



Universiteit Utrecht

Use of GLP-1 receptor agonist as weight reducing agents

Utilizing the COM-B Model and TDF to determine the factors of online purchasing
behaviour of GLP-1 RAs, without medical prescription

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Datum: 29-03-2024

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Abstract

Background: Type 2 Diabetes (T2D) is a chronic health condition affecting hundreds of millions of adults worldwide. Obesity is one of the main risk factors of T2D, underlining the pressing need for effective therapies that treat both conditions. Glucagon Like Peptide Receptor Agonists (GLP-1 RAs) have emerged as promising agents in this regard, showing their potential to improve both glycaemic control and reduce body weight. Mainly the latter has sparked significant interest in GLP-1 RAs, especially on social media. Individuals seeking to bypass regular medical channels, turn to online purchasing, to acquire the medicines without medical prescription. This off-label use has not only been associated with various health and fraudulent risks, but also international shortages.

Aim: This study aimed to explore the factors of the online GLP-1 RA purchasing behaviour, without medical prescription. In this context, the GLP-1 RAs are used as weight reducing agents.

Methods: In this qualitative study, data was obtained from five participants. Five interviews were conducted via the telephone and transcribed. The interview guide was based on domains of the 'Capability, Opportunity, Motivation and Behaviour' (COM-B) Model and the 'Theoretical Domains Framework' (TDF). Thematic analysis was used to code the data, and codes were categorized together to form a specific belief. These specific beliefs were mapped out onto an integrated model of the COM-B and TDF, to eventually establish and explore the underlying determinants of the purchasing behaviour.

Results: Analysis of the interview transcripts revealed multiple dominant specific beliefs, categorized under the COM-B Model domains of Psychological Capability, Reflective Motivation, and Social Opportunity. Notably, participants exhibited a lack of concern regarding potential health and scam risks associated with online purchases. All participants showed optimism regarding the use and purchase of the prescription medicines. Moreover, the awareness of medicine shortages emerged as a potential motivator to resort to online channels for obtaining GLP-1 RAs.

Conclusion: These findings provide a comprehensive understanding of the complex factors driving illegal online purchases of GLP-1 RAs. The identified determinants can serve as a foundation for the development of targeted interventions and communication strategies to address this emerging public health concern.

Samenvatting

Achtergrond: Type 2 Diabetes (T2D) is een chronische aandoening die honderden miljoenen volwassenen wereldwijd treft, waarbij obesitas één van de voornaamste risicofactoren is. Dit benadrukt de dringende behoefte aan effectieve behandelmethoden die beide aandoeningen tegelijk aanpakken. Glucagonachtige Peptide Receptor Agonisten (GLP-1 RAs) lijken op dit gebied veelbelovende middelen, door hun vermogen om zowel glycemische controle te verbeteren als lichaamsgewicht te verminderen. Met name door het laatstgenoemde aspect is er aanzienlijke belangstelling voor GLP-1 RAs ontstaan, vooral op sociale media. Individuen die reguliere medische routes willen omzeilen, maken gebruik van online aankopen om deze medicijnen zonder medisch voorschrift te verkrijgen. Dit off-label gebruik is niet alleen in verband gebracht met verschillende gezondheids- en frauderisico's, maar ook met internationale tekorten van het medicijn.

Doel: Het doel van deze studie was om de factoren te onderzoeken die ten grondslag liggen aan het online aankoopgedrag van GLP-1 RA's, verkregen zonder medisch voorschrift, waarbij deze medicijnen in de context van gewichtsvermindering worden gebruikt.

Methoden: Deze kwalitatieve studie omvatte gegevens van vijf deelnemers, waarbij vijf interviews telefonisch werden afgenomen en vervolgens getranscribeerd. De *interview guide* was gestructureerd op basis van de domeinen van het '*Capability, Opportunity, Motivation and Behaviour*' (COM-B) Model en het '*Theoretical Domains Framework*' (TDF). Thematische analyse werd toegepast om de gegevens te coderen, waarbij codes werden gecategoriseerd om *specific beliefs* te vormen. Deze *specific beliefs* werden vervolgens geïntegreerd in een model van COM-B en TDF om de onderliggende determinanten van het aankoopgedrag verder te onderzoeken.

Resultaten: Analyse van de interviewtranscripten onthulde meerdere dominante specifieke overtuigingen, gecategoriseerd onder de domeinen van het COM-B Model, waaronder *Psychological Capability, Reflective Motivation, en Social Opportunity*. Opmerkelijk was dat deelnemers weinig bezorgdheid toonden over mogelijke gezondheids- en oplichtingsrisico's die geassocieerd zijn met deze online aankopen. Alle deelnemers waren optimistisch over het gebruik en de aankoop van de voorgeschreven medicijnen. Bovendien bleek het bewustzijn van medicijntekorten een mogelijke motiverende rol te spelen om online kanalen te gebruiken voor het verkrijgen van GLP-1 RA's.

Conclusie: Deze bevindingen bieden een diepgaand inzicht in de complexe factoren die illegale online aankopen van GLP-1 RA's stimuleren. De geïdentificeerde determinanten kunnen als basis dienen voor de ontwikkeling van gerichte interventies en communicatiestrategieën om deze opkomende zorg op het gebied van de volksgezondheid aan te pakken.

Preface

Before you lies the master thesis 'Use of GLP-1 receptor agonist as weight reducing agents, utilizing the COM-B Model and TDF to determine the factors of online purchasing behaviour of GLP-1 Receptor Agonists, without medical prescription'. It has been written to fulfil the requirements of the master's program Pharmacy (Farmacie) at the University of Utrecht. I was engaged in researching and writing this thesis from September 2023 to March 2024.

During my master's program, I noticed that besides pharmaceutical, patient focused cases, policy and strategy also interested me. To explore further beyond the pharmacy field, I made the decision to conduct my Research Project at the Healthcare and Youth Inspectorate (Inspectie Gezondheidszorg en Jeugd (IGJ)), part of the Ministry of Health, Welfare and Sport (Volksgezondheid, Welzijn en Sport (VWS)). In agreement with the IGJ, I chose this relevant topic for this research. It's a subject that brings together various disciplines: pharmaceuticals, online illegal purchasing, and behavioural science, all of which deeply interest me. Throughout the process, I gained experience with the Dutch government as a working environment, learned about conducting and analysing qualitative research, and was part of a dynamic team. Therefore, this thesis has taught me valuable lessons both professionally and personally.

I would like to express my heartfelt gratitude to my supervisors at the IGJ, Ron Broere and Hanneke Wanders, for their daily guidance and support throughout the entire process. Whenever I had questions, I could always turn to you both directly. I would also like to thank my referee, Lucy Crane-van Opstal, for her feedback at various points throughout the past months. Furthermore, I want to thank my examiner from Utrecht University, Marcel Bouvy, for the guidance and critical feedback. Finally, I would like to express my gratitude to the entire Advertising Supervision and Intervention (Reclame-toezicht en Interventie) team, and team manager Tom Zwaan, for the pleasant working environment.

Finally, I want to thank my family, partner, friends, and housemates for their continuous support. During tough moments, they always pulled me through. I would also like to thank you, the reader: I hope you enjoy your reading.

Ivy Kan

Utrecht, March 29, 2024

1. Introduction

Type 2 Diabetes (T2D) stands as an escalating global health concern, representing a metabolic disorder characterized by hyperglycaemia resulting from insulin resistance and impaired insulin secretion. This chronic health condition has reached alarming rates worldwide. In the year 2000 the International Diabetes Federation (IDF) released the Diabetes Atlas, which estimated 151 million adults had T2D worldwide. This estimate increased to 537 million adults in 2021, indicating the prevalence had more than tripled (3,56*) over two decades. This number is predicted to increase to 643 million by 2030, and 783 million by 2045 (1). This skyrocketing incidence leads to soaring medical costs, reduced quality of life and increased mortality rates (2).

The cause of T2D is complex and multifactorial. Some risk factors are nonmodifiable, for example age and genetics, and others are modifiable through lifestyle changes, such as following healthy dietary patterns and adequate physical activity levels (3). Overweight and obesity, characterized by high body adiposity, are well-established risk factors for T2D. Sharing genetic and environmental factors in their pathogenesis, obesity amplifies the impact of genetic susceptibility and environmental factors on T2D (4). 20% of patients with obesity have T2D (5) and 89% of patients with diabetes are overweight or obese (6). Therefore, treatments that are beneficial for improving the prognosis of both T2D and obesity or being overweight are preferred.

With the need for effective treatment of T2D while improving body weight management and metabolic health, Glucagon Like Peptide-1 Receptor Agonists (GLP-1 RAs) might predict potential. GLP-1 RAs are a class of medications utilized in the treatment T2D. They offer a treatment option that improves glycaemic control and reduce bodyweight, while having low risk of hypoglycaemia, a common side effect associated with antidiabetic medications. This group of antidiabetics have therefore emerged as attractive options for the treatment of T2D and significant developments continue to be published. Research states that the future of GLP-1 RAs offers broader treatment options for T2D as well as potential in other treatment areas (7).

GLP-1 RAs are agents that mimic the action of a natural incretin hormone called Glucagon Like Peptide-1 (GLP-1), providing the medication with a unique approach of insulinotropic actions, leading to effective improvement of glycaemic control whilst reducing weight. Their effectiveness on the management of obesity is related to the actions of GLP-1. Treatment with GLP-1 RAs has been shown to delay gastric emptying, as well as showing reduced feelings of hunger and to directly increase measures of satiety. These effects can lead to reduced energy intake, thereby facilitating weight loss (8).

Dulaglutide, exenatide, liraglutide, lixisenatide, and semaglutide are GLP-1 RAs approved in the Netherlands for the treatment of T2D. Given their proven clinical efficacy in being associated with weight loss, once-daily subcutaneous administration of liraglutide 3.0mg has been approved by the Food and Drug Administration (FDA) for obesity management since December 2014, under the brand name Saxenda (9). In June 2021 the FDA also approved once-weekly subcutaneous administration of semaglutide 2.4mg for obesity management, under the brand name Wegovy (10). Both treatments are combined with lifestyle interventions, including a reduced-calorie diet and increased levels of physical activity. Although approved since August 2023 by the European Medicines Agency (EMA), Wegovy is

not yet available in the Netherlands (11). GLP-1RAs in the Netherlands are prescription medicines for the treatment of both T2D and overweight or obesity management.

