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ASSESSING POTENTIAL MISUSE IN THE OFF-LABEL USE OF OZEMPIC FOR OBESITY TREATMENT IN NON-DIABETIC INDIVIDUALS

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Abstract

This thesis investigates the potential misuse in the off-label use of Ozempic for weight loss among non-diabetics, focusing on factors driving demand, perceptions of misuse, and ethical and economic implications. Using survey data of 173 primarily young individuals from Germany, it highlights gaps in understanding motivations and behaviors related to off-label use. Key findings illustrate that familiarity with Ozempic increases consideration and risk perceptions, while perceived legitimacy and non-prescription availability enhance acceptability. These results highlight the social and ethical challenges of off-label drug use, emphasizing the need for stricter regulatory healthcare policies and further research into patient safety.

Keywords: Weight Loss, Off-Label Use, Obesity, Diabetes, Misuse, Empirical Study, Supply Shortage, Excess Demand, Ozempic, Drug

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Table of Contents

1 Introduction

Obesity presents significant health challenges for affected individuals and a growing economic burden on healthcare systems and governments globally (Hurt et al. 2010; Tremmel et al. 2017).[1] Rising healthcare costs linked to obesity have become a critical concern, as the increasing prevalence of high body mass index (BMI) drives costly chronic diseases (Dee et al. 2014). [2] These include conditions such as Type 2 diabetes mellitus (T2DM), joint disorders, and cardiovascular disease, which demand substantial financial resources (Organization for Economic Co-operation and Development (OECD) 2019).

In Germany, treating obesity-related conditions will account for 8% of healthcare expenditures, with per capita costs averaging 411.19 USD PPP (OECD 2019). Moreover, their total societal costs in Germany are estimated at 63 billion euros per year as of 2012 (Effertz et al. 2016). T2DM is a condition that is strongly linked to obesity and affects an increasing global population, projected to reach 1.31 billion by 2050 (Deutsche Diabetes Gesellschaft (DDG) 2024; World Health Organization (WHO) 2024b; OECD 2019; Ong et al. 2023). Furthermore, OECD projections indicate that approximately 70% of diabetes-related treatment costs in Germany from 2020 to 2050 will be attributable to obesity, underscoring the need for effective strategies to mitigate the rising healthcare expenditures associated with this epidemic (OECD 2019). One such emerging option is Ozempic (semaglutide), a Glucagon-like Peptide receptor agonist (GLP-1 RA) originally developed for T2DM (Han et al. 2024). Beyond blood sugar control, Ozempic has attracted considerable attention for its significant effectiveness in promoting weight loss, making it an attractive off-label (OL) treatment for obesity (European Medicines Agency (EMA) 2018; Wojtara et al. 2023).[3] However, the increasing use of Ozempic among non-diabetics underscores critical concerns about its potential misuse and

[1] Overweight and obesity are characterized by an abnormal or excessive accumulation of body fat, which poses a health risk. A BMI > 25 is considered overweight, whereas >30 is obese (OECD 2019).
[2] An indicator of overweight and obesity, calculated based on weight divided by height (Apovian 2016).
[3] Use of a medication for an unapproved indication, route of administration, dosage, or age group (EMA n.d.).

economic implications, as the overwhelming OL demand threatens to displace the intended purpose and availability of the drug.

The thesis begins with a concise review of the relevant literature, including elucidating the definition, pathophysiology, and treatment approaches for diabetes, focusing on GLP-1 RA like Ozempic. Regulatory approval, usage restrictions, and insurance coverage are explained, followed by the introduction of the research motivation and question this thesis builds upon. Therefore, the factors driving OL demand and indicators of potential misuse are discussed. Subsequently, the empirical study is described, presenting the survey design, and sample characteristics in detail. Following this, data analysis is performed. Therefore, the methodology is explained and used for descriptive statistics and regression testing. The last section provides a discussion of the findings and the study's limitations and future directions, followed by a conclusion.

2 Literature Review

2.1 Definition, Pathophysiology, and Types of Diabetes

Diabetes mellitus is a chronic condition characterized by persistent hyperglycemia, resulting from the pancreas producing insufficient insulin or the body's cells being unable to use it effectively (National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) 2023). The hormone Insulin regulates blood glucose by helping glucose get into cells to be used for energy (Wilcox 2005).[4] In diabetics, glucose remains in the blood, which leads to higher blood sugar levels (WHO 2024a). This uncontrolled hyperglycemia can lead to serious damage over time, affecting the retina.

Diabetes can be distinguished into different types, including type 1 (see Appendix (A) 2), type 2 and special forms (see A3). T2DM, the most common form, is a metabolic disorder

[4] Glucose serves as the body's main source of energy. Although the body is able to produce glucose itself, it is also obtained directly from food (NIDDK 2023).

characterized by insulin resistance and a progressive decline in pancreatic insulin production (NIDDK 2023). If not treated effectively, this results in increased blood glucose levels (Galicia-Garcia et al. 2020). Unlike Type 1 diabetes, the cells don't use insulin properly (NIDDK 2023). Moreover, this form is linked to lifestyle factors, such as an unhealthy diet, physical inactivity, and increased body weight, although genetic predisposition plays an important role (Chatterjee, Khunti, and Davies 2017).

2.2 Treatment Approaches for Diabetes

Given the significant health and economic impacts of diabetes, effective and sustainable treatment is essential. As nearly two-thirds of T2DM patients are obese and often lead sedentary lifestyles, treatment generally involves a gradual approach that combines lifestyle modifications with medication (Ruze et al. 2023). Dietary adjustments and increased physical activity often serve as the foundation of T2DM therapy. However, these modifications may be supplemented with antidiabetic medications (see A4) or insulin therapy in advanced stages if blood glucose control remains inadequate (Chan and Abrahamson 2003).

2.2.1 Advanced Therapeutic Strategies: GLP-1 Receptor Agonists

One recent advancement in diabetes treatment is the development of GLP-1 RAs, a class of drugs that opened up the therapeutic landscape for T2DM (Garber 2012). By mimicking the hormone GLP-1, these medications offer benefits beyond mere glucose control. GLP-1 RA primarily improve glucose regulation by increasing insulin secretion and inhibiting glucagon release in response to blood glucose levels, thereby reducing hyperglycemia (Filippatos, Panagiotopoulou, and Elisaf 2014). Additionally, they slow gastric emptying, reduce appetite, and consequently lower food intake, which contributes to weight reduction in patients with T2DM (Weghuber et al. 2022).

2.2.2 Specific Role of Ozempic in Diabetes Management

In 2017, Novo Nordisk launched Ozempic, a subcutaneous formulation of semaglutide for primarily managing T2DM (Dhillon 2018). However, Ozempic exhibits dual functionality by

supporting blood glucose control and promoting significant weight loss (Mahapatra, Karuppasamy, and Sahoo 2022; Wojtara et al. 2023). For its OL use in treating obesity, semaglutide targets the hypothalamus, a brain region regulating appetite, and triggers a feeling of fullness. This reduces the desire to eat (Han et al. 2024). Additionally, it prolongs gastric retention, enhancing satiety over a longer period. These mechanisms result in notable weight loss, as evidenced by studies showing strong weight reduction in obese patients using this active substance (Azuri et al. 2023; Borlaug et al. 2023; Palana et al. 2024; Ryan et al. 2024; Wilding et al. 2021). This effectiveness makes Ozempic attractive for OL weight loss, even in individuals without diabetes.

2.3 Overview of Approval, Usage, and Insurance Coverage of Ozempic

The EMA approved Ozempic in 2018, concluding that its benefits outweigh the risks (EMA 2018). In Germany, Ozempic is officially approved only for T2DM treatment as monotherapy or combination therapy (Federal Institute for Drugs and Medical Devices (BfArM) (2023). This is based on clinical evidence from admission studies (Aroda et al. 2019; Marso et al. 2016; Nauck et al. 2021; U.S. Food and Drug Administration (U.S. FDA) 2020). Any other indication, including weight management, represents an OL use. Moreover, Ozempic is prescription-only and therefore exclusively covered by health insurance companies for diabetes treatment. When used for weight loss without a diabetes diagnosis, it is classified as a "lifestyle drug" under § 34 Abs. 1 Satz 7 SGB V, making it legally non-reimbursable (Federal Joint Committee 2024; n.d.).[5] Therefore, patients using Ozempic for weight loss must cover the monthly cost of approximately 300 euros themselves (Innungskrankenkasse classic 2024).

3 Research Motivation and Question

Literature indicates that Ozempic is highly effective in controlling blood glucose and weight loss, driving a significant increase in OL use among non-diabetic patients (Chiappini et al.

[5] Drugs that are primarily used for non-medical purposes (e.g. weight loss) and to improve the quality of life (e.g. appetite suppressants, slimming products) (G-BA 2024).

2023). While OL prescribing is common, the growing demand for Ozempic as a weight loss treatment highlights concerns about its safety and long-term effects (Ashraf et al. 2024; Chothave, Kapadnis, and Jagtap 2024; Tirrell 2024; Ruder 2024; U.S. FDA 2024).

In connection with OL use, there is an increased concern about Ozempic's potential misuse (Chiappini et al. 2023; Wojtara et al. 2023). Misuse, as defined by the WHO (2010), involves using a substance for purposes that deviate from medical or legal standards, such as the non-medical use of prescription medications. This definition captures the nature of Ozempic's OLU-WL, as it is not consistent with the legally approved indication. When OLU-WL is practiced by individuals without a medical need, such as non-overweight persons, it can be defined as a form of 'non-medical' use. This emphasizes that such usage diverges from its intended therapeutic purpose and aligns more closely with misuse. Moreover, OL prescribing may compromise informed consent, as patients might lack the necessary information to make fully educated treatment decisions (Wojtara et al. 2023). This exposes them to unknown risks and side effects, raising ethical concerns also for healthcare providers and pharmacies (see A5).

3.1 Factors Driving Increased Off-Label Demand

The increasing trend of Ozempic's OLU-WL, as highlighted in the literature, underscores the need to examine indicators that may signal potential misuse. To set a fundamental basis for identifying these key drivers and observable patterns, an examination of the factors behind the growing OL demand is therefore needed. These will be discussed in the following section.

3.1.1 Influence of Media and Celebrity Endorsements

The popularity of Ozempic on social media has significantly fueled demand for the drug, particularly for OL uses (Han et al. 2024; Herring 2024). Hashtags like #Ozempic and #Wegovy on TikTok alone have garnered over 600 million views, driven by celebrity endorsements, including Elon Musk's public weight loss results with Ozempic (Schmedt 2023; Tolentino 2023). This rising public interest is also reflected in Google search trends, with a steep rise in searches for "Ozempic" as indicated in Figure 1 from mid-2021 to early 2023, which sharply

accelerates in late 2022. The timing of this uptick coincides with increased media coverage and speculation around celebrity use, including rumors of "Ozempic parties" in Hollywood, highlighting its perceived benefits for weight loss (Noyes 2023). Notably, search volumes strongly correlate with states having higher obesity prevalence, as four of the top five states for Ozempic searches also rank highest in obesity rates (Han et al. 2024). These trends underscore public interest in Ozempic as a weight-loss tool, particularly among populations affected by obesity.

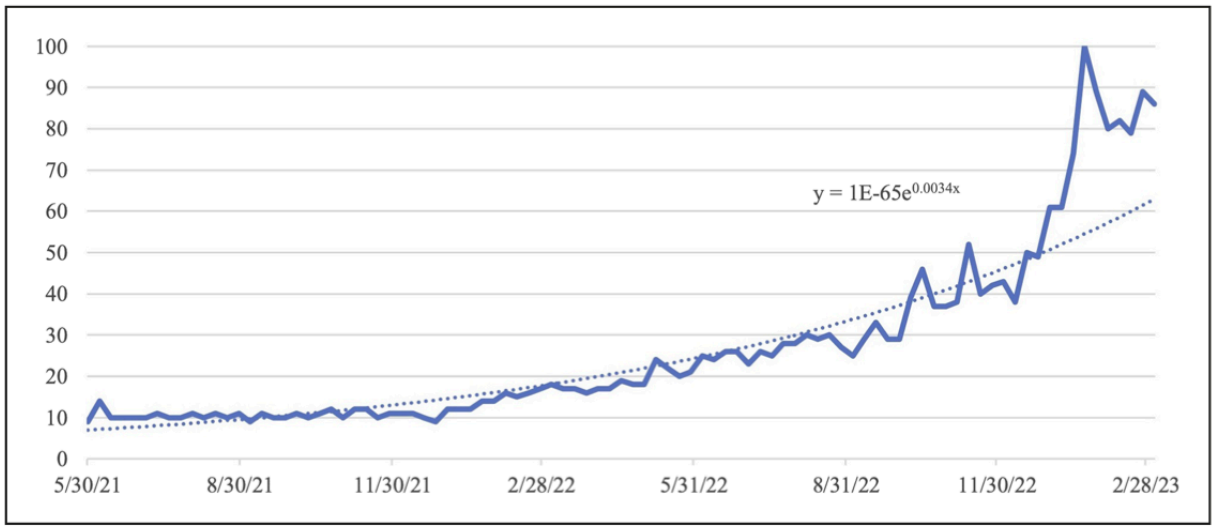

Figure 1: Relative Search Volume of the Term "Ozempic" – 06.2021-02.2023 (Han et al. 2024)

3.1.2 Off-Label Prescription Trends as a Key Driver

Regulatory restrictions limit insurance coverage for Ozempic to approved diabetic indications, yet OL demand for weight loss continues to grow (Muñoz et al. 2024). Studies show that 56% of GLP-1 RA prescriptions, including Ozempic and Mounjaro, were issued without an approved indication (Truveta 2023). Moreover, data from Inovalon's MORE2 Registry® illustrate that 34% of GLP-1 RA prescriptions in 2023 were filled by non-diabetic individuals, an increase from 22% in 2022. Additionally, OL prescription fills tripled between 2022 and 2023 (Inovalon 2024). A rise of 256% in the OL usage of semaglutide from 2018 to 2022 further underscores the substantial and growing interest in GLP-1 RA beyond diabetes management

(see A6). Indirect evidence is provided by news and reports of drug shortages in several countries (Beba et al. 2022; Becker 2024; Therapeutic Goods Administration 2024).

