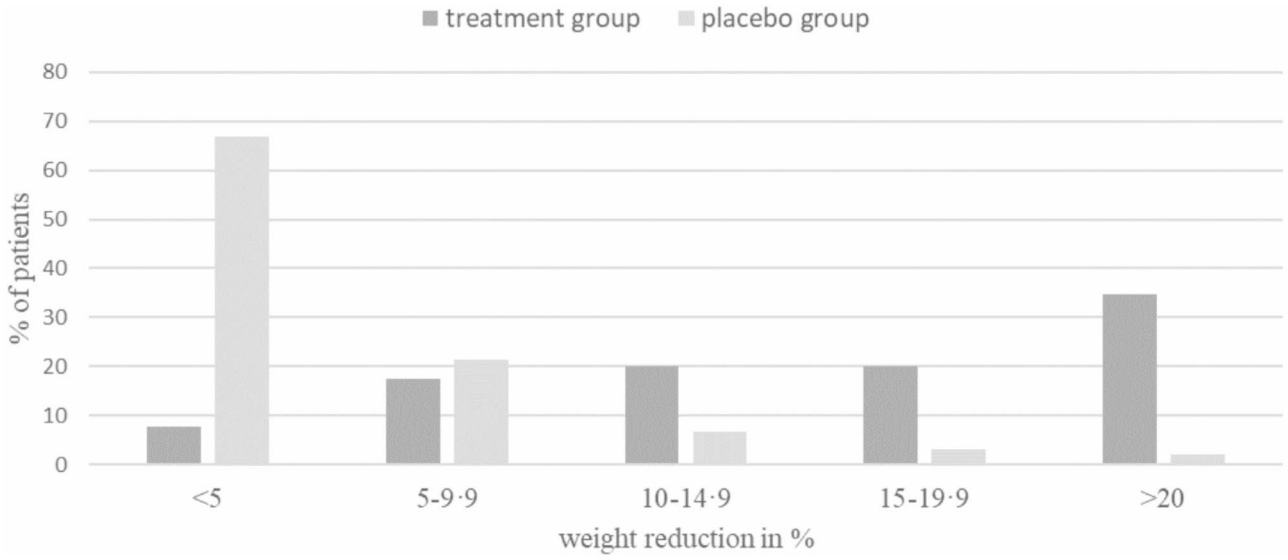


**Fig. 1**. Weight reduction according to Wilding et al.[7]. *Note*: Observed percentages of participants who had bodyweight reductions of less than 5%, 5% to less than 10%, 10% to less than 15%, 15% to less than 20% and over 20% from baseline to week 68 during the on-treatment observation period ($n = 1059$ in the semaglutide group; $n = 499$ in the placebo group).

To account for age and sex-specific differences in cost effects depending on the weight reduction we repeated the assignment of weight reduction to the individuals' body weight in each obesity class one thousand times. We examined the mean share of people who "moved" to lower BMI categories and the 95% confidence intervals. From the Austrian Health Interview Survey population weights, we generated new prevalence rates for each obesity class (by sex and age group) resulting from the following treatment scenarios:

i. "50%-II & 50%-III": 50% of observations categorized as obesity class II (moderate-risk) and III (high-risk) received a dose of 2.4 mg of semaglutide once a week as an adjunct to lifestyle intervention over 68 weeks.
ii. "20%-I & 50%-II & 50%-III": 20% of observations categorized as obesity class I (low-risk) and 50% of observations categorized as obesity class II (moderate-risk) and III (high-risk) received a dose of 2.4 mg of semaglutide once a week as an adjunct to lifestyle intervention over 68 weeks.
iii. "20%-II & 50%-III": 20% of observations categorized as obesity class II (moderate) and 50% of observations categorized as obesity class III (high-risk) received a dose of 2.4 mg of semaglutide once a week as an adjunct to lifestyle intervention over 68 weeks.