Their emergence as effective, non-invasive treatment of obesity without the diagnosis of diabetes, lead to GLP-1RAs arousing great interest (12). On social media various celebrities have promoted their effects and benefits, contributing to a boost in their popularity. The increase in demand is associated with higher levels of non-prescribed GLP-1 RA intake. As a result, the increasing popularity has been associated with problems related to availability throughout traditional prescription channels (13)(14).

Consumers can easily purchase GLP-1 RAs through various online channels, making medical prescription unnecessary. Providing and selling prescription drugs without a doctor's prescription is prohibited in the Netherlands, but many illegal online sources offer various classes of drugs, including ADHD-medication, sleeping pills, drugs for erectile dysfunction, painkillers (including opioids), and weight loss agents (15). This illegal online availability of prescription medicines undermines the conventional prescription process and poses risks for users and problems for pharmaceutical companies.

Consequently, the shortage has been associated with health problems of T2D patients, who are experiencing insufficient access to their medication resulting in poor glycaemic control. Glycaemic control is the primary therapeutic goal for prevention of organ damage and poor control is a crucial determinant of diabetes-related mortality (16).

Health risks are not only seen with T2D patients experiencing problems with availability, but also by those who use non-prescribed GLP-1RAs. Whilst the welcome of GLP-1 RAs as weight loss agents was enthusiastic, there have also been criticisms and concerns (17)(18). Adverse effects still show inconsistency in research, especially regarding long-term effects. Not being monitored and followed up by a medical professional make those who use non-prescribed GLP-1 RAs more vulnerable to damaging long-term side effects. In addition, the online channels providing the prescription drugs can be sources that violate regulations by selling counterfeit, adulterated or unapproved drugs. Misbranded or unapproved prescription drugs have unknown origin, safety, and effectiveness, leading to serious health hazards for users (19).

In the Netherlands the Health and Youth Inspectorate (Inspectie Gezondheidszorg en Jeugd (IGJ)), resorting under the Dutch Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport (VWS)) is responsible for evaluating and promoting good and safe healthcare (20). The department Pharmaceutical Products (Farmaceutische Producten (FP)) oversees the entire chain of drug development, including the proper use of medicines. This includes illegal trade and supply of (prescription) pharmaceuticals. The IGJ supervision concerns both manufacturers, wholesalers, pharmacies and individuals (21). Considering the increasing demand of GLP-1 RAs and therefore also the growing illegal availability online, optimized communication on this matter is necessary.

Utilizing the 'Capability, Opportunity, Motivation and Behaviour' (COM-B) Model for Behaviour Change and 'Theoretical Domain Framework' (TDF) the influencing factors of illegally online purchasing GLP-1 RAs, without medical prescription, are explored. In this context, the GLP-1 RAs are used as weight reducing agents. As such, the following research question will be addressed:

'Utilizing the COM-B Model and TDF, what are the facilitators and barriers of illegally purchasing GLP-1 RAs online, without medical prescription?'

This study aims to gain a deeper understanding of the purchasing behaviour, by identifying the determinants of this behaviour.

2. Contextual background

The following chapter elaborates on the contextual background of this study. It provides an overview of the current situation regarding off-label use of GLP-1 receptor agonists (GLP-1 RAs) as slimming weight agents, and the challenges involved. First, the therapeutic effects of GLP-1 RAs will be discussed. This includes the proposed mechanisms behind the found weight-loss effects and potential long and short-term effects. Second, the contextual background will explore the risks of illegally online purchasing pharmaceutical products, followed by specification of the risks of purchasing GLP-1 RAs online.

2.1 GLP-1 receptor agonists

2.1.1 Therapeutic effects

Glucagon-like peptide 1 (GLP-1) is a hormone belonging to the family of the incretin hormones, produced by intestinal L cells. This family of hormones are gut peptides that are secreted after nutrient intake and stimulate insulin secretion from the beta cells of the pancreas. GLP-1 is one of the most potent incretins stimulating insulin secretion, and as a result of the increased insulin secretion, the glucose concentrations drop (22). These actions of GLP-1 receptor stimulation is one of the three main mechanisms leading to reductions in plasma glucose concentrations. The second mechanism is suppression of glucagon hypersecretion, except during episodes of hypoglycaemia (23). Increased glucagon leads to greater glucose concentration, thus by inhibiting hypersecretion glucose levels decrease. Lastly, the third mechanism includes delaying of gastric emptying. This deceleration was found with less post-meal glycaemic fluctuations (24).

Because of the potential GLP-1 RAs showed in the treatment of T2D, development of GLP-1 RAs resistant to proteolytic inactivation and with slower elimination, rapidly followed. Since the approval of exenatide in the EU in 2006, five more products of the GLP-1 RAs have been approved. The following five active substances are available at this time in the Netherlands: dulaglutide, exenatide, liraglutide, lixisenatide and semaglutide (25)(26).

T2D patients

For patients with T2D the incretin system has become an important target in recent years. This may be the result of the found difference in the incretin effect in patients with T2D compared to healthy individuals. The term 'incretin effect' refers to the finding that there is a greater incretin secretion as a result of oral glucose intake than intravenous glucose administration (27). This effect is a typical finding in healthy individuals. In contrast, patients with T2D have shown a substantially reduced, or in some patients even absent incretin effect (27)(28)(29). This leads to decreased insulin release, and as a result increased blood glucose concentration. The therapeutic potential and added value of GLP-1 RAs for patients with T2D is supported by the pathophysiological finding described above, as the GLP-1 RAs mimics the GLP-1s.

When a medicine like GLP-1 RAs is unavailable, T2D patients are forced to switch to another group of antidiabetics. Switching between the antidiabetics group is not favourable when a T2D patient is well adjusted to the antidiabetic treatment. The optimal management of T2D involves careful selection and titration of antidiabetic medication to achieve glycaemic control. Inadequate treatment puts the patients at increased risk of mostly microvascular complications, which are mainly due to complex and interconnected mechanisms such as insulin-resistance, inflammation, accelerated atherogenesis. The microvascular complications include diabetic nephropathy, retinopathy, and neuropathy with great impact

on the quality of life and overall life expectancy (30). Research has shown that adequate glycaemic control is essential and good adherence of the appropriate antidiabetic treatment is associated with a lower risk of all-cause mortality and hospitalization in patients with T2D (31).

2.1.2 Effects on body weight

Various meta-analyses show that GLP-1RAs have significant influence on body weight, in varying degrees between the GLP-1RAs. Both in patients with T2D, and in overweight or obese persons without diabetes a reduction in body weight was found (32)(33)(34). This makes GLP-1RAs unique in promoting weight loss while reducing glycemia level. Other glucose-lowering agents usually lead to weight gain or do not have effect on weight, except for sodium/glucose cotransporter (SGLT-2) inhibitors (35). This finding is relevant in adequate treatment of T2D because of its common comorbidity obesity. Up to 85,2% of patients with T2D are overweight or obese (36). A body mass index, BMI 25-30 kg/m² classifies to body phenotypic overweight, which can develop into the weight disorder obesity, defined as BMI ≥ 30 kg/m² (37). Weight-loss has shown clinically meaningful implications in the treatment of T2D. Patients with T2D who have lost 5-10% of their bodyweight, not only showed improved glycaemic control, but also showed improved cardiovascular outcomes associated with positive influences on risk factors, including hypertension and dyslipidaemia (38). Other research has shown that patients with T2D who lose weight are more likely to avoid the burden of morbidity and early mortality associated with the diagnoses of diabetes (39).

The found effects of GLP-1RAs on body weight have led to the exploration of the medicines as a novel pharmacological treatment in overweight or obese persons, without the diagnoses of diabetes. It has been proven that finding successful obesity prevention and treatment strategies on the long term is a difficult task (40). Different clinical trials have shown effectiveness and safety in the use of GLP-1 RAs in treating or preventing obesity in different subjects, with and without T2D (41). The mechanisms of weight loss of these medicines in obese persons are not completely understood yet. But research shows that administrating GLP-1RAs decreases appetite, increases satiety, and, as a consequence, reduce food intake. This has been well researched in obese persons (42)(43)(43). Some research also supports this finding in non-obese, healthy persons (44), but the results are inconsistent, as will be discussed in the next section. Earlier is mentioned that the incretin effect in patients with T2D is diminished or completely absent, making GLP-1 RAs an effective theory-based treatment for the diagnosis T2D. Some researchers did a similar observation of an impaired incretin effect in obese persons without T2D (45)(46), although other researchers have found otherwise (47)(48).

Not all the studies confirmed the influence of incretin hormones on weight loss. In one study, the authors suggested that treatment with GLP-1 RAs have influence on weight loss in the starting period, but not on weight loss maintenance (49). In another study administration of GLP-1 RAs in obese persons was not associated with satiety after 16 weeks of treatment (50). This result was also found in non-obese men, who were administered GLP-1 centrally (51). In conclusion, it stays unclear which individual, with what health condition, will benefit from the treatment with GLP-1 RAs.

Weight regain

Multiple studies have shown that after discontinuation of the GLP-1 RAs, the subjects go through weight regain. A clinical trial found that one year after withdrawal of once-weekly

subcutaneous semaglutide 2.4 mg in combination with lifestyle intervention, participants regained two-thirds of their prior weight loss (52). The study therefore suggested long-term treatment for weight loss maintenance. This is supported by findings of a randomized controlled trial (53), and a study done with liraglutide also affirmed this (54). The three mentioned studies included overweight (BMI >27 kg/m) or obese (BMI >30 kg/m) individuals and excluded diabetes patients.

The findings supporting weight loss, although not maintained, make GLP-1 RAs appear to be an argumentative, potential treatment for obese or overweight individuals, even without the diagnosis of T2D. However, there is a need for further research into whom exactly will benefit of the treatment of GLP-1 RAs for weight loss, as the weight loss results and the mechanisms behind this are found inconsistent. It should also be taken into consideration that the adequate treatment of overweight or obese persons with GLP-1 RAs, probably is a chronic and long-term treatment, to prevent regaining weight.