3.1.3 Prescriber Patterns: Family Doctors vs. Specialists' Impact on Demand

Family medicine practitioners play a key role in the OL use of Ozempic, issuing 43.9 % of OL prescriptions compared to only 19.8 % by endocrinologists (Noxon, Moore-Schiltz, and Tkacz 2024) (see A7).[6] Despite their expertise, endocrinologists appear to be more conservative with OL prescribing, while family doctors, as the first point of contact for patients, meet much of the demand (National Institute for Health and Care Excellence 2024). This discrepancy may reflect gaps in risk awareness or expertise, potentially increasing susceptibility to misuse. The fact that less specialized physicians are more inclined to prescribe Ozempic for OL purposes might indirectly suggest a higher risk of medication misuse. However, other factors may also play an important role, such as patient accessibility to specialists, time and cost constraints, and differing prescribing practices. The growing OL use of Ozempic highlights concerning trends, including rising OL prescriptions, heightened public and social media interest, and the predominance of family doctors in prescribing. These factors underscore the need to critically evaluate whether the OL use of Ozempic for weight management leads to misuse.

3.2 Indicators of Potential Misuse in Ozempic Usage

Building on the factors driving the increased OL demand, it is important to investigate indicators of potential misuse. As illustrated in A8, high OL demand sets off a chain reaction that can trigger misuse patterns. The following section analyzes these key signals of misuse.

3.2.1 Supply Shortages

One important indicator are supply shortages and bottlenecks reported by the manufacturer Novo Nordisk that highlight the impact of OL demand on access to medication (BfArM 2023; EMA 2024). The growing use of Ozempic for rapid weight loss, particularly by non-diabetic

[6] Specialists with expertise in diabetes and GLP-1 RA (Van De Loo and Harbeck 2020).

individuals, has significantly limited availability for diabetic patients (Durvy et al. 2024). For instance, 48% of T2DM patients have faced difficulties filling their Ozempic prescriptions due to this high demand (Sermo 2023). Such situations could be considered a form of "legal misuse," where prescriptions for OL use in obesity treatment contribute to shortages that seriously affect access for T2DM patients.

3.2.2 Adverse Event Reports

Adverse Event Reports (AERs) offer valuable insight into potential misuse patterns by documenting side effects linked to both approved and OL use of Ozempic. Studies show that higher doses of semaglutide are linked to greater weight loss (Mailhac et al. 2024; Wilding et al. 2021). As a result, individuals using Ozempic primarily for weight reduction may seek higher doses, increasing the likelihood and risk of intensified side effects (Tomicki 2024). An increase in reported side effects within AERs could thus serve as an indicator of OL use of the drug. Chiappini et al. (2023) analyzed 31,542 AERs from 2018 to 2022, with 26.1% of these reports involving semaglutide. Notably, semaglutide was the only drug among these flagged for OL use, observed in 483 out of 8,249 cases (5.85%). Moreover, drug misuse-related events were predominantly reported for semaglutide, with high rates for 'drug withdrawal syndrome', 'drug abuse', and 'prescription drug used without a prescription'. These misuse signals were identified 3.5 times more frequently than for any other drug in the dataset.

3.2.3 Rising Demand in the Black Market as an Indicator of Illicit Use

The demand for OL use, combined with supply shortages, has also facilitated the emergence of a black market for Ozempic, where it is often marketed as a "weight loss injection" (Norddeutscher Rundfunk 2024; Walsh and Rai 2023; Thier 2024). This shift from legal to "illegal misuse" reflects how supply constraints and heightened interest in OL are driving illicit access channels. Some people are willing to circumvent medical supervision to obtain the drug, which raises additional concerns about its safety. This willingness to purchase unregulated and potentially dangerous products may suggest medication misuse, as people are prepared to take

significant risks. Public reports and agency alerts indicate these patterns: in March 2023, the French National Agency for Drug Safety announced increased monitoring for semaglutide following concerns over misuse and forged prescriptions (Brafman 2023).

As Ozempic is subject to prescription, its misuse of Ozempic is evident in attempts to circumvent this. This happens in various forms: 1) Counterfeit prescriptions and prescription evasion are unlikely among patients with legitimate diabetic or weight loss needs who can obtain official prescriptions.[7] Thus, an increase in these prescriptions could be interpreted as an indicator of potential misuse and non-medical applications of the drug. Such activities may reflect the interest of a target group that is not eligible for the primary indication and is willing to use illegal methods to gain access to Ozempic. The Allgemeine Ortskrankenkasse (AOK) Nordost warns of nationwide counterfeiting of paper prescriptions for medicines such as Ozempic. Since September 2023, they have reported over 1,700 forged recipes worth more than 400,000 euros, mainly concerning medicines like Ozempic (Becker 2024). The FDA also warned about counterfeit versions of Ozempic found in the legal supply chain in the United States (US) (U.S. FDA 2024). This surge in counterfeit products underscores the high demand for Ozempic, particularly for non-diabetic uses, as individuals seek out even unregulated sources when legal supplies are limited.

In addition to counterfeit prescriptions, 2) Counterfeit and relabeled products play a crucial role: the availability of counterfeit products on the black market, such as insulin relabeled as Ozempic shows how criminal activity adapts to demand (Grill and Uhlmann 2024). These products are often of inferior quality, improperly stored, or contain unsafe ingredients, which can cause serious side effects and be life-threatening for non-diabetics (Deutsches Ärzteblatt 2023). Although exact figures on misuse through these channels are difficult to determine, these

[7] A medicinal product that has been fraudulently mislabeled, meaning that false information is provided regarding identity, ingredients, and/or origin (WHO, 2008).

trends highlight how excessive OL demand has led to supply shortages. This encourages misuse and supports the growth of a black market, possessing significant public health risks.

4 Empirical Study

Analyzing the potential misuse of Ozempic requires a structured approach, distinguishing between legitimate OL use and misuse. OL use is legally permissible and not misuse per se, as it can serve valid medical purposes when prescribed by a physician. However, the high demand for Ozempic's OL application has increased the potential for misuse and market distortion.

Therefore, understanding the misuse requires more than an examination of sales, prescription (see A9), and adverse event data. These data reveal usage patterns and related outcomes but fail to capture individual motivations and decision-making processes. Insights directly from individuals who are driving these trends are essential to gain a deeper understanding of these dynamics and capture the full picture of Ozempic's OLU-WL. Following a comprehensive examination of the existing scientific and grey literature, several knowledge gaps that remain unaddressed can be identified. Current literature addresses usage trends, regulatory concerns, supply shortages, and the emergence of a black market, but lacks insights into individual attitudes and perceptions related to Ozempic's OL nature, particularly among younger individuals.

To address these key gaps, an online survey was designed, aiming to answer unresolved questions in the literature: Are young people willing to use Ozempic OL? Are they using it as a weight management tool, and if so, do they perceive its use for weight loss as a legitimate health strategy? How aware are they of the potential side effects and intended use? By directly engaging individuals, the survey seeks to bridge the gap between existing aggregate data and the realities of individual behaviors.

The data was collected using a quantitative research method in the form of an anonymous online survey designed to be self-administered in Qualtrics. The survey was distributed through social

media channels, including Instagram, Facebook, and WhatsApp, and shared on platforms such as LinkedIn and Slack to achieve the highest possible response rate. This study used a convenience sampling and snowball technique. The survey was primarily sent to acquaintances, including friends and family members, who distributed it among their own networks. Responses were collected from 8.11-13.12.2024 in English. Measure such as randomizing answer options minimized bias arising from order effects. The survey gathered information on public awareness, perceptions, and motivations of Ozempic's OLU-WL, including familiarity, personal use considerations, and perceptions of its side effects and misuse.

4.1 Survey Design

The current chapter describes the structure of the online survey. In compliance with data protection regulations, participants were required to provide their written consent.

The survey is divided into four sections, with the first chapter gathering information about the awareness of Ozempic by examining general familiarity through a seven-point Likert scale (1 = Not familiar, 7 = Very familiar). Additionally, participants are asked if they know someone using Ozempic OL or have considered using it for weight loss. Those considering Ozempic for weight loss answer are displayed with two additional questions about what it would replace in their weight management and whether they would request a prescription for this purpose. In general, the first section aims to establish both the baseline awareness of Ozempic and the extent of its recognition as a weight management tool. The second section evaluates Ozempic's perceived purpose and side effects. Participants are asked how likely they would be to try Ozempic for weight loss if it didn't require a prescription. Next, they are prompted to identify the potential side effects of Ozempic and asked whether they perceive Ozempic as a medical treatment, a quick fix for weight loss, or both equally. The third section addresses the perception of misuse and its contributing factors. Therefore, a clear operational definition of "misuse" is used to ensure a standardized understanding. Participants are asked about the risk of Ozempic misuse for weight loss using a seven-point Likert scale (1 = No risk, 7 = Very high risk) and

are prompted to identify contributing factors. Lastly, participants are asked whether using Ozempic for weight loss is a legitimate health strategy. The last chapter gathers demographic data such as age, gender, and nationality to identify correlations between demographic variables and perceptions of Ozempic. For clarity in analysis, each survey question is assigned a corresponding variable name, with a complete legend in A10.

4.2 Sample Description

The sample size is N = 173. Although 185 people started the survey, N = 7 were excluded for completing less than half of the survey, and 5 persons did not agree to participate. In addition, the dropout rate was minimized to 4% by keeping the processing time short (3-5 minutes).

The demographic distribution (see A11) illustrates that participation is nearly balanced in terms of *Gender*. Regarding *Age* characteristics, most participants (N = 147, 84.97 %) are between 18 to 27, reflecting the survey's target population: primarily students and individuals of similar ages within my social network. In terms of *Nationality*, most participants (75.72 %) come from Germany, followed by Brazil (5.78 %). Nonetheless, as a convenience sample conducted within a limited circle, this study is exploratory and may not fully represent the broader population.

5 Data Analysis and Results

The following section describes the analysis and results of the data obtained from the survey. Various statistical analyses and testing procedures were applied to evaluate the data. These will be presented and explained in their primary function and application. Although further descriptions are omitted, reference is made to the relevant statistical literature.

5.1 Method

The data were analyzed using IBM SPSS Statistics, applying descriptive and inferential methods such as correlation-, mean difference-, and regression calculations, testing for significance (see A12). A preliminary pilot study with two participants was conducted to ensure clarity, leading to adjustments to the order of questions to improve the logical flow for

participants. Additionally, variable transformation and coding were performed to enable a more structured analysis, as detailed in A13. For all statistical tests employed, the null hypothesis is rejected only if the probability of error is below the alpha level of .05 (Hirschauer et al. 2016).

5.2 Descriptive Statistics

To gain a comprehensive understanding of participants' familiarity with and attitudes toward Ozempic, they were asked about their knowledge of the drug. These questions aimed to identify the survey's target group and evaluate their level of familiarity and prior exposure to Ozempic.

5.2.1 General Awareness, Usage, and Perceptions of Ozempic

In a sample with N = 173, familiarity with Ozempic varied, with 50.29 % reported moderate to high familiarity (level >= 5) and 39.88 % indicated limited or no familiarity (level <= 3). N = 17 reported a neutral familiarity, selecting a score of 4. A14 provides a graphical representation to illustrate the familiarity level. On average, participants indicated a level of 4.01. The median (5) for this question is larger than the mean (4.01), which indicates left-skewed data distribution (see A15) (Hippel, 2011). Responses related to higher familiarity were thus more prominent. The summary statistics are the following:

		Frequency	Percentage
Level of Familiarity	1	32	18.50
	2	20	11.56
	3	17	9.83
	4	17	9.83
	5	39	22.54
	6	29	16.76
	7	19	10.98

Table 1: Frequency of Levels of Familiarity with Ozempic, N = 173

Results with regard to the perceived commonality of Ozempic's OL use among social circles indicate that it is not widely known. A clear majority of 69.9 % stated they do not know anyone who uses the drug for this purpose, while only 19.7 % confirmed that they know someone (see A16). Similar patterns can be seen about question 3. Figure 1 indicates that the majority (57.23 %) has not yet considered using Ozempic for weight loss.