These scenarios represent a range of possible realisations, as patients might not be eligible for, opt for or receive reimbursement for pharmaceutical treatment or may not show long-term adherence.

## Relative risks

Based on findings of a systematic literature search, we extracted relative risk data from more than 400 meta studies. A detailed description of the search and data can be found in our former study[17]. To summarize, meta-analyses provided relative risk data by obesity class regarding esophageal adenocarcinoma, pancreatic cancer, pancreatic mortality, endometrial cancer, endometrial cancer mortality, liver cancer mortality, breast cancer, breast cancer mortality, prostate cancer mortality, renal cell carcinoma mortality, sudden cardiac death, atrial fibrillation, heart failure, stroke mortality, other vascular disease (no ischemic heart disease or stroke), gallbladder disease, gallbladder cancer mortality, acute pancreatitis, incontinence, type-2-diabetes mortality, influenza-related pneumonia, liver cirrhosis mortality, gout, and end stage renal disease mortality.

We used relative risks resulting from cohort studies regarding asthma, chronic kidney disease and end stage renal disease, kidney stone, colorectal cancer mortality, liver cancer mortality and leukemia, ovarian cancer mortality and leukemia mortality, renal cell carcinoma, multiple myeloma, and psoriasis. We drew on results from hip and knee replacements as a proxy for hip and knee osteoarthritis and results for polycystic ovary syndrome as a proxy for amenorrhea.

For some other relevant diseases, we assumed a log-linear relation between BMI and relative risks in case we did not find appropriate data in any cohort or meta-analysis, such as for polycystic ovary syndrome, hypertension, pulmonary embolism, ischemic stroke, and non-alcoholic fatty liver disease. For type-2-diabetes we derived a factor regarding the increase in relative risks associated with increasing obesity class given in a cohort study and applied it to the results of a meta-analysis. We applied the same procedure for coronary heart disease and gastro-esophageal reflux disease.

Given the mean relative risk per obesity class, we applied polynomial regressions to estimate the relative risks per BMI value up to a BMI of 50. We chose an upper bound to avoid estimating a decrease of relative risks beyond a BMI of 50. For all other diseases, for which we did not find any evidence of increasing relative risks associated with increasing BMI or obesity class, we used constant values for relative risks and distinguished only between overweight and obesity the way the respective studies provided them[17].

## Population-attributable fraction

For each scenario ("50%-II & 50%-III", "20%-I & 50%-II & 50%-III", "20%-II & 50%-III"), we calculated the reduction of the notional costs by assigning lower BMI values, and thus risks, to the corresponding persons with obesity using the approach of population-based attributable fractions. In general, the difference in the observed costs of our base year 2019 and the hypothetical costs without obesity yielded the costs of obesity (a detailed description of the underlying data, method, and the analysis over the lifecycle are given in the appendix A).

In this study, we generated the treatment effect by calculating the difference between attributable costs of the population which moves from higher to lower BMI values (Eq. (1)). The attributable costs decline with decreasing BMI values associated with decreasing relative risks for comorbidities.

$$\text{Treatment Effect} = -\text{Costs}^*\text{AF}_{\text{reduced}} + \text{Costs}^*\text{AF}_{\text{added}} \tag{1}$$

In Eqs. (2) and (3) we show an example for a decrease in prevalence in obesity class II and the corresponding increase in prevalence in obesity class I:

$$AF_{reduced} = \frac{[-]\,in\ prevalence\ BMI\ 35 * (RR_{BMI\ 35} - 1) + \ldots + [-]\,in\ prevalence\ BMI\ 39 * (RR_{BMI\ 39} - 1)}{prevalence_{normalweight} + prevalence_{BMI\ 25} * (RR_{BMI\ 25}) + prevalence_{BMI\ 26} * (RR_{BMI\ 26}) + \ldots + prevalence_{BMI\ 50} * (RR_{BMI\ 50})} \tag{2}$$

$$AF_{added} = \frac{[+]\,in\ prevalence\ BMI\ 30 * (RR_{BMI\ 30} - 1) + \ldots + [+]\,in\ prevalence\ BMI\ 34 * (RR_{BMI\ 34} - 1)}{prevalence_{normalweight} + prevalence_{BMI\ 25} * (RR_{BMI\ 25}) + prevalence_{BMI\ 26} * (RR_{BMI\ 26}) + \ldots + prevalence_{BMI\ 50} * (RR_{BMI\ 50})} \tag{3}$$