2.1.3 Adverse effects

The findings supporting successful weight loss, especially in the introduction period, have led to growing popularity for treatment with GLP-1RAs for overweight or obese individuals. However short- and long-term safety should be taken into consideration before starting treatment. Research into short-term adverse effects will first be discussed, followed by research into long-term effects.

Short-term adverse effects

GLP-1 RAs are available in the Netherlands since 2006. The use of this relatively new class of drugs leads to caution about adverse effects. In clinical trials the most frequently reported side effects associated with the use of GLP-1 RAs are gastrointestinal symptoms (55). Among these symptoms, nausea and diarrhoea were very common ($\geq 1/10$). Relatively common ($\geq 1/100$ to $< 1/10$) were vomiting, constipation, abdominal pain, and dyspepsia (56). The frequency of these adverse events was higher in the beginning of the treatment with GLP-1 RAs, but the gastrointestinal symptoms gradually decreased as therapy continued. Nausea was reported the most out of all gastrointestinal symptoms, leading 4% of the participants to discontinue in clinical trial. The nausea seems to be dose-dependent and decreases with ongoing treatment (57)(58). Researchers have formulated a hypothesis that the delay in gastric emptying is linked to the nausea (56). However, this has not been researched yet.

Another adverse event mentioned in clinical trials is headache, but it usually did not lead to discontinuations in clinical trials. Injection site reactions also mainly did not lead to discontinuations, although they were found to be a common side effect. The most reported injection site reactions included rash, erythema or itching at the injection site (56). Lastly GLP-1 RAs trials have reported upper respiratory and urinary tract infections. Nasopharyngitis, influenza, cystitis, and also viral infections were commonly reported (56). Up to now, no cause-effect relation is found.

Long-term adverse effects

There have been concerns expressed regarding GLP-1 RAs and multiple possible long-term effects. Research on these long-term adverse events will now be discussed.

Thyroid disorders

The association between GLP-1 RAs and the occurrence of various kinds of thyroid disorders is a controversial topic. Concerns have been expressed regarding a possible link between treatment with GLP-1 RAs and medullary thyroid cancer (59). Liraglutide and exenatide have been associated with the development of thyroid C-Cell tumours, when given in above therapeutic doses (60). However, these studies are mainly based on rodents.

A meta-analysis of 25 studies done in 2012 (61) showed no significant association between GLP-1 RAs and an increased risk of thyroid cancer. There were no thyroid malignancies reported with exenatide. More recently, in 2022, a meta-analysis of 45 studies done by Hu et al. (62) also showed no increased risk of six types of thyroid disorders (thyroid cancer, hyperthyroidism, hypothyroidism, thyroiditis, thyroid mass and goiter) related to the use of GLP-1 RAs. However, they did conclude that the incidence of these diseases was low, and that the findings need to be examined further.

Retinopathy

Concerns have been expressed about the potential worsening of diabetic retinopathy caused by GLP-1 RAs. Diabetic retinopathy is a microvascular complication of diabetes. It is a common complication of diabetes and the number of patients diagnosed with diabetic retinopathy continues growing (63).

Results of studies on the long-term impact on retinopathy are inconsistent. A cohort study done by Zheng et al. (64) showed a significantly lower risk of diabetic retinopathy for patients treated with GLP-1 RAs, concluding that GLP-1 RAs have a protective effect. However, some clinical trials have suggested an increased risk of diabetes retinopathy with GLP-1 RAs treatment (65). The increased risk of retinopathy may be attributed to rapid glycaemic control (66).

A systematic review and meta-analysis done by Yoshida et al. (67) included 13 randomized clinical trials examining the effect of GLP-1 RA treatment on adverse events including diabetic retinopathy and diabetic retinopathy complications. They found that the use of GLP-1 RAs may be associated with an increased risk of progression of diabetic retinopathy. The GLP-1 RAs found with this association were liraglutide, semaglutide and dulaglutide. Another meta-analysis of randomized clinical trials (68) also showed a significant association between GLP-1 RAs use and increased risk of early-stage diabetes retinopathy, and early-stage retinal adverse events compared to placebo. Surprisingly, they also found that GLP-1 RAs protected against late-stage diabetes retinopathy, in comparison with treatment with insulin. Both the increased and decreased risk on retinopathy were attributable to albiglutide. Albiglutide was already discontinued in 2017. Not including albiglutide, the researchers found the other GLP-1 RAs not to be significantly associated with increased risk.

As has become clear, results of clinical trials and meta-analyses are inconsistent, pointing out the need for further data from large-scale, long-term, well-designed clinical studies. In these studies, diabetic retinopathy and retinal adverse events should be the primary outcomes and potential confounding factors should be taken into consideration.

Gallbladder disorders

The risk of the development cholelithiasis with the use of GLP-1 RAs have been detected through a meta-analysis of the results of different randomized clinical trials (69). All the trials

included T2D patients as participants. Whether increased risk of gallbladder disorders is associated with a class effect of GLP-1 RAs has not been established (70).

A meta-analysis of 43 randomized controlled trials done by Nreu et al. (71) confirms the association of an increased risk of cholelithiasis with the use of GLP-1 RAs. Another systematic review and meta-analysis done by He et al. (72) investigated the associations of GLP-1RAs use with the risk for gallbladder or biliary diseases. 76 clinical trials were included in the meta-analysis. Results showed an association of an increased risk of the composite outcome of gallbladder or biliary diseases and for cholelithiasis, cholecystitis, and biliary diseases. They also found that the risk was higher in trials with GLP-1 RAs for weight reduction, than in trials of patients treated for T2D. Higher doses and longer duration of GLP-1 RAs were also associated with increased risk of gallbladder or biliary diseases, but this association was not found statistically significant. This is relevant because the dose used to treat obese or overweight patients is higher than the dose used to treat T2D patients, and as discussed earlier, for optimal weight reduction chronic treatment of GLP-1 RAs may be considered.

Pancreatitis and pancreatic cancer

Some animal studies have shown that exenatide administration increases inflammation of pancreatic cells (73) and leads to the formation of pancreatic intraepithelial neoplasia (74). Similarly, liraglutide was associated with an increased risk of pancreatitis in mice (75). These observations pointed to a potential harmful effect of GLP-1 RAs on pancreatic tissue. Some observational studies among human patients confirmed this association, reporting an increased risk of pancreatitis linked to the use of GLP-1 RAs (76) (77), which raised concerns about the safety.

In contrast to the above results, several meta-analyses have found no association between pancreatitis and the use of GLP-1 RAs. Li et al. (78) designed a systematic review and meta-analysis and included 55 randomised controlled trials. They found that the incidence of pancreatitis among patients using incretins is low, and that use of GLP-1 RAs did not lead to an increased risk of pancreatitis. This finding was confirmed in another meta-analysis done by Monami et al. (79), which included 113 randomized controlled trials. An updated meta-analysis done in 2020 by Nreu et al. (80) included 43 randomized controlled trials. The endpoints of these study were pancreatitis and pancreatic cancer reported as serious adverse events. No evidence of risk for pancreatitis was observed, whereas data on pancreatic cancer were too scarce to draw a conclusion. Lastly, another systematic review and meta-analysis of 12 randomized controlled trials (81) found no association of GLP-1RAs and pancreatic cancer. The researchers did mention that further research is needed, including studies with longer duration. The mean follow-up of the included trials in this study was fairly short (1.7 years).

Generally, there is no direct cause and effect relationship found between the use of GLP-1 RAs and pancreatitis. Larger research with longer follow-up is needed to draw a conclusion regarding the link between the use of GLP-1 RAs and pancreatic cancer. Moreover, T2D and hypertriglyceridemia are independent risk factors for acute pancreatitis (82). It may be expedient to be cautious of the use of GLP-1 RAs in patients with several risk factors for pancreatitis, for example heavy alcohol consumption or hypertriglyceridemia.

Cardiovascular system

As opposed to the potential harmful long-term effects associated with GLP-1 RAs, the class

of antidiabetics have also been associated with cardioprotective effects. A meta-analysis done by Kristensen et al. (83) in 2019 included a total of 56,004 participants including placebo-controlled trials reporting major adverse cardiovascular events (MACE; a composite of cardiovascular death, stroke, or myocardial infarction). They found an overall reduction of 12% of MACE in the seven included trials, reflecting a beneficial effect on death from cardiovascular causes (relative risk reduction 12%) and a reduction in the risk of stroke (16% relative risk reduction for fatal or non-fatal stroke). The reduction in myocardial infarction (9% relative risk reduction for fatal or non-fatal myocardial infarction) was less robust, although was directionally concordant. They concluded that the GLP-1 RAs are clearly cardioprotective medicines, and they suggested, by the time course of their effects and the types of cardiovascular events prevented, that the GLP-1 RAs mainly have an anti-atherothrombotic effect, but the precise mechanism remains unclear. An updated meta-analysis confirms the found benefits of GLP-1 RAs on cardiovascular outcomes (84).

In conclusion, it is imperative to take the short- and long-term effects of GLP-1 RAs seriously, especially given the limited understanding of their long-term consequences. It's important to note that research on the effects of GLP-1 RAs has primarily been conducted with patients diagnosed with T2D. However, the treatment of overweight and obese individuals involves higher doses of these medications, and therefore the short- and long-term effects may not be directly generalizable to healthy individuals using GLP-1 RAs solely for weight loss purposes. Additionally, professor obesity and stress, Liesbeth van Rossum states the risks may be justifiable for patients with severe obesity or T2D, because it outweighs the conditions the patients already have or could develop. However, this may not be the case for healthy individuals who only use the GLP-1 RAs to lose weight, as the benefits do not outweigh the disadvantages (85).

2.2 The illegal purchase of prescription pharmaceuticals online

In the next subchapter the risks of illegally buying pharmaceutical products will be discussed, followed by specification of the risks of purchasing GLP-1RAs online. This latter section will concern risks other than the already discussed potentially harmful short- and long-term effects.

In this chapter, and research overall, illegal online purchase of pharmaceuticals will be defined as pharmaceutical products sold by websites or other social platforms that violate regulations by selling counterfeit, adulterated or unapproved drugs or dispensing prescription drugs without a valid description. These websites and social platforms do not meet national or international pharmacy regulations, nor have they been subjected to the requisite regulatory review/licensure and/or certification. These providers are not licensed with the national competent authorities in the EU Member States (86) which is required to be a licensed online pharmacy. Several studies have shown evidence of the availability of different types of prescription medicines without the need for prescriptions, presenting substandard, illegal, unapproved, or counterfeit drugs (87)(88).