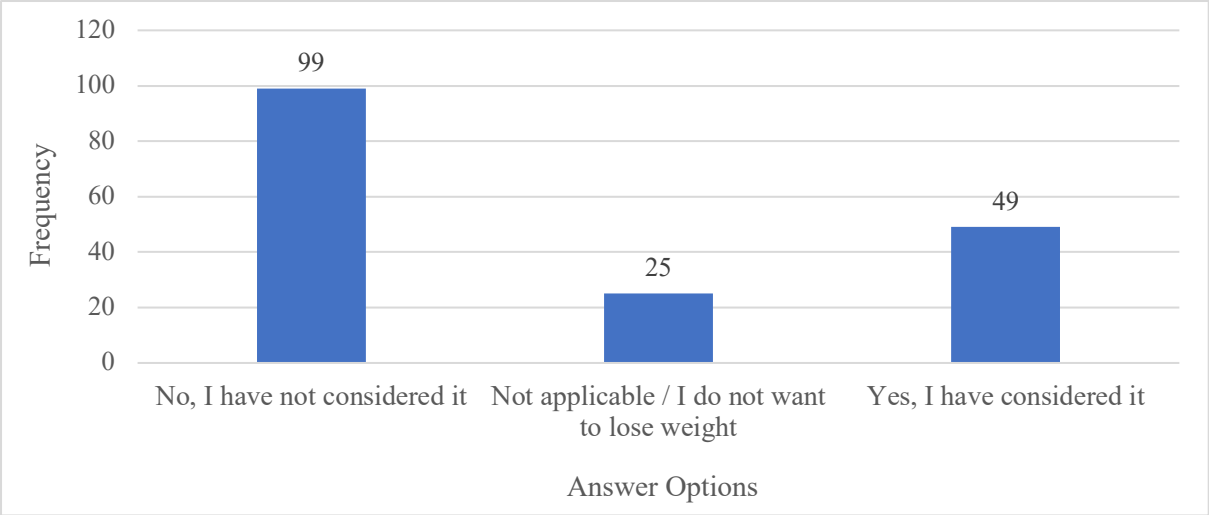

Figure 2: Frequency Distribution of Consideration for Using Ozempic for Weight Loss

Gender-based differences were observed in *Familiarity* with and *Consideration* of Ozempic. Specifically, a larger proportion of male participants (25.88 %) reported having no familiarity with Ozempic, compared to women (11.36 %) (see A17) and more men (68.24 %) had not considered using Ozempic, in contrast to women (46.59 %) (see A18). Moreover, twice as many women (35 vs. 14) reported having considered using Ozempic. This indicates that men generally show less familiarity with and consideration of Ozempic for weight loss purposes compared to women. These results align with recent literature indicating that men show reduced engagement in weight control methods (Simon et al. 2006; Pagoto et al. 2012) and women are more likely to participate in structured weight loss programs or take prescription diet pills (Tsai et al. 2016).

To gain a deeper understanding, those who considered Ozempic for weight loss were asked two follow-up questions. Regarding the first question, most participants indicated they would replace "no specific method" (40.82 %) or "traditional dieting" (42.86 %) with Ozempic (see A19). Regarding the participants' willingness to seek a doctor's prescription for Ozempic for weight loss, the data reflects that the majority (77.55 %) is open to that idea (see A20).

Moreover, the data indicates a strong hesitance among participants to ask a doctor for Ozempic if it were available without a prescription. Most respondents (41.04 %) stated they were "very unlikely" to do so. In contrast, only 18.5 % were "very likely" to ask a doctor under these

conditions. This distribution suggests that even in a non-prescription context, most participants are hesitant to seek Ozempic for weight loss from their doctor.

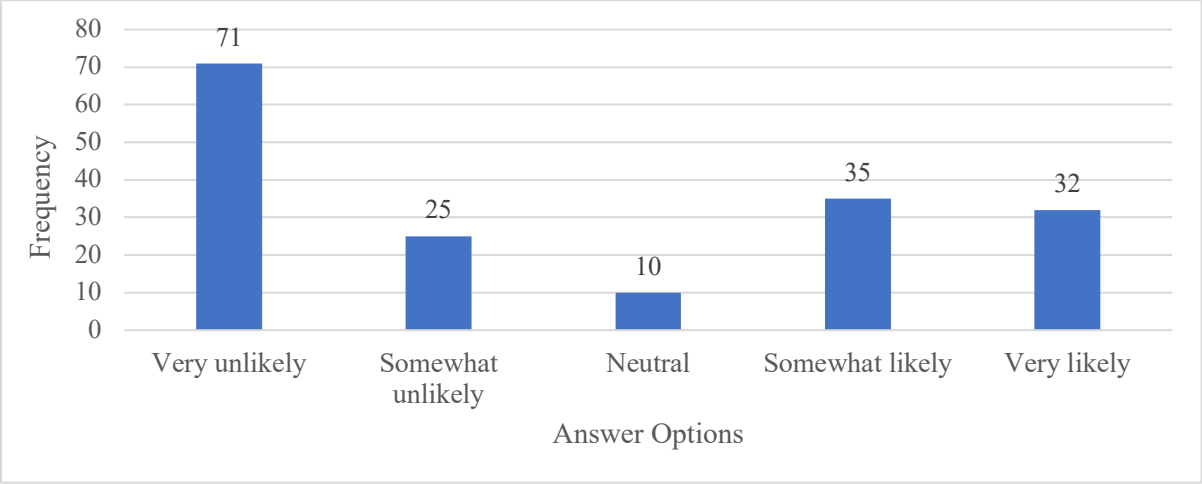

Figure 3: Frequency Distribution of Participants' Willingness to Ask a Doctor for Ozempic Without a Prescription, N = 173

A21 indicates a general concern about side effects, as 53.18 % of respondents perceive either mild or severe side effects. Additionally, the high proportion of respondents who are unsure (15.61 %) or unaware (23.7 %) of the potential side effects suggests a lack of confidence in the safety profile of Ozempic, which could contribute to hesitation or concern. This highlights the need for targeted education and awareness campaigns.

5.2.2 Misuse, Risk Perception, and Legitimacy of Ozempic Use

The findings from Questions 8 to 12 are presented here in brief, as further regression analysis will be conducted to explore these variables in more detail: the analysis reveals that most respondents view Ozempic primarily as a medical treatment (48.55 %) (see A22). In terms of awareness, many respondents (33.53 %) believe that young people havea limited understanding of Ozempic's primary use, with "not very aware" being the most common response (see A23). Regarding the perceived *Risk Of Misuse*, respondents rated this risk relatively high, with an average score of 5.14 on a 7-point scale. The median response is 6, indicating left-skewed data distribution (Hippel 2011): responses related to a higher risk of Ozempic misuse were thus more prominent (see A15). The most frequently cited factors contributing to this risk were "desire to lose weight quickly" and "social media promotion," suggesting that external

influences and the appeal of fast results heighten the risk perception (see A24). Finally, most respondents (50.29%) do not believe that using Ozempic for weight loss is a legitimate health strategy (see A25).

5.3 Regression Analyses and Key Variable Relationships

The following chapter addresses the detailed examination and testing of the research questions. For this purpose, binary and ordinal logistic regression analyses were performed. As a threshold value for individual dual statistical significance, .05 is used. Thus, a p-value ≤ .05 is considered significant (Janssen and Laatz 2013). Full regression outputs can be found in the Appendices. The correlation table (see A26) highlights key relationships, like *Consideration* & *Likelihood of Usage Without Prescription, Perceived Risk of Misuse* & *Legitimacy*, and *Willingness to Ask a Doctor* & *Perception of Ozempic's Use*. These preliminary correlations suggest areas for deeper analysis, which will be expanded through regression testing in subsequent sections. The logistic regression model aims to use the logistic distribution function to determine the effect of explanatory variables $x_{i1}, \dots, x_{ik} (i = 1, \dots, n)$ on the probability of an outcome occurring in the dependent variable. This approach is used to assess the influence of predictors on binary or categorical outcomes, providing insights into the strength and direction of these relationships.

$$F(n_i) = \frac{exp(n_i)}{1 + exp(n_i)} = \pi_i, \text{ with } n_i = \beta_0 + \beta_1 * x_1 + \cdots + \beta_k * x_k, \text{ (Groß 2010).}$$

Familiarity* and *Consideration. For this purpose, the variable *Consideration* was assigned the values 0 (= no consideration) and 1 (= consideration). Data from respondents not engaging in any weight management activities were excluded. *Familiarity* (F) was included as a set of dummy variables, with *F = 1* (lowest familiarity) serving as the reference category. Additionally, *Age* and *Gender* were included as control variables. This binary logistic regression models the likelihood of considering Ozempic *(C = 1)* based on *Familiarity (F)* with the drug (see A27). The positive coefficients for *Familiarity* levels, *F6* and *F7*, indicate that

higher *Familiarity* significantly increases the likelihood of *Consideration*. Respondents in Familiarity level *F6 (F7)* are approximately 8.2 (8.9) times more likely to consider Ozempic compared to those in the reference group (*F1*). Moreover, the overall model is statistically significant ($p < .001$).

Predicting *Willingness to Ask a Doctor.* From the regression output, it can be observed that none of the predictors are statistically significant ($p > .05$), indicating they have no clear influence on whether individuals would ask a doctor to prescribe the drug for weight loss (see A28). However, the direction of the estimates aligns with the expected relationship, so further investigation with a larger sample size could be crucial (see A29).

Legitimacy* and *Risk of Misuse. The chi-square test shows a significant relationship between perceived *Legitimacy* and *Risk of Misuse* ($p < .001$) (see A30). This finding is further confirmed by the Kruskal-Wallis test ($p = .038$), used due to the lack of normal distribution and small expected cell values (see A31). These results suggest that the belief about the legitimacy of using Ozempic for weight loss influences the perceived risk of misuse. To further explore this potential bidirectional relationship, two regression models were conducted, examining the influence of *Risk of Misuse* on *Legitimacy*, and vice versa.

Predicting *Legitimacy.* This binary logistic regression examines the likelihood of the dependent variable based on perceived *Risk of Misuse, Likelihood of Usage Without Prescription*, and *Side Effects* (see A32). The results indicate that the *Risk of Misuse* is a significant predictor ($p = .003$). The negative coefficient (-.354) shows that a higher perceived *Risk of Misuse* decreases the likelihood of viewing Ozempic as a legitimate health strategy. For the likelihood of usage categories, respondents in the "somewhat unlikely*"*, "somewhat likely*",* and "very likely*"* groups are 4.9, 3.4, and 8.2 times more likely to view Ozempic as legitimate, respectively, compared to the reference group "very unlikely" ($p < .05$).[8] This result

[8] Derived from the Exp(B) column in the logistic regression output, representing odds ratios.

indicates that individuals more willing to try Ozempic without a prescription are also more likely to view its OL use for weight management as legitimate. However, the Neutral group shows no statistically significant effect.

Predicting *Risk of Misuse.* Three regression models were conducted to analyze the influence of various predictors on the *Risk of Misuse* (see A33, 35, 37). The first regression output indicates that the overall model is statistically significant ($p < .001$). For *Legitimacy,* both groups significantly increase the likelihood of being in higher risk categories compared to *Legitimacy* = "yes" (reference group). Their positive coefficients (1.274 and 1.210) indicate that individuals who consider Ozempic as not legitimate or are unsure, are significantly more likely to perceive a higher *Risk of Misuse* (see A33). Among the age groups, only group Age = 31 has a significant negative effect on the likelihood of being in higher risk categories compared to the reference group. For *Familiarity*, significant negative effects can be drawn for levels 1, 2, and 3 ($p < .05$). This means that lower levels of *Familiarity* compared to the reference group of "very high" *Familiarity*, indicate lower odds of belonging to higher risk categories.

For the second regression model (see A35), only the lower levels 1 (= very unlikely) and 2 (= somewhat unlikely) of *Likelihood of Usage Without Prescription* have significant effects on the *Risk of Misuse* compared to the reference group "very likely". Their negative estimates indicate that individuals who are less likely to use Ozempic without a prescription perceive lower risks of misuse. Moreover, *Side Effects* emerge as a significant predictor across nearly all levels. Specifically, the categories "no side effects" ($p < .001$) and "mild side effects" ($p < .006$) significantly reduce the likelihood of perceiving higher risk levels compared to the reference group "severe effects", highlighted by their negative estimates. This underscores that individuals perceiving less severe or no side effects associate lower risks of misuse. While the direction of the estimates aligns with theoretical expectations (see A34, 36, and 38), all other predictors are not significant.