## Study ethics

Our study does not involve human participants or materials but makes use of secondary data only. Any appertaining regulations were followed. Permission for the use of the data of the Austrian Health Interview Survey was granted by the Austrian Statistics Institute, permission for the use of the sick leave data was granted

by the Austrian Health Insurance Fund, the Social Insurance Institution for Self-Employed Persons, and the Work Accident Insurance. Other data we used for this study were of an open domain, no patient consent was required. Studies that use only secondary data already available to research are exempt from our institute's IRB oversight.

## Results

### Effects on obesity prevalence

In our sample of potential treatment patients, the initial total population-weighted numbers were 73,654 persons in obesity class III, 194,029 in obesity class II and further 769,412 in obesity class I category. Table S-1 in the appendix B shows the distribution of potential treatment patients by age and obesity class.

Table 1 provides the resulting prevalence for each treatment scenario. The treatment of 50% of patients with obesity class III (and no diabetes), resulted in a reduction of the prevalence of obesity class III in the population by about a third, from about 1.5% to 1%. Treating 50% of patients with obesity class II (and no diabetes) lowered the prevalence of obesity class II in the population from 4% to 2.7%. The resulting prevalence was 3.6% if only 20% had received the treatment. The prevalence of obesity class I experienced an increase of 1 and 0.5 percentage points in the scenarios "50%-II & 50%-III" and "20%-II & 50%-III", respectively. In contrast, the prevalence of obesity class I decreased by 1 percentage point in the scenario "20%-I & 50%-II & 50%-III".

### Annual cost effects

In 2019, total medical costs and indirect costs (sick leave, disability, and death) related to obesity yielded €2.167 billion (95% CI 2.164–2.169), which were about 6% of Austria's total health expenditures. €837.56 million (95% CI 836.69–838.42) or 39% arose from patients initially in obesity class II (€606 million) and class III (€231 million) respectively (see Table S-2 in the appendix B).

Table 3 shows the annual reduction of costs and deaths by treatment scenario. The treatment of 50% of individuals with BMI 35+ (excl. diabetes patients) results in a reduction of 12.9% (€– 108.7 million) of expenses (medical and indirect costs) related to obesity class II and III, taking into account the residual expenses arising from the patients' remaining excess weight. The cost reduction is twice as high when also the prevalence of obesity class I declines after the treatment of 20% of persons (excl. diabetes patients) with BMI values between 30 and 35. In the scenario, in which only 20% of persons with obesity class II excl. diabetes patients are treated, the total annual cost reduction (medical and indirect costs) amounts to €46.7 million (– 5.6% of costs due to obesity class II and III).

If we divide the total costs (Table 2) by the number of treated patients (Table S-1 in appendix B), the average annual cost reduction lies between €881 and €1,225 per patient.

In 2019, the total number of deaths (under the age of 85) associated with obesity yielded 3950 (95% CI 3948.81–3951.65), of which 29% occurred in patients initially in obesity class II and 12% occurred in patients in obesity class III. After the change in Austria's obesity prevalence according to treatment (i)–(iii), the decline in yearly death cases amounts to (i) 151, (ii) 318 and (iii) 77, respectively (Table 3). In 2019, 4264 (95% CI 4256.76–4271.58) employees (in full-time equivalents, FTE) were lost due to obesity-associated sick leave, disability, or death; 40% of them were in obesity class II or III. The reduction in obesity prevalence in each scenario saves (1) 273, (2) 595 and (3) 141 employees (in FTE), respectively.