The Dutch customs authorities have observed a growing trend in inspecting postal shipments containing medicines or substances with medical claims. Many of these items are purchased online and shipped to individuals' homes by postal carriers, including unapproved medicines. In collaboration with the Dutch customs, the IGJ discovered various prescription medicines, including GLP-1 RAs, during a national action. This is depicted in the next image, see figure 1.



Figure 1. Found pharmaceuticals during an international action by the IGJ and the Dutch customs. Including GLP-1 RA liraglutide under the brandname Victoza. Source: IGJ, FP.

2.2.1 Consumers health safety associated with general online purchasing, without medical prescription

The proliferation of online platforms has facilitated the ease with which individuals can purchase pharmaceuticals without a valid prescription. Although the Internet offers numerous opportunities to improve health, it can also lead to enormous health hazards since it represents an unregulated market with almost no consumer protection (87). The various ways the purchasers' health can be influenced by these pharmaceutical products will now be discussed.

Product authenticity

One of the primary risks associated with illegal, online purchases of pharmaceuticals is the uncertainty surrounding the authenticity of the products. Unlike regulated medications, these pharmaceutical products are not subjected to testing, raising concerns about their quality and safety. Prescription drugs obtained from unauthorized sources may be misbranded or unapproved, with unknown origins and questionable safety and effectiveness. These unapproved drugs can pose various risks, including being counterfeit, containing incorrect amounts of active ingredients, being contaminated with toxic chemicals, or containing dangerous or illegal substances (19). All of these factors contribute to potential health hazards for consumers.

A counterfeit semaglutide pen, under the brandname Ozempic, was discovered in October 2023. An image to depict this is included, see figure 2:

Original:



Fälschung:



Abbildungen von Original und Fälschung des Arzneimittels Ozempic®

Figure 2. An original Ozempic pen compared to counterfeit Ozempic pen. Source: lunch presentation; 'Illegale handel in geneesmiddelen raakt ons toezicht' Jan 23, 2024, IGJ.

Absence of a practitioner

The illegal online offered pharmaceuticals do not require warnings about associated health risks, adequate directions for safe use, and as earlier stated, requirement of valid

prescriptions (87). No need for a valid prescription leads to absence of monitoring and supervision of a practitioner. This can also be harmful for the consumers health through various mechanisms (89). As discussed previously, GLP-1 RAs can lead to adverse effects both on the short and long term. This highlights the importance of close monitoring by healthcare professionals after prescription. Regular follow-up appointments are necessary to ensure proper treatment and to address any emerging health related issues, which are not always recognized by patients as adverse effects of the medication. Additionally, healthcare practitioners are trained to consider patients' comorbidities and potential drug interactions to provide optimal treatment, a critical aspect that is missing when prescription medicines are obtained without proper oversight. Furthermore, some prescription medicines have a narrow therapeutic index, meaning that the therapeutic dose is close to the toxic dose, significantly increasing the risk of serious adverse effects.

2.2.2 Consumers personal economic consequences

A rather self-evident danger of purchasing prescription medicines online, of an unlicensed site, is the risk of consumer fraud. As earlier stated, the quality of the medicines cannot be guaranteed, nor can the arrival of the medicines to the consumer, resulting in consumer fraud and scam (90). Furthermore, consumers may suffer invasion of their privacy, potentially personal medical information. Lack of confidentiality of personal data can even lead to misuse or sale of personal information.

2.2.3 Unauthorized access to prescription drugs

Unrestricted access to prescription drugs through the availability of purchasing online legitimizes unacceptable health practices (91). When there is no longer the need for a prescription, the practitioner is left out of context, which undermines the regular prescription process. This challenges existing regulatory frameworks, and therefore it also challenges public health authorities.

Online acquisition of prescription medicines may also encourage self-diagnosis and treatment, as individuals may attempt to address health concerns without medical guidance (92).

2.2.4 Social, economic threats

The uncontrolled proliferation of the illegal sales of prescription drugs may even have a national effect, by economic loss to the healthcare system. This may be the result of utilizing ineffective treatments, adverse events, and needed remedial care (93).

2.2.5 Consumers health safety associated purchasing GLP-1 RAs online without medical prescription

Apart from the short- and long-term effects of GLP-1RAs, which have been discussed in the previous chapter, various other risks have been identified that can be traced back specifically to misusing GLP-1 RAs as weight loss agents. These risks will now be addressed.

Dose

Because only liraglutide and semaglutide from the GLP-1 RAs are registered for weight loss, only these two agents will be the subjects in this subchapter. These agents also receive the most attention in the media (94).

To receive treatment to lose weight with GLP-1 RAs, an individual should be diagnosed with obesity, which entails a Body Mass Index (BMI) of 30kg/m^2 or higher, or the diagnosis of overweight, meaning a BMI in between 27 up to 30kg/m^2 in combination with a weight related

comorbidity (including T2D, prediabetes, hypertension, dyslipidaemia, or obstructive sleep apnoea). The treatment with GLP-1 RAs is always in addition to lifestyle changes, including diet and physical exercise (95).

As stated earlier, liraglutide has been registered for longer time for the treatment of the diagnosis obesity and overweight, apart from the treatment of T2D. Semaglutide has only been registered recently for the treatment of obesity and overweight, since August 2023. The registered doses of these medicines to lose weight is higher than the registered doses for the treatment of T2D. For liraglutide used for T2D the dose lies between 1.2mg and 1.8mg subcutaneous once daily (Victoza) and the approved maintenance dose for obesity is 3.0mg (Saxenda). A higher dose is also seen with semaglutide. For the treatment of T2D the max dose of semaglutide administered subcutaneously (Ozempic) is 2mg weekly. For the treatment of obesity or overweight the maintenance (and maximum) dose is 2.4mg weekly (Wegovy).

The in this research included clinical trials reporting short- and long-term effects often include patients with T2D, who receive the lower dose of the GLP-1 RAs. The effects found may therefore not be directly extrapolated to another group, the individuals without T2D.

Administration

Semaglutide and liraglutide in the treatment of obesity are administered subcutaneously. Subcutaneous administration can be convenient, providing slow and steady drug release, due to the absorption process from the injection site (96). This delayed response leads to reduced frequency of administration. Furthermore, subcutaneous administration requires no medical personnel, in contrast to intravenous and intramuscular administrations, the injections are less painful, the risk of infection is lower in subcutaneous than intravenous injections, and, if this occurs the infection is generally limited to a local infection rather than a systematic infection (97).

However, subcutaneous administration is also associated with various risks, mainly injection site reactions, including pain. Besides a direct effect of the drug itself, several factors may be associated with the sensation of pain after subcutaneous injections including injection technique and site, volume injected and injection speed. A meta-analysis showed that injection site reactions, such as rash, erythema, or itching at the injection site, are common with GLP-1 RAs, but that these adverse effects usually did not lead to discontinuation in the included trials (56). However, as with any injection procedure, properly administering the drug is essential to ensure the drug's effectiveness and minimise the risk of complications. Safe administering and recognizing potential injection site reactions cannot be guaranteed when the medicines are illegally purchased online, without medical prescription and guidance.

3. Theoretical background

In this chapter, two theories are explored through available academic literature, forming the foundation for the methodology and data analysis of the study, thereby contributing to the essential theoretical understanding of this research. First, the 'Capability, Opportunity, Motivation, and Behaviour' (COM-B) Model for Behaviour Change is examined. This model is acknowledged as a component of the 'Behaviour Change Wheel' (BCW). Subsequently, the Theoretical Domain Framework (TDF) is discussed, followed by an overarching model that integrates the COM-B model and the TDF.

Relevance of using behavioural models

The supply of chain of prescription medicines available online is complex and hard to track, which makes it impossible to keep the Internet free of illegal websites selling medicines (90). One possible solution could come from focusing on the potential purchasers themselves, as they are the ones who ultimately make the decision to purchase.

Utilizing behavioural sciences has the potential to improve health-related interventions, as evidenced by numerous studies demonstrating the effectiveness of behaviour change interventions in promoting health-related behaviour (98)(99)(100). However, it is noted that many behaviour change interventions lack theoretical grounding or fail to adequately operationalize the behaviour change principles (101). According to Glanz and Bishop (102), this could potentially hinder the effectiveness. Despite ongoing uncertainties regarding the superior effectiveness of theory-based interventions to achieve behaviour change (103), there is international consensus on the relevance and value of using evidence-based knowledge from behavioural sciences to inform public health programs and policies (104). According to the knowledge-to-action framework, key steps in designing knowledge translation strategies include conducting research on factors associated with knowledge uptake, such as facilitators and barriers (105), which constitutes the main subject of this research. Once these factors are identified, an essential aspect involves developing mechanisms to adapt evidence-based knowledge to the context of the target audience (105). One theory-based framework commonly used for behaviour change is the COM-B model, which serves to contextualize individual-level change and uncover the underlying determinants of the target behaviour. The TDF builds on the constructs identified by the COM-B model, to further uncover facilitators and barriers of evidence-based change.

3.1 Capability, Opportunity, and Motivation (COM-B) Model

The COM-B Model is a theoretical framework that proposes there are three key components underlying any behaviour: Capability, Opportunity, and Motivation. The comprehensive model guides in understanding the behaviour of interest and identifies specific targets within this behaviour that serve as the foundation for intervention strategies. Situated at the core of the Behaviour Change Wheel (BCW), the COM-B Model often serves as the starting point of intervention development (106).

Each of the three core components of the COM-B Model can be further subdivided into two components. Capability encompasses both psychological and physical capability to perform the behaviour of interest. Opportunity includes both physical and social environmental factors that either facilitate or hinder the behaviour. Lastly, motivation is divided in automatic and reflective processes, which pertain to how the brain processes information to either facilitate or inhibit the target behaviour. These three main categories and their corresponding six subcategories are organized and illustrated in Figure 3.



Figure 1. The components of the COM-B Model.