***Side Effects*, *Risk of Misuse*, and *Legitimacy*.** For this binary Logit-Model, as displayed in A39, a p-value of $p < .001$ is obtained. For *Side Effects*, it can be seen, that its overall effect is statistically significant ($p = .004$), indicating that the perceived severity of side effects plays a crucial role in the consideration of Ozempic. Specifically, participants perceiving mild side effects are significantly more likely to consider using Ozempic compared to those perceiving severe ones ($p = .007$). The only other statistically significant overall effect observed is for *Gender* ($p = .017$). Male participants are significantly less likely to consider using Ozempic compared to female respondents, indicated by its negative coefficient ($B = -1.094$). Even though the overall effect for *Legitimacy* is not statistically significant ($p = .146$), there is a notable trend for participants who do not consider Ozempic legitimate: the negative coefficient ($B = -1.001$) shows a negative association with the likelihood of considering its use. This result, which is just below the significance threshold, suggests that not seeing Ozempic as a legitimate health strategy for weight loss, decreases the probability of its consideration. Although the other values for the variables are not statistically significant, the direction of the coefficients provides additional insights and will be explored in more detail in the appendix (see A40).

6 Discussion

Familiarity, Consideration, and Risk of Misuse. *Familiarity* consistently influences both *Consideration* and *Risk of Misuse*. These results are consistent with previous literature demonstrating that familiarity increases purchase intention, as consumers are more likely to choose products they know well (Wang, Sun, and Hou 2021). Additionally, *Familiarity* enhances understanding of a product's characteristics, thereby enabling better risk assessment (Palazzo and Scherer 2006). However, these findings also warrant consideration of the drivers of *Familiarity*. If familiarity stems predominantly from social media influence emphasizing weight loss benefits, it may prioritize popularity over accurate medical information. This

narrow focus could result in misinformed familiarity, potentially increasing the likelihood of misuse rather than mitigating it. These concerns are further supported by the study's findings, which identify social media promotion and the perceived effectiveness of rapid weight-loss outcomes as primary drivers of misuse. Future research should therefore explicitly evaluate the credibility of information, disseminated through various channels.

Legitimacy and Consideration. *Legitimacy* significantly predicts *Consideration* but does not influence the *Risk of Misuse*. The former is consistent with existing research, indicating that individuals are more likely to adopt practices they perceive as legitimate due to alignment with their moral and social frameworks (Palazzo and Scherer 2006). However, these findings also underscore the importance of further investigating the underlying drivers of perceived legitimacy for evaluating its broader social acceptance and potential implications.

Accessibility and Legitimacy. The study revealed that Ozempic's *Likelihood of Usage*, if no prescription was required, significantly predicts perceived *Legitimacy*. This suggests that accessibility might influence social or medical acceptability. Non-prescription status may be associated with reduced medical risk or increased safety for consumers, thus suitable for unsupervised use. Future research should explore the underlying reasons behind this association, as it has important implications for regulatory and public health policies.

Economic Implications of Misuse. While the study primarily focuses on the misuse of Ozempic, its financial implications form an integral part of the broader discussion. Misuse, as a subset of the broader economic burden, underscores the importance of addressing this topic in future research. Due to space constraints, a comprehensive analysis of Ozempic's economic impact is provided in the appendix (see A41). Ozempic's financial implications pose significant challenges for healthcare systems and insurers, particularly regarding reimbursement for OL use. Nationwide reimbursement is estimated to cost €45.8 billion – equivalent to the total annual pharmaceutical expenditure of Germany's statutory health insurance (SHI) funds (AOK 2024). This raises ethical and economic questions, especially if the drug is used for weight loss in non-

diabetics. A key consideration is therefore whether the long-term health benefits of Ozempic, such as reducing obesity-related complications and hospitalizations, outweigh its high upfront costs. Given that obesity imposes a substantial financial burden, with direct costs exceeding €29 billion annually in Germany (DDG 2024), Ozempic's potential to alleviate these costs makes it a critical area for further research. Initial findings from Incremental Cost-Effectiveness Ratio analyses indicate that, despite higher upfront costs, semaglutide offers significant long-term savings by preventing costly complications (see A42). Moreover, as specific cost-effectiveness studies on Ozempic in Germany are limited, obesity-related cost analyses serve as a valuable proxy (see A43). These could provide baseline data to estimate the potential savings Ozempic could generate by reducing obesity-related healthcare expenditures.

7 Limitations and Future Directions

The study's findings are limited in generalizability due to a small, non-representative sample predominantly from Germany, consisting mainly of young participants drawn from my social network. This restricted subset of society leads to selection bias. Future studies should target diverse populations across different countries and cities to increase sample size, enabling to statistically detect even small differences. The survey primarily captures attitudes and perceptions rather than actual behaviors. While valuable, these insights must be complemented by behavioral data, such as prescription patterns and usage histories, to provide a more comprehensive understanding. For example, analyzing prescription histories could identify behaviors like "doctor shopping," a known indicator of drug misuse (Biernikiewicz et al. 2019; Sansone 2012). Additionally, an experimental rather than a self-reporting survey could enable greater internal validity and investigate cause-and-effect relationships. Conducting experiments in real-world settings (e.g. within fitness studios, doctor's offices, or pharmacies) could reduce bias and would allow to compare self-reported behavior with actual decision-making. Moreover, this one-time and cross-sectional study restricts insights into changes in consumer

attitudes over time (Setia 2016). As such, a longitudinal study could address this limitation (Caruana et al. 2015). Also, the absence of questions on participants' weight or BMI prevents determining whether those considering Ozempic for weight loss meet the clinical criteria for obesity. However, this omission was due to the sensitivity of such questions. It is not just weight, but also the body image people have of themselves that is difficult to ask and could be considered too invasive in this setting. Social desirability bias can be identified as another limitation, as participants may feel pressured to give socially acceptable responses rather than honest answers regarding weight loss intentions. This sensitivity could lead participants to respond in ways that do not accurately reflect their personal views and true behaviors. Similarly, the broad WHO definition of 'misuse', may have led to varied interpretations, as it does not clearly distinguish between legal OL and illegal misuse in the context of Ozempic. Therefore, responses may be influenced by participants' own assumptions about whether the term “misuse” includes legally prescribed OL use or refers only to illegal, unsupervised use. Future studies could therefore use more nuanced definitions or categories that distinguish between these forms of misuse. Furthermore, the study lacks insights from healthcare providers, such as pharmacists and physicians. Understanding how often these professionals receive requests for OL prescriptions of Ozempic, their views on misuse, and their willingness to prescribe Ozempic to non-diabetic patients would offer a more comprehensive view. Finally, participants’ responses in a hypothetical survey may differ from real-world decisions, potentially overestimating certain attitudes or behaviors toward Ozempic. Since data is collected that the participants provide about themselves (self-reported data), inaccuracies can occur, even under anonymity, as participants may withhold information about their actions or motives.

8 Conclusion

This study highlights critical issues for Ozempic’s OL-WL, driven by social media promotion and its effectiveness in rapid weight reduction. Literature and study findings align in identifying

these factors as key drivers of misuse, reflecting a concerning trend in the inappropriate use of this drug (Han et al. 2024). Supply shortages and forged prescriptions further reflect the growing OL demand, leading to serious problems such as black-market activity and the circulation ofcounterfeit drugs (EMA 2024). The study's results reveal that many young people are unaware of Ozempic's primary medical use, as its reputation for weight loss overshadowed its intended role. Furthermore, the perceived legitimacy of Ozempic to lose weight strongly predicts its consideration. Accessibility plays a significant role in this dynamic, as non-prescription availability is linked to higher acceptability. These findings emphasize the need for targeted awareness campaigns, educational initiatives, and stricter regulation on non-prescription availability to address misconceptions about Ozempic's intended use and strengthen its responsible use. While there are clear indications of misuse, it is crucial to acknowledge that obese individuals may have legitimate reasons for seeking such treatments. These insights are essential when devising policy measures without pushing individuals toward unsafe alternatives, such as black-market purchases. Policy responses must therefore balance between regulating OL use and ensuring equitable access to Ozempic for diabetics. Additionally, stricter regulations on social media advertising for prescription drugs are necessary to curb the spread of misleading information. Pomoting global cooperation between regulatory authorities could further strengthen the fight against misuse and counterfeit medicines. In addition, funding for long-term studies on the safety and efficacy of Ozempic is essential to enable evidence-based policy making. Only through collaborative efforts between policymakers, healthcare providers, and social media platforms can we ensure that innovative treatments such as Ozempic are used ethically, effectively and equitably. To conclude, addressing the challenges of obesity and diabetes on a global scale requires a holistic approach that combines public education, robust regulation, and improved access. If used appropriately and proven safe over the long-term, Ozempic has the potential to become a transformative tool in the fight against obesity and diabetes, offering new hope to patients worldwide.

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Appendix

Appendix 1: List of Abbreviations

Abbreviation	Definition
AER	Adverse Event Report
AOK	Allgemeine Ortskrankenkasse
BfArM	Federal Institute for Drugs and Medical Device
BMI	Body Mass Index
DDG	Deutsche Diabetes Gesellschaft
EMA	European Medicines Agency
FDA	Food and Drug Administration
GLP-1 RA	Glucose-like Peptide Receptor Agonist
MACE	Major Adverse Cardiovascular Events
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
OECD	Organization for Economic Co-operation and Development
OL	Off-Label
OLU-WL	Off-Label Use for Weight Loss
SHI	Statutory Health Insurance
T2DM	Type 2 Diabetes Mellitus
WHO	World Health Organization

Appendix 2: Type 1 Diabetes

Type 1 diabetes is a condition - usually diagnosed in children and young adults - in which the body's immune system attacks and destroys the insulin- producing cells in the pancreas. As a result, the body produces little to no insulin. Therefore, this form requires daily administration of insulin to effectively manage blood sugar levels (NIDDK 2023).

Appendix 3: Special Forms of Diabetes

Other types include gestational diabetes and monogenic diabetes. Gestational diabetes develops during pregnancy but usually disappears after delivery. However, this increases the risk of developing T2DM later on in life. Monogenic diabetes, on the other hand, is caused by a single gene mutation (NIDDK 2023).

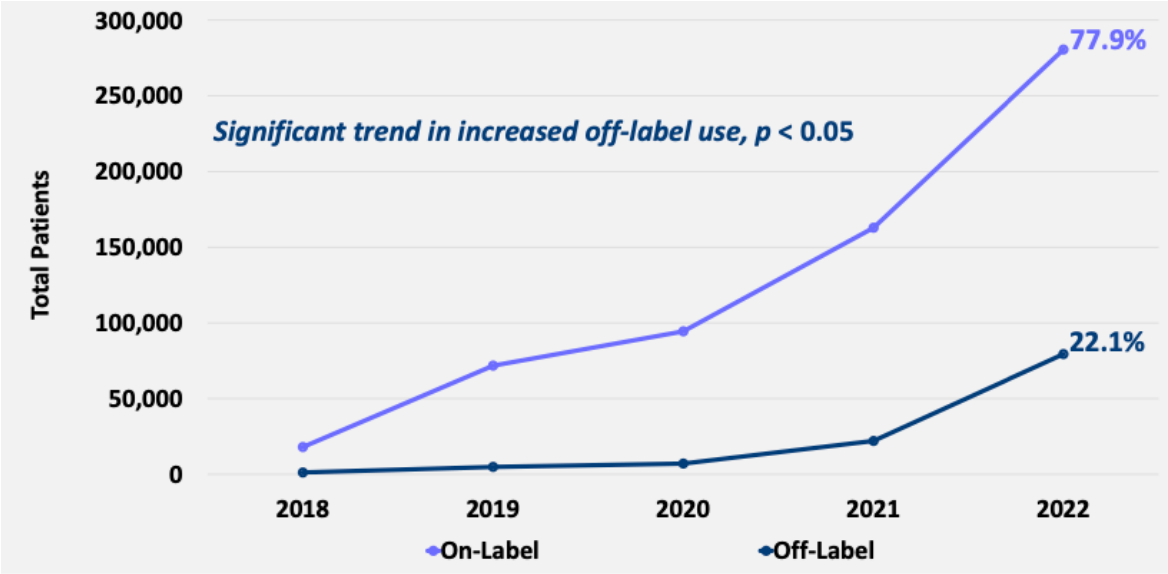
Appendix 4: Antidiabetic Medications

Antidiabetic medications work through various mechanisms to regulate blood glucose levels effectively. They target different aspects of glucose regulation, aiming to lower blood sugar and minimize long-term complications associated with diabetes, such as coronary heart disease and diabetic kidney disease (Chan and Abrahamson 2003; Tomic, Shaw, and Magliano 2022).