### Cost effects over the life cycle

Considering that the patient had not lost weight and remained in his or her obesity class, we estimated the total economic costs over one's lifetime. Since most of these avoidable costs occur several decades after the treatment and future costs are worth less for the individual as well as for society from today's perspective, we used a discount rate of 3%[18]. Fig. 2 provides the corresponding results regarding direct medical costs as well as indirect costs arising from sick leave, disability, or death during working age, by sex and over age groups. Life-cycle costs increase up to the age of 60, according to our findings.

| | Normal weight | Overweight | Obesity class I | Obesity class II | Obesity class III |
|---|---|---|---|---|---|
| 50%-II & 50%-III | NA* | 42,951 | 67,025 | – 79,519 | – 30,527 |
| | | (42,157–43,745) | (65,766–68,285) | (– 79,648–79,389) | (– 30,557–30,496) |
| 20%-I & 50%-II & 50%-III | 42,993 | 137,435 | – 70,383 | – 79,519 | – 30,527 |
| | (40,506–45,479) | (135,995–138,875) | (– 71,269–69,745) | (– 79,684–79,389) | (– 30,557–30,496) |
| 20%-II & 50%-III | NA* | 17,243 | 35,709 | – 22,494 | – 30,527 |
| | | (16,924–17,562) | (34,957–36,460) | (– 22,824–22,163) | (– 30,557–30,496) |

**Table 1**. Estimated absolute change over overweight and obesity classes in three treatment scenarios. The underlying weighted sample of the Austrian Health Survey covers adults between 20–74 years and excludes diabetes patients. The mean (95% CI) result from 1000 iterations of random assignment to weight reduction per treatment scenario: 7.6% received a weight-reduction below 5%, 17.6% received a weight-reduction between 5% and 10%, 20% received a weight-reduction between 10% and 15%, 20% received a weight-reduction between 15% and 20% and 34.8% received a weight-reduction between 20% and 25% *not applicable.

| | Normal weight | Overweight | Obesity class I | Obesity class II | Obesity class III |
|---|---|---|---|---|---|
| 2019 prevalence | 43.964% | 36.717% | 13.866% | 4.000% | 1.453% |
| 50%-II & 50%-III | 43.964% | 37.397% (37.384–37.409) | 14.922% (14.907–14.947) | 2.741% (2.739–2.743) | 0.970% (0.969–0.970) |
| 20%-I & 50%-II & 50%-III | 44.645% (44.606–44.685) | 38.893% (38.970–38.916) | 12.751% (12.737–12.765) | 2.741% (2.739–2.743) | 0.970% (0.969–0.970) |
| 20%-II & 50%-III | 43.964% | 36.990% (36.985–36.995) | 14.431% (14.419–14.443) | 3.644% (3.638–3.649) | 0.970% (0.969–0.970) |

**Table 2**. Resulting prevalence of obesity class I, II, III. The table shows the prevalence of obesity class I, II, III of the Austrian population 20–74 years (incl. diabetes patients) in different scenarios compared to the status quo prevalence of 2019. The mean (95% CI) result from 1000 iterations of random assignment to weight reduction per treatment scenario: 7.6% received a weight-reduction below 5%, 17.6% received a weight-reduction between 5% and 10%, 20% received a weight-reduction between 10% and 15%, 20% received a weight-reduction between 15% and 20% and 34.8% received a weight-reduction between 20% and 25%.

| | Medical costs* | Indirect costs* | Deaths |
|---|---|---|---|
| 50%-II & 50%-III | 75.95 (75.94–75.96) | 32.79 (32.78–32.79) | 150.7 (150.6–150.7) |
| 20%-I & 50%-II & 50%-III | 151.76 (151.73–151.78) | 69.24 (69.24–69.29) | 317.1 (317.0–317.1) |
| 20%-II & 50%-III | 28.98 (28.98–28.99) | 17.68 (17.68–17.69) | 76.8 (76.81–76.83) |