Elaborating on the (sub)categories of the COM-B Model, capability comprises the knowledge, skills, and abilities required to engage in the target activity. Psychological capability encompasses aspects such as knowledge, memory, attention, and behavioural regulation, while physical capability pertains physical strength and abilities or proficiencies acquired through practice.

The second core component, opportunity, refers to the factors that enable the behaviour. Physical opportunity encompasses the environmental context and available resources, while social opportunity includes social influences, such as social pressure, norms, and conformity.

Lastly, motivation, the third core component, consists of automatic and reflective aspects. Motivation refers to all brain processes that energize and direct behaviour. Automatic motivation includes emotions, incentives, and reinforcement mechanisms such as rewards, whereas reflective motivation comprises beliefs about capabilities and consequences, intentions, goals, and optimism (107).

The three main categories of the COM-B Model interact with each other to facilitate behaviour. As depicted in Figure 4, Capability and Opportunity exert influence on motivation. It's important to note that not only do all three components influence behaviour, but they are also influenced by changes that occur.

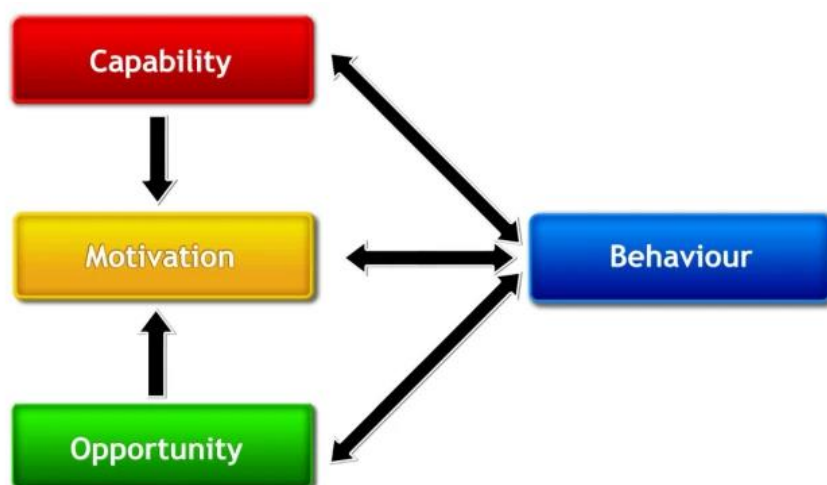


Figure 2. Interactions of the COM-B Model leading to behaviour. Source: <https://implementationscience.biomedcentral.com/articles/10.1186/1748-5908-6-42/figures/1>

The COM-B Model is commonly used at an early stage to investigate the facilitators and barriers of the target behaviour, which can serve as the groundwork for designing behaviour change intervention strategies (107). A given intervention might change one or more (sub)categories in the COM-B model, and the causal links within the system can either stimulate or reduce the effect of the intervention. When applying the model during intervention design, it is crucial to consider the behavioural target and which categories of the COM-B Model should be focal points to achieve behavioural change effectively. Therefore, the target behaviour should not be the desired behaviour but rather the behaviour that demonstrates change after an effective intervention. The COM-B Model was designed to be accessible to individuals from any discipline (108). This accessibility is one of the reasons why this behavioural change model is utilized in this research.

As previously noted, interventions aimed at behaviour change are often designed without analysis of either the behaviour itself or the theoretically predicted mechanisms of action. Instead, they tend to rely on common-sense and rational models of behaviour (109). To provide theoretical underpinning, the COM-B Model is the behavioural theory selected in this research. While multiple theories exist to explain health behaviours, such as the Health Belief Model (110), the Social Cognitive Theory (111), and the Theory of Reasoned Action (112), most of these theories are insufficient to comprehensively explain all the possible influences on behaviour (113). Recognizing this limitation and the lack of overlapping constructs among these theories, there have been calls for an integrated theoretical framework. To address this challenge, Robert et al. developed the COM-B Model as part of the Behaviour Change Wheel (BCW) (107), illustrated in Figure 5. The primary advantage of the BCW is its provision of clear guidance in developing, delivering, and evaluating interventions targeting health behaviours. The BCW consists of three layers, with the (sub)categories of the COM-B Model situated at the centre.

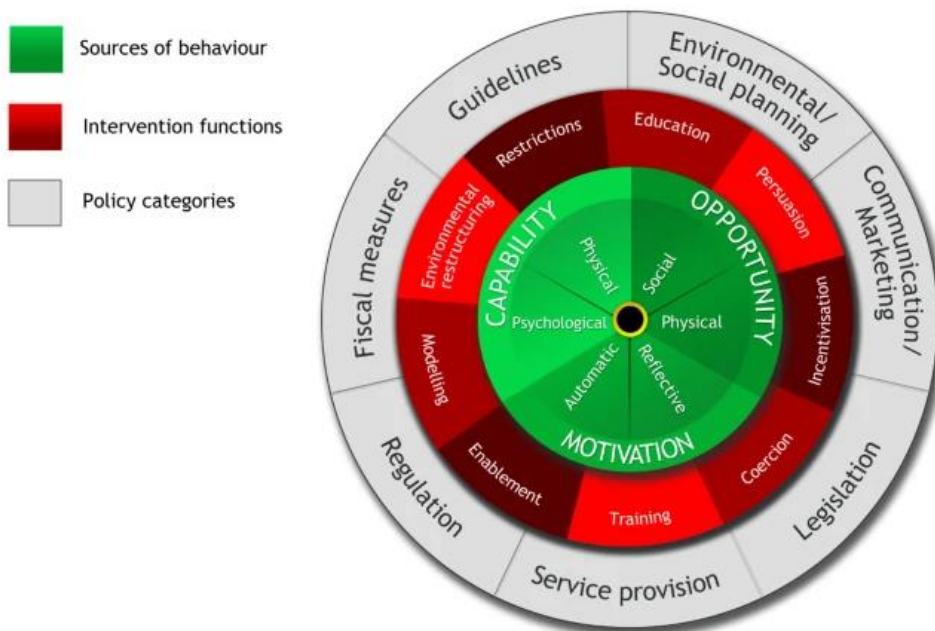


Figure 3. The BCW, and the COM-B Model centered in the wheel. Source: <https://implementationscience.biomedcentral.com/articles/10.1186/1748-5908-6-42>

Positioned around the COM-B Model are nine intervention functions aimed at addressing the (sub)categories established through the use of the COM-B Model. Additionally, seven categories of policy are identified to enable these interventions (114). Examples of successful utilisation of the BCW include interventions within the English Department of Health’s 2010 tobacco control strategy (115) and the National Institute of Health and Clinical Excellence’s guidance on reducing obesity (116).

Although this research does not involve finding an appropriate intervention strategy to inhibit the purchase of GLP-1 RAs online, it focuses on providing factors of the target behaviour. While the choice of intervention strategies will not be addressed in this research, the decision was made to use the COM-B model as part of the BCW as the theoretical foundation of this research, and therefore the findings of this research can potentially serve as starting points in future research.

3.2 Theoretical Domains Framework (TDF)

The Theoretical Domains Framework (TDF) builds upon the three constructs identified by the COM-B model to further elucidate the determinants of evidence-based change. Developed by 18 psychological theorists in collaboration with 16 health service researchers and 30 health psychologists, the TDF was created to enhance healthcare researchers’ access to psychological theory (117)(118). Synthesizing insights from 33 behavioural theories and 128 key theoretical constructs related to behaviour change, the framework aims to assess implementation and other behavioural issues and inform intervention design. As a result, it comprises 14 domains that encompass overlapping constructs within behavioural theories. In this research TDF serves as a conceptual lens for identifying specific determinants on purchasing GLP-1 RAs online by expanding upon the systems identified in the COM-B Model. The domains and definitions of the TDF that are utilized in this research can be found in Table 1. The definitions have been sourced from Almomani et al. (119) and supplemented with data from Phillips et al. (120) where necessary. The original sources are data extracted from Cane et al. (118) and Michie et al. (117).

Table 1. Theoretical Domains of the TDF and their definitions

Theoretical Domains	Definition
1. Skills	Cognitive or physical abilities acquired via practice
2. Memory, Attention, and Decision Processes	The ability to retain information, focus selectively on aspects of the environment, and choose between two or more alternatives
3. Knowledge	The knowledge of the existence of something, the risks associated with it, and the procedural knowledge
4. Behavioural Regulation	Anything aimed at managing or controlling specific actions (e.g., facilitators and barriers)
5. Beliefs about Capabilities	Acceptance of the truth, reality or validity about an ability, talent, or facility that a person can put to constructive use
6. Optimism	The confidence that things will happen for the best or that desired goals will be attained
7. Beliefs about consequences	Positive or negative outcomes of a specific behaviour
8. Goals	Target that an individual wants to achieve

9. Social/professional identity	A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting
10. Emotion	A complex reaction pattern, involving experiential, behavioural and physiological elements, by which the individual attempts to deal with a personally significant matter or event
11. Reinforcement	Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus
12. Social influences	Those interpersonal processes that can cause individuals to change their thoughts, feeling, or behaviours
13. Environmental conditions	Any environmental condition that discourages or encourages the development of skills, abilities, or adaptive behaviour
14. Intentions	A conscious decision to perform a behaviour or a resolve to act in a certain way

3.3 Integration of COM-B and TDF

In previous studies the domains of the TDF are mapped against the COM-B model as shown in F1 in order to unpack the COM-B model (121). This allows research to go into more detail of the influences of the target behaviour. This integrated model is depicted in Figure 6, created by Almomani et al.