Appendix 5: Ethical Considerations and Stakeholders in the Off-Label Context of Ozempic

	Stakeholder Description	Ethical Principle Involved	Impact on Ethical Principles
Patient	Those who use Ozempic for weight loss without fully understanding its mechanism of action.	Autonomy: The right of patients to make self-determined decisions about their medical treatment (Daniels 2017).	A lack of complete information can affect patients' ability to make informed decisions, undermining their autonomy.
Healthcare Provider	Those prescribing Ozempic without adequately informing patients about uncertainties and risks or without sufficient medical evidence.	Nonmaleficence: Obligation of a physician to not harm to the patient (Varkey 2020). Beneficence: "Obligation of physician to act for the benefit of the patient and (…) prevent harm" (Varkey 2020).	When off-label prescribing occurs without sufficient information and evidence, it can cause unintended harm.
Pharmacy	Sellers providing Ozempic to patients without them having proper prescription.	Justice: fair, equitable, and appropriate distribution of healthcare resources (Daniels 2017).	Off-label prescribing can cause shortages of the drug for patients with legitimate medical needs (e.g. diabetes).

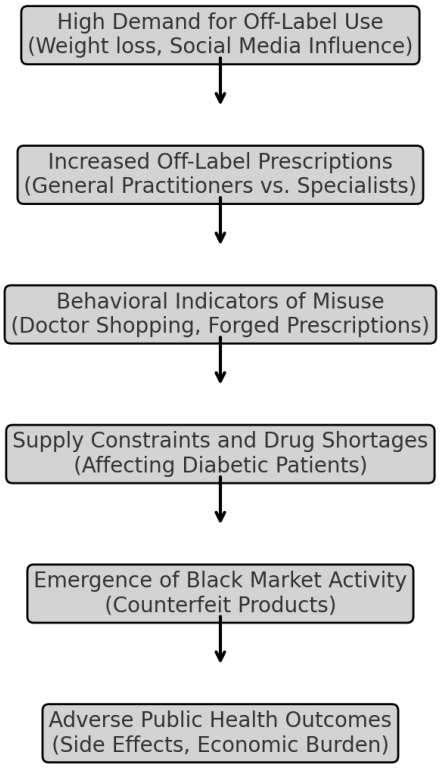
Appendix 6: Trends in On-Label vs. Off-Label Ozempic Prescriptions (2018–2022) (Noxon, Moore-Schiltz, and Tkacz 2024)



Appendix 7: Provider Specialties by Label Status Cohorts (Noxon, Moore-Schiltz, and Tkacz 2024)

Provider Specialty	**Off-Label Cohort**	**On-Label Cohort**
Family medicine	43.9 %	37.1%
Endocrinology, Diabetes, & Metabolism	19.8 %	37.9 %
Medical	7.4 %	6.4 %
Others	13 %	7.4 %

Appendix 8: Pathways from Off-Label Demand for Ozempic to Misuse and Public Health Risks



Appendix 9: Prescription Data for Ozempic's OLU-WL

Prescription data at a general level captures patterns in overall prescribing practices and associated diagnostic information. It is crucial as it provides a detailed view of medications prescribed by healthcare providers and subsequently dispensed in pharmacies. This often includes the provider specialty, which allows to identify the type of healthcare professional that is prescribing Ozempic, particularly for OL uses. Key institutions like the SHI-Arzneimittelindex provide valuable insights into pharmaceutical trends and drug utilization in Germany (Pharmatechnik n.d.).

These records are invaluable for tracking trends in medication consumption. Since prescription data often includes diagnostic information in the form of diagnosis codes, it is essential to determine the reasons, extent, and specific use of each Ozempic prescription. These codes indicate whether patients are prescribed the medication for approved primary use, as diabetes treatment, or for OL purposes, such as weight loss in individuals without diabetes or obesity.

Appendix 10: Variable Legend

Question	Variable Name
Q1	Familiarity
Q2	Personal Knowledge
Q3	Consideration
Q4	Replacement in Weight Management
Q5	Willingness to Ask a Doctor
Q6	Likelihood of Usage Without Prescription
Q7	Side Effects
Q8	Perception of Ozempic's Use
Q9	Youth Awareness of Ozempic's Use
Q10	Risk of Misuse
Q11	Factors for Misuse
Q12	Legitimacy
Q13	Age
Q14	Gender
Q15	Nationality

Appendix 11: Demographic Sample Distribution, N = 173

Variable	Frequency	Percentage
Gender		
male	85	49.13 %
female	88	50.87 %
non-binary/ other	0	0 %
Prefer not to say	0	0 %
Age		
<18	0	0 %
18 - 27	147	84.97 %
28 - 34	18	10.40 %
35 - 44	3	1.73 %
45 - 59	4	2.31 %
60 - 78	1	0.58 %
78+	0	0 %
Prefer not to say	0	0 %
Country of Nationality		
Austria	8	4.62 %
Brazil	10	5.78 %
Germany	131	75.72 %
Portugal	7	4.05 %
Prefer not to answer	4	2.31 %
Other	13	7.51 %

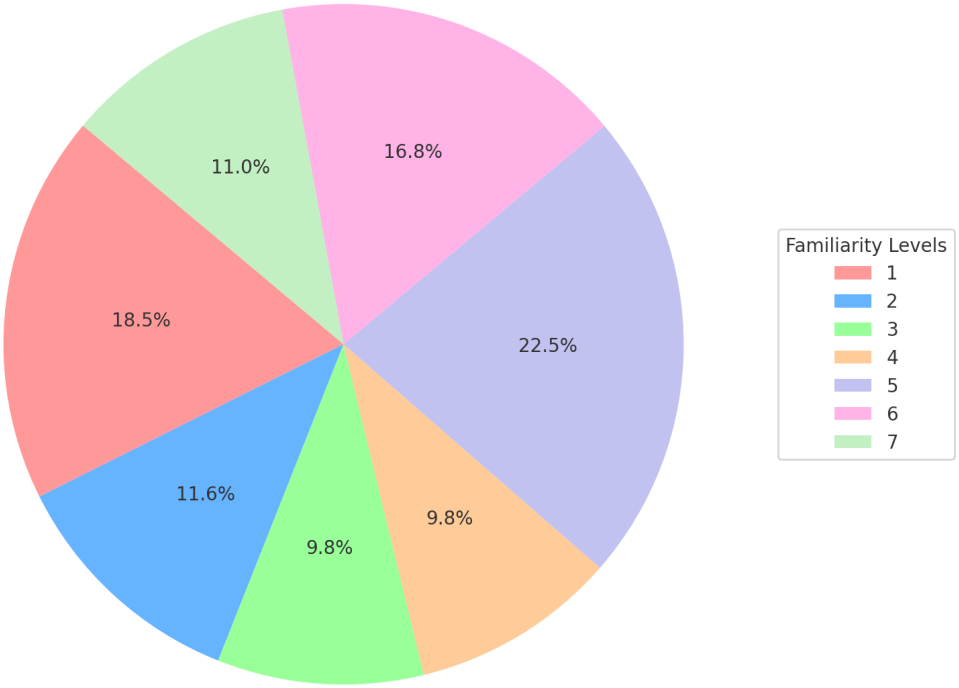
Appendix 12: Overview of Different Methods Used

Using the Kolmogorov-Smirnov Test and Shapiro-Wilk Test, it was examined whether the collected data can be considered as normally distributed. For comparing mean ranks of more than two independent samples, the Kruskal-Wallis H Test was employed (McKight and Najab 2010). Correlations between variables were assessed using Kendall's Tau-b, Spearman's Rho, and Pearson's Point-Biserial correlation coefficients to evaluate the strength and direction of associations (Janssen and Laatz 2013). Additionally, the Chi-Square Test of Independence was conducted to examine significant associations between categorical variables.

Appendix 13: Variable Transformations and Coding

Gender was recoded into a dummy variable, with 0 representing males and 1 representing females. Additionally, a set of three dummy variables was introduced for *Age*, categorized into the following groups based on averages: Age Group 1 (= 22.5) (ages 18–27), Age Group 2 (= 36) (ages 28–44), and Age Group 3 (= 62) (ages 45–78). The variable *Risk of Misuse* was transformed into three categories: low risk (= 1) (Likert scale scores of 1 and 2), medium risk (= 2) (scores of 3–5), and high risk (= 3) (scores of 6 and 7).

Appendix 14: Visual Representation of *Familiarity*, N = 173



Appendix 15: Descriptive Statistics for Likert and Ordinal Scale Variables

Statistics

	Familiarity	Likelihood of Usage Without Prescription	Risk of Misuse
Description	7-point Likert scale (1 = very low, 7 = very high)	0 = very unlikely, 4 = very likely	7-point Likert scale (1 = very low, 7 = very high)
N	173	173	173
Mean	4.01	1.61	5.14
Median	5.00	1.00	6.00
Minimum	1	0	1
Maximum	7	4	7

Appendix 16: Frequency Table of *Personal Knowledge of Ozempic Users*

	Frequency	Percentage
No	121	69.94%
Unsure	11	6.36%
Yes	34	19.65%
Do not know/ do not answer	7	4.05%
Total	173	100

Appendix 17: Gender-Based Differences in *Familiarity*, N = 173

		Female	Male
Level of Familiarity	1	10	22
	2	9	11
	3	6	11
	4	10	7
	5	23	16
	6	17	12
	7	13	6
Total		88	85

Appendix 18: Gender-Based Differences in *Consideration*, N = 173

		Female	Male
Consideration	No, I have not considered it	41	58
	Not applicable / I do not want to lose weight	12	13
	Yes, I have considered it	35	14
Total		88	85

Appendix 19: Frequency Table of *Replacement in Weight Management*, N = 49

	Frequency	Percentage
I would not replace any specific method	20	32.26
Other weight-loss methods	6	9.68
Regular exercise	15	24.19
Traditional dieting	21	33.87
Total*	62	100

*Multiple answer options were possible.

Appendix 20: Frequency Table of *Willingness to Ask a Doctor,* N = 49

	Frequency	Percentage
No, I would not ask	10	20.41
Unsure	1	2.04
Yes, I have already asked	11	22.45
Yes, I would consider asking	27	55.10
Total	49	100

Appendix 21: Frequency Table of Perceived *Side Effects* of Ozempic, N = 173

	Frequency	Percentage
Severe side effects (e.g., gastrointestinal issues)	54	31.21
Mild side effects (e.g., nausea)	38	21.97
No side effects	13	7.51
I am unsure about the potential side effects	27	15.61
I do not know the potential side effects	41	23.7
Total	173	100

Appendix 22: Frequency Table of *Perception of Ozempic's Use*, N = 173

	Frequency	Percentage
Primarily a medical treatment	84	48.55
Both equally	34	19.65
Mainly a weight loss tool	38	21.97
Not sure	13	7.51
Do not know/ do not answer	4	2.31
Total	173	100

Appendix 23: Frequency Table of *Youth Awareness of Ozempic's Use*, N = 173

	Frequency	Percentage
Not aware at all	38	21.97
Not very aware	58	33.53
Somewhat aware	56	32.37
Very aware	15	8.67
Do not know/ do not answer	6	3.47
Total	173	100

Appendix 24: Frequency Table of *Factors of Misuse*, N = 173

	Frequency	Percentage
Desire to lose weight quickly	136	26.36
Social media promotion	128	24.81
Perceived effectiveness in rapid weight loss	110	21.32
Doctors prescribing off-label for weight management	57	11.05
Advice/ influence from friends/ relatives	52	10.08
Perceived safety	33	6.40
Total*	516	100%

*Multiple answer options were possible.

Appendix 25: Frequency Table of *Legitimacy*, N = 173

	Frequency	Percentage
No	87	50.29
Unsure	38	21.97
Yes	48	27.75
Total	173	100

Appendix 26: Correlation Table of Variable Pairs

Variable 1	Variable 2	Correlation Coefficient (r)	Significance Level (p-value)	Significance	Interpretation of the Direction of Coefficients
Consideration (Q3)	Likelihood of Usage Without Prescription (Q6)	Kendall's Tau-b: 0.564 Spearman's Rho: 0.620	Kendall's Tau-b: < 0.001 Spearman's Rho: < 0.001	Yes	The higher the value in Q3, the higher the value in Q6 tends to be. Respondents considering Ozempic are more likely to try it without a prescription.
Perception of Ozempic's Use (Q8)	Risk of Misuse (Q10)	Kendall's Tau-b: -0.112 Spearman's Rho: -0.125	Kendall's Tau-b: 0.051 Spearman's Rho: 0.060	No	A higher value in Q8 suggests a lower value in Q10. Respondents viewing Ozempic as a weight-loss drug tend to perceive a lower risk of misuse.
Risk of Misuse (Q10)	Legitimacy (Q12)	Pearson (Punkt-Biserial): -0.247	< 0.001	Yes	The negative relationship indicates that a higher perceived risk of misuse tends to be associated with lower approval of using Ozempic as a health strategy.