**Table 3**. Annual reduction of costs and deaths by treatment scenario. The underlying weighted sample of the Austrian Health Survey covers adults between 20–74 years and excludes diabetes patients. The mean (95% CI) result from 1000 iterations of random assignment to weight reduction per treatment scenario: 7.6% received a weight-reduction below 5%, 17.6% received a weight-reduction between 5% and 10%, 20% received a weight-reduction between 10% and 15%, 20% received a weight-reduction between 15% and 20% and 34.8% received a weight-reduction between 20% and 25%. *in € million, base year is 2019.

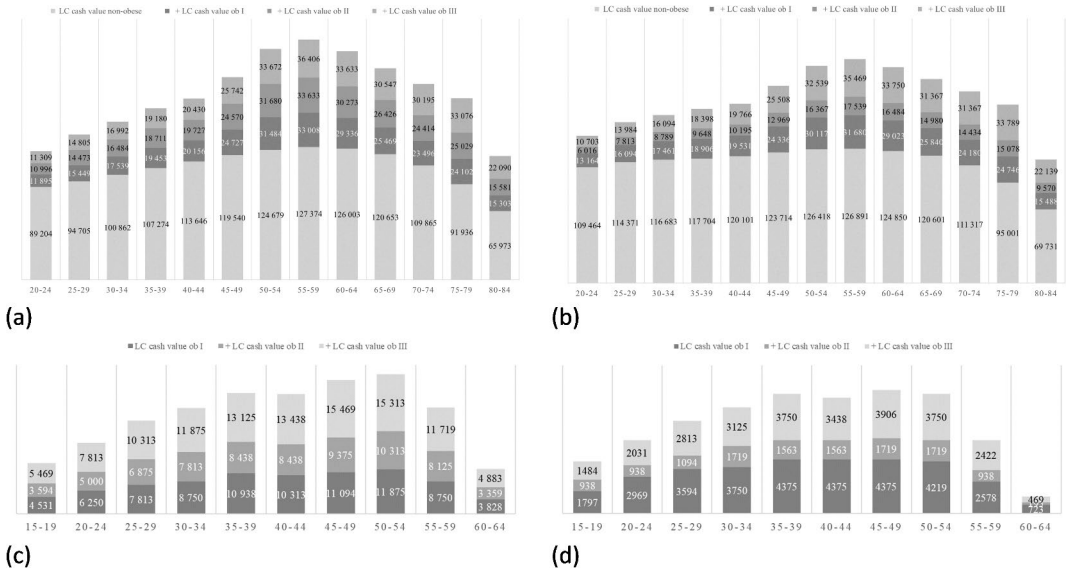


**Fig. 2**. Life-cycle direct medical costs of men (**a**) and women (**b**), and indirect costs of men (**c**) and women (**d**), by age group and obesity class; base year 2019; excl. diabetes patients.

The results for the age group 30–34 were further highlighted in Tables 4 and 5, since we assume that adults at this age still have relatively few established complications. Furthermore, these tables show the uncertainty intervals based on lower and upper bounds of intervals concerning relative risks and discount factors ("sensitivity interval", SI). We applied the lower and upper bounds of 95% CI intervals of morbidity risks of diseases (using a discount rate of 3%), and a discount rate of 4% and 0% (using, at the same time, average relative risk values). A discount rate of zero reflects the raw sum of costs, i.e. current and future costs are valued equally.