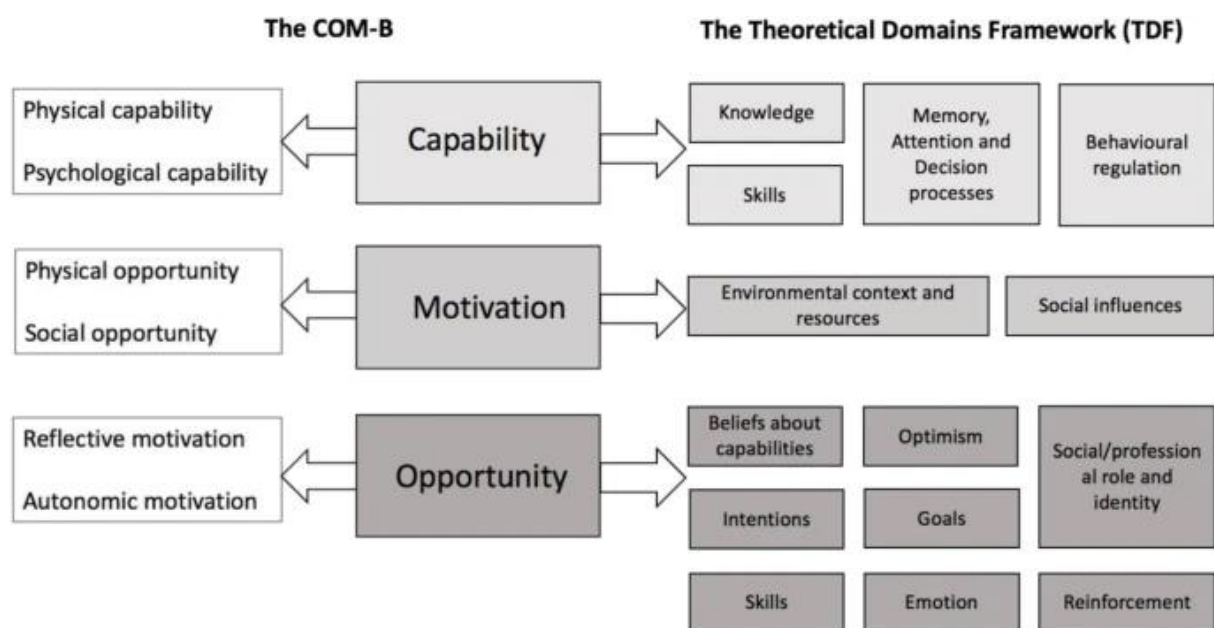


Figure 4. Integration of the COM-B and TDF. Source: <https://implementationsciencecomms.biomedcentral.com/articles/10.1186/s43058-020-00100-x>

4. Methods

4.1 Study design

Given the exploratory nature of the research question, qualitative methodology was applied to enable the collection of in-depth information to understand and interpret the facilitators and barriers of illegally purchasing GLP-1 RAs online. Semi-structured, in depth-interviews were conducted with individuals who have purchased GLP-1 RAs online in the past, or persons who did not purchase it online but are or were motivated to purchase it online and had views and opinions about the purchase.

Based on the COM-B model and the theoretical domains of TDF the topics for the semi-structured interviews were developed, guided by an in-depth literature search of various qualitative research articles. The topic guide was reviewed by Hanneke Wanders (HW), Lucy Crane-van Opstal (LC) and Tamara Rochement (TR). HW and LC both obtained their doctoral degrees and have experience with quantitative research. TR has experience in conducting and analysing qualitative data. She has conducted multiple (semi-structured) interviews. All had provided feedback on the topic guide, which was taken into account and incorporated into the final version. The topic guide is included in Appendix 1.

Defining target behaviour

As stated earlier, the target behaviour of research utilizing the COM-B Model and TDF is not the desired behaviour, but rather the behaviour that demonstrates change after an effective intervention. In this research that encompasses the behaviour of purchasing a GLP-1 RA online, without medical subscription

4.2 Sampling and recruitment

This study was conducted between September 2023 and March 2024.

4.2.1 Recruitment of participants - Attempt one

Participants were enlisted via recruitment posts on various Facebook groups. The recruitment message (see Appendix 2) was posted in these groups, which were created to provide support and guidance to individuals interested in weight loss using GLP-1 RAs. Within these groups, members share their experiences and engage in discussions related to weight loss using a GLP-1 RA. These groups were identified using the following keywords on Facebook:

- Ozempic
- Saxenda
- Rybelsus
- Gewichtsverlies
- Nederland

Various combinations of the keywords lead to 15 search results or Facebook groups. Upon initial screening, 7 groups were excluded for either including content unrelated to the research subject or predominantly using a language other than Dutch, the language used in the interviews. This research is focused on the Dutch population. Subsequently, 8 groups out of the initial 15 were deemed relevant and therefore included in the study.

Access to these 8 groups required completion of a short survey comprising 1 to 5 questions, ensuring that interested individuals intended to seek or provide help regarding the use of GLP-1 RAs for weight loss. The researcher provided answers to these questions, aiming to

enhance the possibility of group admission. However, challenges getting access to some groups were encountered, as one group rejected the request, reasoned the account was 'too new', while another group denied access without providing a reason. Eventually, admission was gained to 6 out of the 8 groups. However, administrators of 3 of these groups either prevented the posting of the recruitment message (see appendix 2) or deleted the recruitment message shortly after posting. In the remaining 3 groups, the researcher gained admission and successfully posted the message. However, this effort resulted in only one response from a prospective participant who ultimately did not engage further.

4.2.2 Recruitment of participants - Attempt two

After one week, the researcher noted minimal response to the recruitment posts on Facebook. Consequently, the researcher decided to offer monetary compensation for participation. Each participant was digitally sent a €15 'VVV-cadeaubon' gift voucher upon completion of the interview, reimbursed by the IGJ. The original message posted earlier was revised to align with the group's context and shortened to maintain reader engagement (see Appendix 3). This modified message was shared in the 8 included groups mentioned earlier. Additionally, the message was posted in 2 'beauty-focused' groups to broaden the outreach. These groups cover a wide range of personal care topics and had previously discussed GLP-1 RAs as weight loss agents.

Despite this revised approach from a few interested individuals, overall response remained limited. The first five individuals who expressed interest by contacting the researcher, and met the criteria, were included in the study.

In- and exclusion criteria of the participants

The study included people who have purchased GLP-1 RAs as weight loss agents online in the past, without medical subscription and/or people who did not purchase GLP-1 RAs online, but are motivated to do so, and therefore have views and opinions about this kind of purchase online. No strict exclusion criteria have been applied, related to the limited overall response.

4.3 Data collection

The form of data collection was a semi-structured interview, guided by topics that were established beforehand (see Appendix 1).

Before initiating data collection, LC reviewed the interview guide to ensure relevance and integrity of the questions. The phrasing of the questions and format of the guide were discussed with TR, who possesses experience in conducting and analyzing semi-structured interviews. The interviews were conducted over the telephone. Following a brief introduction and stating the purpose of the interview and study, the interviewer informed the interviewee about ensuring their privacy and data storage. The verbal given consent was audio-recorded, and subsequently, the researcher began the semi-structured interview, adhering to the predetermined guide. Each interview lasted approximately between 20 and 30 minutes. To ensure accuracy during data-analysis, all interviews were audio-recorded. After successful transcription the audio-recordings were deleted. Transcriptions were generated partly by Microsoft Transcript and supplemented manually when necessary. Field notes were not utilized, and transcripts were not returned to participants for feedback.

4.4 Data analysis

Data were analyzed using thematic analysis. Initially, the transcripts were read, and reread for familiarity, while taking notes. Subsequently, the transcripts were uploaded into NVIVO software for coding. These initial codes were then collated to form specific beliefs. These preliminary specific beliefs were evaluated in relation to the constructs of the theoretical domains of the TDF, with each belief being assigned to a (sub)domain based on its perceived relevance. A brief description of the TDF domains can be found in Table 1. Some specific beliefs were found to intersect with multiple theoretical domains, as evident in the results table (see Appendix 4) where a specific belief may be categorized into two or more domains, indicated by corresponding numbers ((1), (2), (3) etc.). Following the completion of the analysis, the codes, specific beliefs, and corresponding domains were reviewed and discussed with HW, who provided feedback on her perspectives regarding the mapping of the codes and specific beliefs into domains. Differences in opinion arose between the researcher and HW, especially regarding the classification of specific beliefs. After discussing it together, the researcher decided whether to incorporate or omit the feedback.

5. Results

5.1 Participants

Five participants (4 female; 1 male) were recruited via Facebook platforms to participate in the semi-structured interviews. Their ages range between 23 between 30. To protect participant privacy, gender-neutral pronouns 'they/them' will be used when referring to participants. Additionally, participant ages will not be linked to the identities.

5.2 Coding of utterances

A total of 246 utterances from the 5 interviews were coded. These utterances were categorized into 63 specific beliefs. Four of the specific beliefs were found to be irrelevant for the target behaviour, which focused on purchasing the GLP-1 RAs online for weight loss purposes. The remaining 59 specific beliefs were categorized into the fourteen TDF domains.

5.3 Identifying specific beliefs into their domain

Specific beliefs arising from the interviews with the purchasers of GLP-1 RAs online were categorized within twelve theoretical domains: Memory, attention and decision processes, Knowledge, Behavioural regulation, Beliefs about capabilities, Optimism, Beliefs about consequences, Goals, Social/professional identity, Emotions, Social factors, Environmental conditions, and Intentions (see Appendix 4). Two TDF domains, Skills and Reinforcement, are not included because no key themes as no specific beliefs were attributed to them.

5.4 Map of domains

The relations between the theoretical (sub)domains and the target behaviour, which is purchasing the GLP-1 RA online without medical prescription, is illustrated in figure 7.