Risk of Misuse (Q10)	Youth Awareness of Ozempic's Use (Q9)	Kendall's Tau-b: 0.010 Spearman's Rho: 0.016	Kendall's Tau-b: 0.437 Spearman's Rho: 0.420	No	Very weak positive relationship. A higher perceived risk of misuse tends to be associated with higher awareness of Ozempic's primary use for diabetes.
Willingness to Ask a Doctor (Q5)	Risk of Misuse (Q10)	Kendall's Tau-b: -0.022 Spearman's Rho: -0.027	Kendall's Tau-b: 0.431 Spearman's Rho: 0.428	No	The weak negative coefficient suggests that respondents who are willing to ask a doctor, perceive a slightly lower misuse risk.
Willingness to Ask a Doctor (Q5)	Legitimacy (Q12)	Kendall's Tau-b: 0.039 Spearman's Rho: 0.041	Kendall's Tau-b: 0.388 Spearman's Rho: 0.389	No	The weak positive correlation coefficients suggest that respondents' willing to ask a doctor, have a slightly higher belief in the legitimacy of using Ozempic for weight loss.
Willingness to Ask a Doctor (Q5)	Perception of Ozempic's Use (Q8)	Kendall's Tau-b: 0.069 Spearman's Rho: 0.076	Kendall's Tau-b: 0.304 Spearman's Rho: 0.302	No	The weak positive correlation coefficients suggest that respondents' willingness to ask a doctor is not meaningfully associated with their perception of Ozempic's use.
Willingness to Ask a Doctor (Q5)	Likelihood of Usage Without Prescription (Q6)	Kendall's Tau-b: 0.226 Spearman's Rho: 0.248	Kendall's Tau-b: 0.047 Spearman's Rho: 0.043	Yes	Respondents who are willing to ask a doctor for Ozempic are slightly more likely to also consider using Ozempic if it were available without requiring a prescription.

Appendix 27: Binary Logistic Regression – *Familiarity* Predicting *Consideration*

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	29.836	8	**<.001**
	Block	29.836	8	**<.001**
	Model	29.836	8	**<.001**

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	158.107[a]	.183	.254

a. Estimation terminated at iteration number 5 because parameter estimates changed by less than .001.

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	**Level of Familiarity (Overall)**			17.037	6	**.009**	
	2	.238	.908	.068	1	.794	1.268
	3	.852	.935	.829	1	.363	2.344
	4	.186	.907	.042	1	.838	1.204
	5	1.218	.733	2.759	1	.097	3.380
	6	2.103	.753	7.799	1	**.005**	8.193
	7	2.182	.805	7.356	1	**.007**	8.866
	Gender (Female)	1.006	.411	5.992	1	**.014**	2.736
	Age (Overall)			1.521	2	.467	
	28-44	-.437	.727	.360	1	.548	.646
	45-78	-1.294	1.179	1.203	1	.273	.274
	Constant	-2.323	.685	11.501	1	**<.001**	.098

a. Variable(s) entered on step 1: Levels of Familiarity (1-7), Gender, Age.

Reference Category = First: Level of Familiarity = 1, Gender = Male, Age = 18–27

Appendix 28: Ordinal Regression Model – *Perception of Ozempic's Use* and *Legitimacy* Predicting *Willingness to Ask a Doctor*

Model Fitting Information

Model	-2 Log Likelihood	Chi-Square	df	Sig.
Intercept Only	37.899			
Final	32.313	5.586	5	.349

Link function: Logit.

Goodness-of-Fit

	Chi-Square	df	Sig.
Pearson	22.405	25	.612
Deviance	18.359	25	.827

Link function: Logit.

Parameter Estimates

			Estimate	Std. Error	Wald	df	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Threshold	Willingness to Ask a Doctor	No	-1.961	.786	6.225	1	**.013**	-3.502	-.421
		Unsure	-1.675	.768	4.760	1	**.029**	-3.180	-.170
Location	Perception of Ozempic's Use	Medical treatment	-.407	.869	.219	1	.640	-2.110	1.297
		Both equally	.124	1.153	.011	1	.915	-2.137	2.384
		Weight-loss tool	0[a]	.	.	0	.	.	.
	Legitimacy	No	-.159	.901	.031	1	.859	-1.924	1.606
		Unsure	-2.175	1.114	3.807	1	.051	-4.359	.010
		Yes	0[a]	.	.	0	.	.	.
	Gender	Male	.762	.847	.809	1	.368	-.898	2.422
		Female	0[a]	.	.	0	.	.	.

Link function: Logit.

a. This parameter is set to zero because it is redundant.

Appendix 29: Analysis of the Direction of Estimates for *Perception of Ozempic's Use* and *Legitimacy*

The negative estimate for *Perception of Ozempic's Use* = "medical treatment" (-.407) indicates that individuals who perceive Ozempic primarily as a medical solution are less likely to fall into higher categories of *Willingness to Ask a Doctor* (e.g., "yes") compared to those who view Ozempic as a weight loss tool (reference category, *Perception of Ozempic's Use* = "weight-loss tool"). This suggests that a shift in perception from viewing Ozempic as a weight loss tool to perceiving it as a medical treatment decreases the likelihood of asking a doctor for a prescription.

The negative estimate for *Legitimacy* = "no" (-.159) suggests that individuals who perceive Ozempic as not legitimate for losing weight are less likely to fall into higher categories of *Willingness to Ask a Doctor* (e.g., "yes") compared to those who view Ozempic as a legitimate (reference category, Legitimacy = "yes"). This indicates that perceiving Ozempic as illegitimate for weight loss reduces the likelihood of asking a doctor for a prescription. However, these results are not statistically significant.

Males, with an estimate of .762 are more likely to fall into higher categories of *Willingness to Ask a Doctor* compared to female counterparts. This trend could be explained by risk-taking behaviour. As studies suggest, men are generally more likely to engage in such behaviours than women (Byrnes, Miller, and Schafer 1999). This phenomenon may be reflected in a greater willingness to utilize off-

label or unconventional treatments such as Ozempic, as men may perceive fewer barriers or concerns in exploring alternative health strategies.

Appendix 30: Chi-Square Test – *Risk of Misuse & Legitimacy*

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	43.460[a]	12	**<.001**
Likelihood Ratio	42.573	12	**<.001**
Linear-by-Linear Association	10.522	1	**.001**
N of Valid Cases	173		

a. 8 cells (38.1%) have expected count less than 5. The minimum expected count is 1.32.

Appendix 31: Kruskal-Wallis Test for *Risk of Misuse & Legitimacy*

Tests of Normality

		Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Legitimacy	Statistic	df	Sig.	Statistic	df	Sig.
Risk of Misuse	Low	.245	87	**<.001**	.831	87	**<.001**
	Medium	.211	38	**<.001**	.855	38	**<.001**
	High	.223	48	**<.001**	.842	48	**<.001**

a. Lilliefors Significance Correction

Hypothesis Test Summary of Kruskal-Wallis Test

	Null Hypothesis	Test	Sig.[a,b]	Decision
1	The distribution of *Risk of Misuse* is the same across categories of *Legitimacy*.	Independent-Samples Kruskal-Wallis Test	.038	Reject the null hypothesis.

a. The significance level is .050.
b. Asymptotic significance is displayed.

Independent-Samples Kruskal-Wallis Test Summary

Total N	173
Test Statistic	6.528a
Degree Of Freedom	2
Asymptotic Sig.(2-sided test)	**.038**

a. The test statistic is adjusted for ties.

Appendix 32: Binary Regression Model - *Likelihood of Usage Without Required Prescription*, *Side Effects*, *Risk of Misuse* Predicting *Legitimacy*

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	39.888	9	**<.001**
	Block	39.888	9	**<.001**
	Model	39.888	9	**<.001**

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	164.437[a]	.269	.297

a. Estimation terminated at iteration number 5 because parameter estimates changed by less than .001.

Variables in the Equation

			B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]		Risk of Misuse	-.354	.117	9.066	1	**.003**	.702
	Likelihood of Usage Without Prescription	Somewhat unlikely	1.586	.613	6.696	1	**.010**	4.883
		Neutral	.921	.901	1.046	1	.306	2.513
		Somewhat-likely	1.233	.573	4.636	1	**.031**	3.431
		Very-likely	2.108	.607	12.067	1	**<.001**	8.230
	Side Effects	Unsure	.284	.704	.163	1	.687	1.328
		No effects	1.079	.844	1.635	1	.201	2.942
		Mild effects	.671	.616	1.186	1	.276	1.956
		Severe effects	.041	.612	.005	1	.947	1.042
		Constant	-.589	.692	.723	1	.395	.555

a. Variable(s) entered on step 1: Risk of Misuse, Likelihood of Usage Without Prescription, Side Effects. Reference categories: for Likelihood of Usage = Very unlikely, for Side Effects = I don't know.

Appendix 33: Ordinal Regression Model – *Familiarity, Consideration,* and *Legitimacy* Predicting *Risk of Misuse*

Model Fitting Information

Model	-2 Log Likelihood	Chi-Square	df	Sig.
Intercept Only	224.312			
Final	183.761	40.550	12	**<.001**

Link function: Logit.

Goodness-of-Fit

	Chi-Square	df	Sig.
Pearson	192.324	124	**.003**
Deviance	146.541	124	.380

Link function: Logit.

Parameter Estimates

			Estimate	Std. Error	Wald	df	Sig	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Threshold	Risk of Misuse	Low	-3.905	1.271	9.443	1	**.002**	-6.396	-1.414
		Medium	-1.914	1.240	2.382	1	.123	-4.344	.517
Location	Legitimacy	No	1.274	.436	8.540	1	**.003**	.420	2.129
		Unsure	1.210	.518	5.468	1	**.019**	.196	2.224
		Yes	0[a]	.	.	0	.	.	.
	Consideration	Other	.215	.439	.240	1	.624	-.645	1.075
		Yes	0[a]	.	.	0	.	.	.
	Gender	Male	.072	.380	.036	1	.850	-.673	.816
		Female	0[a]	.	.	0	.	.	.
	Age	18-27	-2.035	1.137	3.202	1	.074	-4.264	.194
		28-44	-2.973	1.238	5.766	1	**.016**	-5.400	-.546
		45-78	0[a]	.	.	0	.	.	.
	Level of Familiarity	1	-1.817	.697	6.803	1	**.009**	-3.183	-.452
		2	-1.504	.737	4.163	1	**.041**	-2.949	-.059
		3	-1.546	.783	3.898	1	**.048**	-3.081	-.011
		4	-1.032	.739	1.950	1	.163	-2.480	.416
		5	-.039	.664	.004	1	.953	-1.340	1.261
		6	1.091	.769	2.012	1	.156	-.416	2.599
		7	0[a]	.	.	0	.	.	.

Link function: Logit.

a. This parameter is set to zero because it is redundant.

Appendix 34: Analysis of the Direction of Estimates for *Familiarity* and *Consideration*

The output for Legitimacy shows significant positive estimates for both groups (Legitimacy = "no" and "unsure") compared to the reference group Legitimacy = "yes" (perceiving Ozempic as legitimate). This suggests that individuals who either view Ozempic as illegitimate or are unsure about its legitimacy are more likely to associate higher risks of misuse compared to those who see it as legitimate.

The positive estimate for *Consideration* (.215) indicates that individuals who have not considered Ozempic as a weight-loss tool (*Consideration* = "other") perceive a higher risk of misuse compared to those who have considered it. This aligns with the notion that individuals who take into account the use of Ozempic as a weight-loss option may also be more familiar with it and, therefore, aware of its likelihood of being misused.

Moreover, the output indicates a significant relationship between Familiarity levels 1,2, and 3 and the perception of misuse. The negative estimates for these Familiarity levels suggest that individuals with lower levels of Familiarity perceive a lower risk of misuse compared to the reference group (Familiarity level = 7). This implies that as Familiarity with Ozempic increases, individuals may become more aware of its potential for OL use or misuse, leading to heightened concerns.

For *Gender* the results indicate no significant effect ($p = .850$), suggesting that there is no meaningful difference between males and females in their perception of misuse risk. Regarding *Age*, only the estimate for Age = "28-43" is significant, indicating that individuals in this age group perceive significantly lower risks of misuse compared to the reference group (Age = "44-78"). Even though the effect for Age = "18-27" is not statistically significant, the estimate indicates a similar trend of lower perceived risk compared to the reference group.

Appendix 35: Ordinal Regression Model - *Likelihood of Usage Without Required Prescription*, *Side Effects*, *Legitimacy* Predicting *Risk of Misuse*

Model Fitting Information

Model	-2 Log Likelihood	Chi-Square	df	Sig.
Intercept Only	149.318			
Final	114.744	34.574	8	**<.001**

Link function: Logit.

Goodness-of-Fit

	Chi-Square	df	Sig.
Pearson	62.757	38	**.007**
Deviance	60.197	38	**.012**

Link function: Logit.

Parameter Estimates

								95% Confidence Interval	
			Estimate	Std. Error	Wald	df	Sig.	Lower Bound	Upper Bound
Threshold	Risk of Misuse	Low	-3.753	.675	30.876	1	**<.001**	-5.077	-2.429
		Medium	-1.794	.622	8.307	1	**.004**	-3.014	-.574
Location	Likelihood of Usage Without Prescription	Very unlikely	-1.397	.533	6.863	1	**.009**	-2.442	-.352
		Somewhat unlikely	-1.427	.596	5.740	1	**.017**	-2.595	-.260
		Neutral	-.917	.798	1.323	1	.250	-2.481	.646
		Somewhat likely	-.827	.551	2.251	1	.134	-1.906	.253
		Very likely	0[a]	.	.	0	.	.	.
	Side Effects	Do not know	-.874	.439	3.971	1	**.046**	-1.734	-.014
		Unsure	-.388	.508	.583	1	.445	-1.384	.608
		No Side effects	-3.603	.706	26.056	1	**<.001**	-4.987	-2.220
		Mild effects	-1.278	.466	7.532	1	**.006**	-2.191	-.365
		Severe effects	0[a]	.	.	0	.	.	.