We excluded expenses associated with diabetes and incorporated the effects of obesity-associated decreased life expectancy. Accordingly, it turned out that an untreated man with obesity class I in his early 30's yielded an

| | Medical costs* | Indirect costs* | Total* |
|---|---|---|---|
| Obesity class I | 17,539 | 8750 | 26,289 |
| RR low–RR high | 10,625–24,297 | 8125–10,313 | 18,750–34,610 |
| $r = 4\%$–$r = 0\%$ | 12,539–56,563 | 7813–17,813 | 20,352–74,376 |
| Obesity class II | 34,023 | 16,563 | 50,586 |
| RR low–RR high | 20,977–41,914 | 14,063–17,188 | 35,040–59,102 |
| $r = 4\%$–$r = 0\%$ | 24,082–113,750 | 14,063–32,500 | 38,145–146,250 |
| Obesity class III | 51,016 | 28,438 | 79,454 |
| RR low–RR high | 30,703–73,223 | 24,063–32,188 | 54,766–105,411 |
| $r = 4\%$–$r = 0\%$ | 35,625–176,875 | 23,125–55,938 | 58,750–232,813 |

**Table 4**. Life-cycle costs results—males. The table shows discounted life-cycle costs ($r = 3\%$) of a 30–34-year-old man with obesity (excl. diabetes), by obesity class and by sensitivity according to upper and lower bound of relative risks' 95% CI and discount rates at 4% and 0% (i.e., the raw sum of costs). RR = relative risk. *in € million, base year is 2019.

| | Medical costs* | Indirect costs* | Total* |
|---|---|---|---|
| Obesity class I | 17,461 | 3750 | 21,211 |
| RR low–RR high | 11,367–24,297 | 3281–4844 | 14,648–29,141 |
| $r = 4\%$–$r = 0\%$ | 12,793–53,750 | 3438–7500 | 16,231–61,250 |
| Obesity class II | 26,250 | 5469 | 31,719 |
| RR low–RR high | 18,203–37,266 | 4531–6719 | 22,734–43,985 |
| $r = 4\%$–$r = 0\%$ | 18,906–83,203 | 4375–10,313 | 23,281–93,516 |
| Obesity class III | 42,344 | 8594 | 50,938 |
| RR low–RR high | 27,773–69,023 | 7500–11,094 | 35,273–80,117 |
| $r = 4\%$–$r = 0\%$ | 29,727–143,359 | 7188–15,938 | 36,915–159,297 |

**Table 5**. Life-cycle costs results—females. The table shows discounted life-cycle costs ($r = 3\%$) of a 30–34-year-old women with obesity (excl.diabetes), by obesity class and by sensitivity according to upper and lower bound of relative risks' 95% CI and discount rates at 4% and 0% (i.e. the raw sum of costs). RR = relative risk. *in € million, base year is 2019.

obesity-attributable present value of lifetime costs of about €26,000 (SI €18,750–€74,376) until his expected end of life (Table 4). The costs for an untreated man of the same age with obesity class II are twice as high (SI €35,040–€146,250) and increase by about another €30,000 for a man with obesity class III. Untreated women with obesity are more likely to have lower costs than men in Austria, mainly because of lower expected production losses arising from lower incomes and full-time employment of the base year 2019 (Table 5). Hence, an individual in her early 30s who is untreated in obesity class results in a cost of approximately €21,000 (SI €14,648–€61,250) until her anticipated end of life. Furthermore, an untreated woman with obesity class II adds about €10,000 to her obesity-associated present value of lifetime costs, and an untreated woman with obesity class III adds another €20,000.

## Placebo scenario and sensitivity

We used the weight loss distribution of the placebo sample from Wilding et al.[7] (Fig. 1) in the placebo scenario. About half of the patients would transition to lower obesity classes if they received lifestyle interventions without semaglutide treatment (Table S-3 in appendix B). The total direct and indirect costs decreased from (1) €108.7 to €53.1, (2) €221.0 to €108.5, and (3) €46.7 to €16.6 without AOM in each scenario, respectively (Table S-4). Similarly, avoidable deaths decreased from (1) 151 to 58, from (2) 317 to 143, and from (3) 77 to 49 without semaglutide.