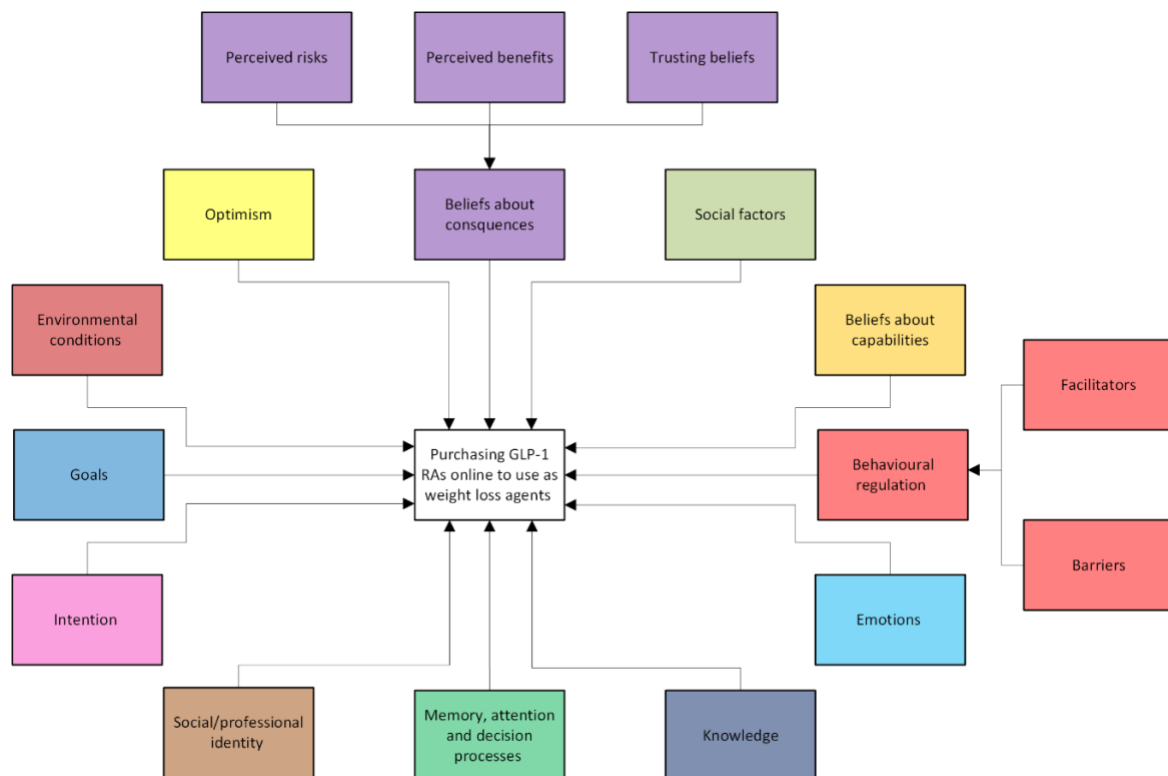


Figure 5. Relations between the identified (sub)domains of the TDFI and the target behaviour.

5.3 Interpreting codes in domains

5.3.1 Memory, Attention and Decision processes

Key themes were identified within the domain Memory, Attention and Decision Processes. Purchasers commonly indicated experiencing hesitation before using the GLP-1 RA. Participants pointed out several safety concerns regarding both the risks and disadvantages of illegally purchasing GLP-1 RAs online, as well as the use of GLP-1 RAs itself. The specific content of these concerns will be addressed in chapter 5.3.6. Perceived risks and disadvantages significantly influenced purchasers' decision-making processes, indicating a clear connection between two domains: Memory, Attention and Decision Processes and Perceived Risks. Participants often followed up on mentioned risks or disadvantages with counterarguments, explaining their eventual decision to purchase or use the GLP-1 RA. This can be illustrated by the following sample quote:

P3:

'Ik zou me een beetje... Dom, wil ik niet zeggen, maar een beetje zwak voelen als ik uiteindelijk echt het medicijn nodig had, en het niet helemaal op eigen kracht kon doen [afvallen]. Dus dat was eigenlijk een soort van constant effect in mijn hoofd. Waar ik dus aan de ene kant heel erg dacht van, joh, doe het gewoon. En aan de andere kant dacht ik, ja, doe het gewoon op de goede manier, de normale manier. Maar ja, toen had ik ook van, joh, het is me al zo vaak niet gelukt... Waarom zou het me nu wel zelf lukken?'

'I would feel rather... Dumb is not the correct word, but strengthless, if I eventually would really need the medicine, and if I wouldn't succeed on my own [to lose weight]. So, that was a constant debacle playing in my head. On the one hand I really thought to myself, hey, just use it. But on the other hand, I thought, why not lose weight in another way, the normal way? But well, that's when I also thought, I failed so many times already... Why would I succeed this time?'

Related to perceived risks and disadvantages and the following decision processes, participants also mentioned the importance of conducting research by themselves before the purchase or use of GLP-1 RAs, showing their ability to retain information.

Specific beliefs were mainly categorized in this domain because participants in the interviews indicated the doubts about using the GLP-1 RA, thereby sharing their decision process and their ability to choose between two or more alternatives.

5.3.2 Knowledge

Several specific beliefs fell under the theoretical domain Knowledge. All participants showed varying levels of familiarity with GLP-1 RAs, with the source of information differing. While some participants conducted extensive online research independently, others relied primarily on information obtained from their social circles. Participants who received informed information about GLP-1 RAs from their (close) social environment appeared to feel less pressure to conduct research themselves, indicating trust in their immediate environment.

Procedural knowledge was identified by most participants. Some participants consulted their general practitioner to obtain a medical prescription for GLP-1 RAs, while others possessed basic knowledge about the diagnoses of diabetes and obesity, recognizing that a medical prescription was not a realistic option. Some participants associated their use of the GLP-1 RA with unethical or narcissistic behaviour because the treatment was not primarily intended for them. This perception is influenced by social norms, therefore categorizing this specific

belief within the domain of Social Influences as well. This can be illustrated by the following quote:

P3:

'Nou, ja, ik klink misschien een beetje narcistisch, maar ik wist zelf ook heel goed dat het eigenlijk een medicijn is wat voor diabetes wordt gebruikt.'

'Well, I might sound a bit narcissistic now, but I knew very well that it is actually a medicine used for the treatment of diabetes.'

All participants appeared to be aware of the shortage of the GLP-1 RAs. Interestingly, no participant exhibited any emotional response regarding their own illegal online purchase. One participant pointed out that the shortage could even be a motivating factor to purchase online. This sentiment can be illustrated by the following quote:

P2:

'Ja, mijn huisarts die zei van, van ja, omdat er ook wel een groot tekort aan is. Ook om die redenen hoor, dat was het dat ik op gegeven moment ook verder ben gaan zoeken.'

'Yeah, my general practitioner said, well, because of the big shortage of it. It is also for those reasons, why I eventually started searching for other options.'

In the context of the GLP-1 shortage, it remains unclear whether the participants deemed the shortage irrelevant for their own use of it, or if they had an association between their illegal online purchase of the medicines and the shortage.

5.3.3 Behavioural Regulation

The theoretical domain Behavioural Regulation includes factors that could enhance or hinder the purchaser's behavioural regulation and level of behavioural control. This domain can therefore be further subcategorized into facilitators and barriers, which will be addressed separately in the following sections. Some researchers [] identify facilitators and barriers within the domain of Environmental Conditions. However, developers of the TDF, Michie et al., 2005, do not specifically categorize facilitators and barriers in domains, leaving the data open for interpretation. In this research, facilitators and barriers collected under the domain Behavioural Regulation, as deemed most appropriate based on the definitions noted in Table 1.

Facilitators

Factors facilitating the behaviour of purchasing GLP-1 RAs online and the benefits associated with this behaviour, which fall under the domain Beliefs about Capabilities, may overlap. When a specific belief aligns with one domain, it does not necessarily preclude its relevance to another domain. Factors are classified as facilitators if they primarily ease the purchasing process or contribute to the weight loss journey, as opposed to being beneficial overall.

One participant mentioned that using GLP-1 RAs for weight loss facilitated their weight loss journey simply because the medication made the process easier. They indicated they did not have to exert as much effort as they would have with other, more traditional methods, such as increasing exercise levels or following a diet plan.

Another identified facilitator was the involvement of healthcare providers. Participants indicated that guidance from a healthcare provider could facilitate their decision to purchase and use GLP-1 RAs. They expressed a preference for being guided by their general practitioner but acknowledged that being guided by another healthcare provider (i.e. employee from the clinic) was also acceptable if the former option was not available. This can be illustrated by the following sample quote:

P2:

'Ik had liever gehoopt via mijn huisarts was, dan ging het nog makkelijker in die zin. Toch wel, maar als het ook begeleid kan worden via een andere weg, waarom niet?'

'I would have preferred it was through my general practitioner, it would have been easier in that sense. But still, if it can be guided in another way, why not?'

Furthermore, participants indicated the ease of purchasing GLP-1 RAs online as a facilitator, emphasizing the convenience of it. They noted that online purchasing saved both time and effort, as illustrated by the following quote:

P1:

'...en ik denk ook wel een stukje gemak want je hoeft in feite, maar op twee knoppen te drukken.'

'...and I also think it's a bit of convenience because, basically, you only have to press two buttons.'

Another facilitator is provided by online sellers, which entails access to prescription medication online. GLP-1 RAs typically require a medical prescription and supervision, which can be circumvented when purchased online.

Additionally, several participants mentioned that the availability of GLP-1 RAs was also a significant factor. During the interviews participants expressed disappointment about not being able to obtain the GLP-1 RAs through medical prescription. The assurance of availability therefore played a role in facilitating their online purchasing behaviour.

Barriers

Interestingly, only one barrier of the purchasing or using behaviour was identified. Participants indicated that they hadn't considered what factors would hinder them from purchasing and using GLP-1 RAs when specifically asked about thus by the interviewer. No barriers were identified in other sections of the interview either. One common barrier mentioned by several participants was self-financing the GLP-1 RA treatment, in contrast to a medical prescribed treatment.

5.3.4 Beliefs about Capabilities

In this domain one specific belief was mentioned by several participants. They shared various perspectives on the administration of the GLP-1 RA and therefore showed acceptance about an ability. Two participants indicated they were anxious about injecting the pen in their body, especially because they had no knowledge and experience. Injecting in the wrong spot, too deep or not deep enough in their abdomen were mentioned when expressing their concerns. Nevertheless, both the participants also mentioned they had overcome these feelings of fear because the motivation to lose weight was greater.

In contrast, two participants mentioned they were not anxious at all about injecting the GLP-1 RA. One of these participants indicated they had no problem with the administration route, because they had seen their family injecting themselves before.

5.3.5 Optimism

Three aspects associated with GLP-1 RA purchase or use were mentioned by the participants and identified in the domain of Optimism.

First, one participant expressed optimism about online purchasing in general. They were confident that the online purchase of prescription medicines would unfold without any negative consequences, foreseeing no risks associated with it. This optimism is related to trusting beliefs in the purchasing environment, a subdomain of the domain Beliefs about Consequences.

The second aspect involves participants' optimism regarding the potential side effects associated with GLP-1 RA use. Two participants mentioned they had researched the common side effects of GLP-1 RAs but believed the likelihood of experiencing them themselves would be low. This sentiment is exemplified by the following quote:

P4:

'Maar ik ben eigenlijk wel van nature een persoon met een hele hoge pijngrens. Dus ik dacht van, oh, ik kan het [de bijwerkingen] wel aan, zal vast niet zo erg zijn. Dus ik had het een beetje onderschat.'