Link function: Logit.

a. This parameter is set to zero because it is redundant.

Appendix 36: Analysis of the Direction of Estimates for *Likelihood of Usage Without Prescription, Side Effects* and *Legitimacy*

The negative estimates for *Likelihood of Usage Without Prescription* indicate, that as the likelihood of obtaining Ozempic without a required prescription decreases, perceived misuse risk also decreases compared to the reference category. This negative association is however just statistically significant for the categories "very unlikely" and "somewhat unlikely". Their estimates show that a lower likelihood of seeking Ozempic if no prescription would be required is linked to reduced perceived misuse risk.

For *Side Effects*, which has five levels, the reference category (*Side Effects* = "severe effects") represents a perception of very severe side effects associated with Ozempic. Compared to this baseline, responses in other *Side Effects* Levels, which represent unknown, uncertain, no, or milder side effects, are associated with a lower perceived misuse risk. The strongest negative coefficient can be seen for the category of mild *Side Effects*. Thus, individuals perceiving milder side effects tend to view the misuse risk as lower compared to those who perceive the risks as severe.

Appendix 37: Ordinal Regression Model – *Perception* and *Youth Awareness of Ozempic's Use* Predicting *Risk of Misuse*

Model Fitting Information

Model	-2 Log Likelihood	Chi-Square	df	Sig.
Intercept Only	118.387			
Final	109.387	9.001	6	.174

Link function: Logit.

Goodness-of-Fit

	Chi-Square	df	Sig.
Pearson	53.865	22	**<.001**
Deviance	61.894	22	**<.001**

Link function: Logit.

Parameter Estimates

			Estimate	Std. Error	Wald	df	Sig.	95% Confidence Interval Lower Bound	95% Confidence Interval Upper Bound
Threshold	Risk of Misuse	Low	-1.232	.610	4.074	1	**.044**	-2.428	-.036
		Medium	.440	.600	.538	1	.463	-.735	1.615
Location		Do not know	1.034	.620	2.780	1	.095	-.181	2.249
	Perception of Ozempic's Use	Medical treatment	.755	.397	3.617	1	.057	-.023	1.534
		Both equally	.274	.454	.364	1	.546	-.616	1.164
		Weight-loss tool	0[a]	.	.	0	.	.	.
	Youth's Awareness of Ozempic's Use	Not aware at all	-.370	.606	.372	1	.542	-1.558	.818
		Not very aware	.465	.578	.649	1	.420	-.667	1.597
		Somewhat aware	.033	.565	.003	1	.954	-1.075	1.141
		Very aware	0[a]	.	.	0	.	.	.

Link function: Logit.
a. This parameter is set to zero because it is redundant.

Appendix 38: Analysis of the Direction of Estimates for *Perception* and *Youth Awareness of Ozempic's Use*

In *Perception of Ozempic's Use*, the reference category is "weight-loss tool". The positive, non-significant estimates of the other groups suggest that viewing Ozempic as a non-weight loss tool might be associated with a higher perceived misuse risk compared to the reference category. However, these effects are not statistically significant, which indicates limited evidence to support this association.

For *Youth Awareness of Ozempic's Use*, the reference category = "very aware". It can be seen that lower levels of *Youth Awareness of Ozempic's Use* is associated with a higher perceived misuse risk, except for the category "not very aware." However, none of the predictors is statistically significant.

Appendix 39: Binary Logit Model - Predicting *Consideration* Using *Side Effects*, *Risk of Misuse*, *Legitimacy,* and the Control Variables *Age* and *Gender*

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	37.810	15	**<.001**
	Block	37.810	15	**<.001**
	Model	37.810	15	**<.001**

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	150.133[a]	.225	.313

a. Estimation terminated at iteration number 5 because parameter estimates changed by less than .001.

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	**Level of Risk of Misuse (Overall)**			4.063	6	.668	
	1	-.647	1.206	.288	1	.592	.523
	2	-.624	.826	.570	1	.450	.536
	3	-.486	1.323	.135	1	.714	.615
	4	.174	.915	.036	1	.850	1.190
	5	-.925	.678	1.864	1	.172	.396
	6	.306	.539	.323	1	.570	1.358
	Legitimacy (Overall)			3.854	2	.146	
	No	-1.001	.518	3.728	1	.053	.368
	Unsure	-.865	.647	1.788	1	.181	.421
	Age (Overall)			2.375	2	.305	
	18-27	1.583	1.171	1.830	1	.176	4.871
	28-44	.899	1.393	.417	1	.519	2.458
	Gender (Male)	-1.094	.459	5.667	1	**.017**	.335
	Side Effects (Overall)			15.588	4	**.004**	
	Do not know	-.704	.685	1.054	1	.304	.495
	Unsure	-.257	.647	.157	1	.692	.774
	No side effects	1.349	.888	2.308	1	.129	3.855
	Mild side effects	1.518	.558	7.400	1	**.007**	4.564
	Constant	-1.267	1.217	1.085	1	.298	.282

a. Variable(s) entered on step 1: Risk of Misuse, Legitimacy, Age, Gender, Side Effects. Reference Category = Last, Level of Familiarity = 7, Legitimacy = Yes, Age = 44-78, Gender = Female, Side Effects = Severe Side Effects

Appendix 40: Analysis of the Coefficients for *Risk of Misuse*, *Age*, and *Side Effects*

With regards to the perceived *Risk of Misuse*, it can be seen, that none of the Likert scale levels have a significant influence, with p-values $> .05$. The perception of misuse risk does not appear to have a direct influence on the *Consideration* of Ozempic. The same applies to the variable *Age*, which also has no significant influence on the decision to use Ozempic. The negative coefficients for respondents who are unsure about Ozempic's side effects ($B = -.257$) or do not know them ($B = -.704$) indicate that they are less likely to consider using Ozempic compared to those perceiving severe side effects (reference category). In contrast, respondents who perceive no or mild side effects are more likely to consider it. These findings align with existing literature, which highlights that individuals often avoid decisions involving unknown or uncertain risks (Büchter and Wiegard 2020). This aversion leads to a preference for decisions with clearly quantifiable risks over those with uncertain outcomes. In the context of Ozempic, this is evident from the observation that quantifiable risks, such as mild or severe side effects, increase the likelihood of considering its use. Conversely, when the side effects of Ozempic are unknown or unclear, the likelihood of consideration decreases, as the inability to assess the associated risks makes the decision more challenging.

Appendix 41: Economic Considerations of Ozempic

To systematically analyze the economic impact of Ozempic, a cost-benefit framework can be applied:

Net Benefit (Ozempic) = ((Direct Cost Savings + Indirect Cost Savings + Long-Term Healthcare Savings + QALY Gains) - (Cost of Ozempic + Costs of Side Effects)) – Net Benefit (Alternative Treatments)

For the treatment of diabetes are already established and cost-effective alternatives. One example of this is insulin, which can be used as a baseline or point of comparison when evaluating the cost-effectiveness of Ozempic specifically for diabetes. This procedure is based on the assumption that patients who do not use Ozempic would instead rely on other previously established standard treatments, such as insulin therapy or alternative medications. However, what distinguishes Ozempic from other diabetes drugs is its dual action: it not only treats T2DM but also supports weight loss. Given that obesity is a major risk factor contributing to the rising prevalence of T2DM, the analysis emphasizes the economic burden associated with obesity. This focus is particularly relevant as obesity-related costs constitute a substantial proportion of total healthcare expenditures. Regarding the comparison point for obesity, my study provides

useful insights, as most respondents indicated that they would replace traditional dieting or would not replace any particular method. This lack of specificity makes it challenging to establish a clear and concrete comparison point for evaluating the economic impact of Ozempic on obesity.

1. **Direct Medical Cost Savings**

   Addressing diabetes and obesity forms the largest share of the economic benefits associated with Ozempic. By analyzing healthcare costs for individuals with obesity, baseline expenditures can be used to assess which services might be reduced or increased through treatment with Ozempic. For example, a study by ING Bank highlights that annual healthcare costs due to obesity in Germany (€2,400) exceed the costs associated with Ozempic (€1,100), suggesting short-term cost savings (Stadig 2024). These findings underline Ozempic's potential to mitigate obesity-related healthcare costs.

2. **Costs of Potential Side Effects**

   Like any medication, Ozempic is associated with potential adverse effects, such as gastrointestinal issues, which may require additional treatments or interventions, thereby increasing healthcare costs (DDG, 2024). Establishing a direct causal link between Ozempic and these effects remains challenging due to limited studies, but future long-term research is essential for a comprehensive understanding.

Cost Type	Cost Drivers	Source
Direct Costs Savings	Treatment of obesity and its comorbidities, major adverse cardiac events (MACE)[9], stroke and various types of cancer.	(Ritchie and Roser 2017; OECD 2019; Colditz 1992)
	More visits to primary and specialty care clinics, outpatient specialists and more inpatient stays, undergo more surgeries and use more diagnostic and home health services.	(Bertakis and Azari 2005; Cecchini 2018)
	Higher costs per visa, hospitalization, and medication costs.	(Jonsson 1998)
	Increased prescription frequency (2.4x).	(Cecchini 2018)
Indirect Costs Savings	Loss of quality of life, lower employment rates, reduced productivity due to sickness-related absence, early retirement.	(Sortsø et al. 2016; American Diabetes Association 2018)
	Reduced productivity (absenteeism, presenteeism).	(Goettler, Grosse, and Sonntag 2017)
	Increased tax burden (+0.62%), additional USD 359 PPP per person per year in OECD countries.	(OECD 2019)

[9] E.g. death, stroke, heart failure, or myocardial infarction (Moltó-Balado et al. 2023).

	Psychological conditions (depression, anxiety).	(Simon et al. 2006; Vogelzangs et al. 2009)
Costs of Side Effects	Adverse, gastrointestinal effects.	(DDG 2024)

The studies in appendices 42 and 43 provide valuable insights to shed light on the components of the Net Benefit equation above. Direct cost savings can be derived from studies like Bain et al. (2019), which highlight reductions in diabetes-related costs, saved compared to liraglutide, due to fewer complications. Indirect cost savings can be informed by studies on productivity gains or reduced absenteeism resulting from weight loss, as commonly linked to obesity-related cost reductions. Long-term healthcare savings are supported by studies such as Pulleyblank et al. (2023), which emphasize reduced costs due to fewer cardiovascular complications over time. QALY gains are reported in studies like Evans et al. (2023) and Gaede et al. (2019), showing quality-of-life improvements with Ozempic compared to alternatives. The cost of Ozempic is detailed in Guzaukas et al. (2021), with annualized treatment costs available for reference. Costs of side effects, such as gastrointestinal issues, are acknowledged in studies that highlight additional treatment costs. Lastly, the net benefit of alternative treatments, such as liraglutide or empagliflozin, provides a baseline for comparison, as demonstrated by Bain et al. (2019). Although these studies provide valuable insights for estimating the components of the net benefit equation, it is important to consider potential limitations, such as the variability of cost estimates across health systems, differences in study populations, and generalizability.