The sensitivity of the results obtained with semaglutide is presented in Table S-5 in the appendix, wherein we have modified the weight loss and relative risk parameters. The utilization of categorical weight loss variables resulted in a slight reduction in total expenses, namely, (1) €101.6, (2) €207.9, and (3) €41.7 in each scenario, respectively. For the scenarios (1)-(3), the utilization of the lower and upper bounds of the 95% confidence intervals of morbidity risks resulted in total expenses ranging from (1) €88.1 to €126.8, (2) €175.8 to €269.69, and (3) €35.5 to €57.91.

## Discussion

Our study showed the potential of newer AOM together with a lifestyle intervention program to lower the prevalence of moderate- to high-risk obesity in the population. To focus on obesity therapy, we excluded diabetes patients to isolate the effect of AOM on obesity, i.e. we included only patients that would be prescribed

semaglutide as a treatment for obesity, not for diabetes. For example, the treatment of 50% of individuals with BMI 35+ resulted in an annual reduction of 12.9% (€− 108.7 million) of expenses related to obesity class II and III. Thereby, we considered the weight loss distribution (e.g. 7.6% of patients lose below 5% of weight) and we assumed that none of the patients quit during the treatment period of 68 weeks. Moreover, our life-cycle analysis for patients of each obesity class revealed a large potential for cost savings through weight reduction.

One limitation of our study is, however, that our model does not consider cumulative increases in risks over time but is based on population-average risk values. Weight loss has turned out to significantly reduce the risks for the majority of obesity-related diseases[16,19]. Nevertheless, we may overestimate the overall risk reduction because some patients who lose weight may not reach the average risk of each disease after a long period of moderate- or high-risk obesity. Conversely, using average-population risk may also underestimate the risk reduction for some patients.

Moreover, will weight loss effects of the clinical trial be achievable in the population? New evidence from electronic health records indicates that the treatment with semaglutide has resulted in a lower effect on weight loss compared to the effect of clinical trials[20]. In the same study, moreover, weight loss from the treatment with tirzepatide has been achieved comparable to our model assumptions based on clinical trial effects of semaglutide. Therefore, the choice of AOM will matter to make our modelled weight loss achievable, and, even more, treatment adherence of the patients.

So far, we made no probabilistic assumptions about treatment adherence during the treatment period and about weight maintenance after the treatment period. However, we have chosen scenarios with a maximum of 50% of the respective target patients which we interpret as 50% (or 20%) of patients who completed initial treatment and would be able to maintain their weight loss. This corresponds with new findings from an electronic health-record database showing that 56.2% of patients either remained around the same weight or continued to lose additional weight after stopping semaglutide[21].

Furthermore, manufacturers must keep up with the demand for AOM and they must be affordable (e.g., through health-insurance coverage) to allow such a moderate- to high-risk population treatment program in real life. Since obesity is a chronic disease, a single treatment period of 68 weeks, however, will not be enough. Therefore, the medication must be affordable and available for the moderate- to high-risk population, maybe lifelong. Treatment costs will change over time as market competition and the expiration date of the patent right will probably lead to price reductions in future[22].

We showed the potential of a treatment program for a large share of the population with moderate- to high-risk obesity based on quite novel data assessing the effect of semaglutide. More research will be needed, though, to address weight maintenance in the longer run and actual treatment costs over time.

## Data availability

Prepared data regarding cost factors as well as Stata code files can be requested from the corresponding author. Prevalence data can be retrieved from the Austrian Statistics Office. Relative risk data can be found in the supplementary online appendix. Austrian Health Interview survey data are available from Eurostat: https://ec.europa.eu/eurostat/web/microdata/european-health-interview-survey.

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## Author contributions
SR contributed to conceptualisation, data curation, formal analysis, methodology, project administration, resources, software, validation, visualisation, writing the original draft and editing.TC contributed to conceptualisation, data curation, methodology, project administration, resources, validation, funding acquisition, investigation, reviewing and editing draft and supervision.

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## Declarations

## Competing interests
The authors declare no competing interests.

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