Appendix 42: Summary of Cost-Effectiveness Analyses Semaglutide Compared to Other Treatments

Author, Publication Year, Country	Drug Comparison (GLP-1 RA vs. Comparator)	QALYs (Quality-Adjusted Life Years)	Direct Costs	Payer Perspective Costs	Healthcare Sector Savings	Cost-effective profile
(Bain et al. 2020), United Kingdom (UK)	Oral Semaglutide vs. Empagliflozin, Sitagliptin, Liraglutide	0.09 QALYs vs. empagliflozin; 0.20 QALYs vs. sitagliptin; 0.07 QALYs vs. liraglutide	GBP 971 higher vs. empagliflozin ; GBP 963 higher vs. sitagliptin; GBP 1,551 lower vs. liraglutide	GBP 11,006/QALY vs. empagliflozin; GBP 4,930/QALY vs. sitagliptin; dominant (more effective, less costly) vs. liraglutide	Reduced incidence of diabetes-related complications	Cost-effective versus empagliflozin and sitagliptin, and dominant versus liraglutide.
(Evans et al. 2023), UK	Semaglutide vs. Liraglutide	Improvements of 0.06 vs. dulaglutide	GBP 280 saved	Not specified	Avoidance of diabetes-related complications	Yes, semaglutide as a dominant treatment option.
(Gæde et al. 2019), Denmark	Semaglutide vs. Dulaglutide, Exenatide ER,	Improvements of 0.11 (0.5 mg),	DKK 289 (0.5 mg) and DKK 13,416	Not specified	Not specified	Yes, showing clinical advantages over dulaglutide, exenatide

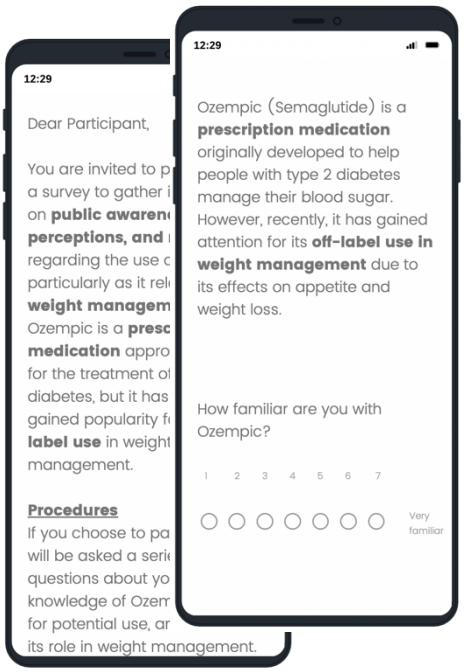
	Liraglutide, Lixisenatide	0.34 (1 mg) vs. dulaglutide	(0.1 mg) saved			ER, liraglutide, and lixisenatide for treating type 2 diabetes.
(Guzauskas et al. 2021), US	Oral semaglutide vs. (a) background antihyperglycemic treatment, (b) sitagliptin, (c) empagliflozin, (d) liraglutide	Oral semaglutide: 4.11 QALYs; comparators: 3.70–4.03	Oral semaglutide: $311,300; comparators: $262,800–$287,800	Not specified	Reduced MACE and cardio-vascular deaths for oral semaglutide	Cost-effective compared with liraglutide and moderately cost-effective vs. sitagliptin and background therapy ($100,000–$150,000/QALY). Not cost-effective vs. empagliflozin.
(Johansen et al. 2019), Canada	Semaglutide vs. Dulaglutide	11.10 vs. 11.07 (Low Dose) (+0.04); 11.12 vs. 11.07 (High Dose) (+0.05)	CAN$113,287 vs. CAN$113,690 (Low Dose); CAN$112,983 vs. CAN$113,695 (High Dose)	CAN$403 (Low Dose); CAN$711 (High Dose)	Not specified	Semaglutide is dominant over dulaglutide in most simulations and cost-effective at a threshold of CAN$50,000.
(Johansen et al. 2020), UK	Semaglutide vs. Liraglutide	0.3 (discounted) compared with liraglutide	GBP 140 saved	GBP 279 saved	Reduction in diabetes-related complications	Yes, it is a cost-effective treatment option.
(Kim et al. 2022) , US	Semaglutide vs. no treatment, diet and exercise (D&E), and 3 branded Anti-obesity medications (liraglutide 3 mg, phentermine-topiramate, and naltrexone-bupropion).	QALY gain of 0.138 to 0.925 vs. comparators	Higher costs by US$3,254 to US$25,086 over 30 years	Incremental cost per QALY from US$23,556 to US$144,296	Not specified	Yes
(Pulleyblank and Larsen 2023), Denmark	Oral Semaglutide vs. Empagliflozin, Sitagliptin; Subcutaneous Semaglutide vs. Sitagliptin, Canagliflozin	Higher lifetime QALYs with semaglutide	Higher lifetime treatment costs with semaglutide	DKK 150,618/QALY (€20,189) vs. Empagliflozin; DKK 95,093/QALY (€12,746) vs. Sitagliptin (oral); DKK 79,982/QALY (€10,721) vs. Sitagliptin (subcutaneous); DKK 167,664/QALY (€22,474) vs. Canagliflozin	Lower complication costs with semaglutide	Semaglutide is likely to both increase cost and health benefits within commonly accepted thresholds based on clinical trials.
(Viljoen et al. 2019), UK	Semaglutide 0.5 mg & 1 mg vs. Dulaglutide	0.04 QALYs (0.5 mg) and 0.10 QALYs (1 mg) vs. dulaglutide	GBP 35 saved (0.5 mg); GBP 106 saved (1 mg)	Not specified	Fewer diabetes-related complications due to better glycemic control.	Both doses of once-weekly semaglutide are considered dominant vs dulaglutide.
(Yang et al. 2021), Taiwan	GLP-1 RA vs. Insulin	N/A	US$54,851 (mortality) US$29,115 (hypoglycemia)	US$54,851 (Mortality), US$29,115 (Hypoglycemia)	US$19,391 (Mortality), US$10,293 (Hypoglycemia)	Yes

Appendix 43: Characteristics of the Included Studies for the Component "Direct/ Indirect Cost Savings" for Germany *(Tremmel et al. 2017)*

Author, Publication Year	Objective	Perspective	Cost as Reported (Costing Year)	Direct Costs Included Items	Method	Indirect Costs Included Items
(Effertz et al. 2016), Germany	To estimate annual societal costs.	Third-party payer	Total costs: €63.04 billion; Direct costs: €29.39 billion; Indirect costs: €33.65 billion (-)	Nursing costs, rehabilitation treatments, financial compensations for job integrations, accidents, medication	Prevalence-based, bottom-up approach, retrospective	Sickness absence, nursing care, early retirement pension, pension for widows and orphans, rehabilitation, unemployment, premature mortality.
(Konnopka, Bödemann, and König 2011), Germany	To estimate annual societal costs.	Societal	Total costs: €9.873 million Direct costs: €4.854 million Indirect costs: €5.019 million (2002)	Inpatient and outpatient costs, rehabilitation, administration, and research.	Prevalence-based, top-down approach, retrospective	Loss of productivity due to sickness absence, early retirement, and premature mortality.
(König et al. 2015), Germany	To estimate societal costs.	Societal	Direct per-capita costs: €1244 (2008)	Inpatient and outpatient costs, medication, dental prostheses, professional community nursing home care, and informal care	Population-based, bottom-up approach, retrospective	Not included
(Lehnert et al. 2015), Germany	To estimate annual societal costs.	Societal	Total costs: €12.2 million Direct costs: €6.05 million Indirect costs: €6.19 million (2008)	Inpatient and outpatient costs, rehabilitation, health protection, ambulance, administration, research, investments, and education	Prevalence-based, top-down approach, retrospective	Loss of productivity due to sickness absence, early retirement and premature mortality.
(Wolfenstetter 2012), Germany	To estimate the correlation between changing BMI and future (in)direct costs.	Societal	Total direct costs per user: €1029-(healthy weight), €1093-(overweight) and €1040-(obesity) Future costs in the utilization of general practitioners per user at higher obesity levels (€72; €75; €96)	General practitioner visits, internist visits, overall health care utilization	Cross-sectional, population-representative health surveys (MONICA/KORA S3 survey, KORA F3 survey)	Loss of productivity
(von Lengerke and Krauth 2011), European countries	To estimate direct medical costs.	Healthcare sector	Moderate obesity: €1,080.14; Severe obesity: €2,572.19	Physician visits, receipt and purchase of drugs, inpatient days in hospital	Cross-sectional health survey	Not included

Appendix 44: Survey Questionnaire

Dear Participant,



You are invited to participate in a survey to gather information on **public awareness, perceptions, and motivations** regarding the use of **Ozempic**, particularly as it relates to **weight management**. Ozempic is a **prescription medication** approved primarily for the treatment of type 2 diabetes, but it has recently gained popularity for its **off-label use** in weight management.

Procedures

If you choose to participate, you will be asked a series of questions about your knowledge of Ozempic, reasons for potential use, and views on its role in weight management. The survey will take approximately **5 minutes** to complete.

Voluntary Participation

Your participation in this study is entirely **voluntary** and you can end the survey at any time without any penalty or consequence.

Confidentiality

All data collected in this survey is **anonymous.** No personally identifiable information will be collected, and your responses will be used solely for scientific research purposes. The results of this study may be published, but individual responses will not be disclosed, and data will not be shared with any third parties.

Risks and Benefits

There are **no anticipated risks** associated with your participation in this survey. While you may not receive any direct benefits from participating, your responses will contribute to a better understanding of public perceptions and potential issues related to the off-label use of medications for weight management.

Contact Information

If you have any questions or concerns regarding this survey or your participation, please feel

free to contact the researcher, Greta Westermann, at 60472@novasbe.pt.

Consent

By selecting "I agree to participate," you acknowledge that you have read and understood this information, and you consent to participate in the survey. If you do not wish to participate, you may select "I do not agree to participate," which will end the survey.

Thank you!

- ○ I have read the information given above and agree to participate in the study
- ○ I do not agree to participate, I do not wish to participate

Skip To: End of Survey, If = I do not agree to participate, I do not wish to participate.

Ozempic (Semaglutide) is a **prescription medication** originally developed to help people with type 2 diabetes manage their blood sugar. However, recently, it has gained attention for its **off-label use in weight management** due to its effects on appetite and weight loss.

Q1 How familiar are you with Ozempic?

	1	2	3	4	5	6	7	
Not familiar at all	○	○	○	○	○	○	○	Very familiar

Q2 Do you personally know anyone who is using/ has used Ozempic for purposes other than type 2 diabetes treatment?

- ○ No
- ○ Unsure
- ○ Yes

Q3 Have you ever considered or are you currently considering using Ozempic for weight loss?

- ○ No, I have not considered ->Q6
- ○ Yes, I have considered it/ I am considering it -> Q4
- ○ Not applicable / I do not want to lose weight -> Q6

Q4 What would Ozempic primarily replace in your approach to weight management?

- ○ Traditional dieting
- ○ Regular exercise
- ○ Other weight-loss methods
- ○ I would not replace any specific method
- ○ Do not know/ do not answer

Q5 Would you consider asking or have you already asked a doctor to prescribe Ozempic for weight loss, even though it's approved primarily for diabetes treatment?

- ○ No, I would not ask

- ○ Unsure
- ○ Yes, I have already asked
- ○ Yes, I would consider asking

Q6 How likely would you be to try Ozempic for weight loss if it didn't require a doctor's prescription?

- ○ Very unlikely
- ○ Somewhat unlikely
- ○ Neutral
- ○ Somewhat likely
- ○ Very likely
- ○ Do not know/ do not answer

Q7 What do you believe are the main potential side effects of Ozempic?

- ○ No side effects
- ○ Mild side effects (e.g., nausea)
- ○ Severe side effects (e.g., gastrointestinal issues)
- ○ I am unsure about the potential side effects
- ○ I do not know the potential side effects

Q8 Do you think Ozempic is mainly a medical treatment, or could it also be seen as a quick fix for weight loss?

- ○ Primarily a medical treatment
- ○ Mainly a weight loss tool
- ○ Both equally
- ○ Do not know/ do not answer

Q9 How aware do you think young people are of Ozempic's primary use for diabetes compared to its weight-loss potential?

- ○ Very aware
- ○ Somewhat aware
- ○ Not very aware
- ○ Not aware at all
- ○ Do not know/ do not answer

Misuse is defined as the use of a substance for purposes that are not in accordance with legal or medical guidelines (source: World Health Organization, 2024).

Q10 In your opinion, how high is the risk of misusing Ozempic for weight loss, especially among those who are not diabetic?

	1	2	3	4	5	6	7	
No risk at all	○	○	○	○	○	○	○	Very high risk

Q11 What do you believe contributes to the risk of misuse of Ozempic?

- ○ Social media promotion
- ○ Advice/ influence from friends/ relatives
- ○ Perceived safety
- ○ Perceived effectiveness in rapid weight loss
- ○ Doctors prescribing off-label for weight management
- ○ Desire to lose weight quickly

Q12 Do you believe that using Ozempic for weight loss is a legitimate health strategy, even though it is not approved for this purpose?

- ○ No
- ○ Unsure
- ○ Yes

Q13 What is your age?

- ○ Under 18
- ○ 18-27
- ○ 28-34
- ○ 35-44
- ○ 45-59

○ 60-78

○ 78+

○ Prefer not to say

Q14 What is your gender?

○ Male

○ Female

○ Non-binary / third gender

○ Prefer not to say

Q15 What is your nationality? (Please select country of nationality below, or select "Prefer not to answer" if you prefer not to disclose it.)

▼ Drop-down menu of all countries, including the option 'Prefer not to answer”

Appendix 45: Full SSPS Output File Download Link

https://docs.google.com/document/d/1bZm1rDkS3K2SBLS84-udhcZjSTwyTgIZ/edit?usp=sharing&ouid=103110929574786958615&rtpof=true&sd=true

Declaration of Authorship

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During the preparation of this work project, I utilized Chat GPT 4.0 exclusively as a tool to enhance the readability and refine the language of the text. The generation of ideas, the development of the structure, and the creation of the content were entirely my own. After using this tool for language-related improvements, I carefully reviewed and edited the content to ensure its accuracy and alignment with the intended message. I take full responsibility for the originality, quality, and integrity of the thesis.

Greta Westermann	Lisbon, 16.12.2024 
first and last name	city, date, and signature