'But naturally, I am a person with a very high pain threshold. So, I thought, oh, I can handle it [the side effects], it cannot be that bad. So, I had underestimated that a bit.'

One participant also expressed optimism regarding the therapeutic effects of the GLP-1 RA, showing confidence in its potential benefits for weight loss. They were convinced that the medication would benefit them in helping them achieve their weight loss goals.

5.3.6 Beliefs about Consequences

Beliefs about Consequences encompasses positive and negative outcomes associated with the target behaviour. This domain can be further subdivided into three subdomains: perceived risks, perceived benefits, and trusting beliefs. All three subdomains are relevant to both the purchase and the use of the GLP-1 RA.

Perceived risks

Regarding the risks associated with purchasing medicines online, participants expressed a specific concern. Two participants mentioned the possibility of receiving a product that is not the original GLP-1 RA, indicating uncertainty and distrust toward the seller or the selling environment. Trust toward the seller or selling environment will be further discussed in the next subchapter Trusting Beliefs. The perceived risk of receiving a non-original product, and the subsequent decision-making process, can be illustrated by the following quote:

P4:

'Ja, kijk, ik wist niet zeker of het een echt origineel product was. Dus dat kan ook natuurlijk uit China of namaak of iets zijn.'

'Yeah, you see, I wasn't sure if it was the original product. So, it could be from China or a counterfeit or something.'

Several risks were also perceived regarding the use of the GLP-1 RA. One participant expressed concerns about health-related risks, mentioning skepticism about uncertainties regarding the effects on their bodies, although no specific concerns were discussed. Some participants also highlighted the risks associated with the side effects of using the GLP-1 RA, either after conducting online research or through information from their social circles. Additionally, one participant mentioned risks associated with medication use in general, suggesting that medicines may have negative consequences on their health:

P2:

'Anders had ik het denk ik niet gedaan, hoor. Nee, zeker niet nee. Want het blijft, uhm, het blijft een medicijn, of hoe je het kan noemen.'

'Otherwise, I would not have done it. No, definitely not. Because it is, uhm, it is still a medicine, or however you want to call it.'

Remarkably, one participant repeatedly emphasized that they did not perceive any risks associated with the online purchase of GLP-1 RA. They also noted their familiarity with the GLP-1 RA, as they had witnessed multiple family members use it and purchase it online before. This sentiment is directly related to the domain Social Influences.

Perceived benefits

Various factors were interpreted by the purchasers as benefits that they might expect if they choose to purchase the GLP-1 RA online. One participant indicated that the ability to choose type of GLP-1 RA played a significant role, therefore favoring purchasing online than getting the treatment medically prescribed. Their preference was Ozempic, as a result of receiving extensive information about it, and when medically prescribed the participant would receive Wegovy. The participant pointed out why they therefore preferred purchasing the GLP-1 RA online rather than getting it prescribed.

Mentioned by several participants is the privacy online purchasing provides. One participant for example preferred online purchasing, because then it would not be noted down in their medical record, and they would be the only one who knew about the GLP-1 RA use. This specific belief is also identified in the domain Environmental Conditions, as the online selling environment encourages adaptive behaviour. This can be illustrated by the following quote:

P5:

'Dus als ik bijvoorbeeld naar de huisarts ging voor de Ozempic, en stel dat dat werd genoteerd in mijn dossier en zo, dat wou ik ook niet eigenlijk. Dus ik ging het gewoon online bestellen en... Dan weet ik het enkel zelf.'

'So, if for example, I went to the general practitioner for Ozempic, and he would note that down in my dossier or something, I did not want that to happen. So, I just ordered it online and... I am the only one that knows.'

Furthermore, participants mentioned it was preferable they could directly start using the GLP-1 RA, discussing the time saved by not having to visit the general practitioner and obtaining any medical controls. One participant specifically emphasized the time saved by not having to follow the lifestyle intervention program, which is mandated when getting the GLP-1 RA medically subscribed:

Researcher:

'En zag je op tegen de leefstijlinterventie [programma] of omdat het zo lang duurde?'

P3:

'Ik was niet per se tegen dat leefstijlprogramma, maar wel het besteden van de tijd die het zou kosten.'

And were you dreading the lifestyle intervention [program] or the time it would take?'

-

'I wasn't against the lifestyle program per se, but I was against spending the time it would take.'

Another participant also mentioned they knew using the GLP-1 RA would lead to faster weight loss than by following other, healthy, methods and therefore preferring the GLP-1 RA.

Trusting beliefs

Lastly, trusting beliefs represent the final subdomain of Beliefs about Consequences. One specific belief identified in the interviews was the confidence and assurance participants gained from observing the use of GLP-1 RA in their close environment. Three participants mentioned having family members or close friends who had previously used a GLP-1 RA and experienced positive results in terms of weight loss. All three participants emphasized that this significantly influenced their perspective on the efficacy of the medication. A commonly shared sentiment during the interviews was: 'If the GLP-1 RA works for others, why would it not work for me?' Additionally, witnessing the weight loss themselves in those using the GLP-1 RA further reinforced their trust in the effectiveness. This is exemplified by the following quote:

P5:

'Echt veel, ja, want ik hoorde echt veel positieve verhalen. Van vrouwen meestal, die waren afgevallen en ook positief. En ik zag dat ook want het is mijn familie, en ik ken hen sowieso. Ik zag dan ook dat die kilo 's echt weg waren. Daarom heb ik het ook geprobeerd.'

'Yeah, quite a bit, because I heard a lot of positive stories. Mostly from women, who had experienced weight loss and spoke positively about it. And I could see it too, because they are my family, and I know them personally. That's how I could really witness them losing the kilos. That's why I tried it as well.'

Participants exhibited diverse opinions regarding their trust in the seller or selling environment of the GLP-1 RA. For instance, one participant expressed distrust in the seller, particularly because communication mainly took place via the social media platform Telegram. They described this environment as 'sketchy' and were reluctant to share personal information, including their address, with the seller. Factors contributing to this participant's distrust included the use of the platform Telegram, the anonymity of the sellers, and the absence of secure payment options. The latter can be illustrated by the following quote:

P3:

'Er werd me ook, en dat hielp eraan mee dat ik het helemaal niet vertrouwde, er werd me meerdere malen gevraagd of ik via Bitcoin kon betalen.'

'At one point, I was asked several times if I could pay with Bitcoin, and that facilitated in me not trusting it at all.'

In contrast to the low levels of trust expressed by one participant, another participant showed minimal doubt in the seller, demonstrating almost instant trust. One factor influencing this behaviour is related to how the participant perceived the seller. The participant indicated that the seller was a well-known 'influencer', which led them to have little to no doubts beforehand about the purchase.

Researcher:

'Zag je risico's in het online kopen?'

P4:

'Ik was er niet echt bang voor omdat het wel, zeg maar, via een bekend persoon, bekende influencer-achtig iets was.'

'Did you think about the risks of purchasing online?'

-

'I wasn't really nervous about that because, you know, it was through a well-known person, some kind of famous influencer-person.'

One participant explained the factors influencing their trust in a GLP-1 RA selling website. Firstly, they mentioned their familiarity with online purchases, which had developed a 'gut feeling' about the security of a selling website. Secondly, they stated they recognize safe websites based on indicators like starting with 'HTTPS'. Additionally, they had downloaded an extension for their computer that identifies unsafe websites, which increased their confidence in recognizing unsafe websites.

5.3.7 Goals

This domain encompasses the target an individual wants to achieve. All participants shared the common goal of losing weight. For them, using the GLP-1 RA and therefore, purchasing it online without medical prescription, was seen as means to achieve this goal.

5.3.8 Social/Professional Identity

One participant expressed concerns regarding their social identity associated with using weight slimming agents, emphasizing their identity within a group. They indicated potentially feeling judged for using GLP-1 RAs instead of losing weight through other conventional methods. This can be illustrated by the following quote:

P2:

'Wat het online kopen moeilijker maakt? Nou ja, ik denk dat dat vooral een sociaal psychologische kwestie is, in mijn geval. Ik had wel op een gegeven moment voordat ik die pillen ging halen dat ik wel even dacht van, oké, nee, moet ik hier wel aan beginnen? Is het wel wijsheid, kom ik wel niet over als een persoon die heel lui is?'

'What made purchasing online more difficult? Well, I think in my case that is mainly a social psychological issue. At some point I did start thinking, okay, do I really want to start this? Is it wise? Am I not going to come across as someone who is just very lazy?'

5.3.9 Emotions

Participants described multiple scenarios during the purchasing process in which they experienced emotional responses. The emotions identified during the interviews were shame, determination, desperation and feeling insecure.

Shame

One participant expressed feelings of shame associated with using the GLP-1 RA. This sentiment is directly related to the domain of Social/Professional Identity, as the participant expressed concerns about how their use of GLP-1 RA might affect their identity within their social circle or professional context. Additionally, the feelings of shame can also be linked to the domain Beliefs about Consequences, as the participant viewed online purchasing as a benefit due to its ability to provide privacy, thereby mitigating feelings of shame associated with purchasing the medication.

Determination and desperation

All participants exhibited determination, especially when discussing the potential risks or disadvantages associated with GLP-1 RA use. Despite acknowledging these concerns, the participants showed strong motivation and therefore determination to use the medication. For one participant, this determination was accompanied by a sense of desperation, as they felt that other conventional methods for weight loss had been ineffective for them. This can be illustrated by the following quote:

P3:

'...dat heeft er wel een soort rol in gespeeld, dat ik eigenlijk altijd al heel graag iets aan mezelf wilde veranderen, maar gewoon niet wist hoe.'

'...that has played a role in it, that I have always wanted to change something about myself, but I just didn't know how.'

Feelings of insecurity

Two participants expressed a lack of confidence in their self-images, indicating feelings of insecurity. They both highlighted the challenge of conforming to the 'ideal body image' and experiencing social pressure. These sentiments are related to social influencing factors, as social pressure and social comparison play a significant role in facilitating the motivation to lose weight and therefore the GLP-1 RA using behaviour. This can be exemplified by the following quote:

P2:

'...en het ideaalbeeld van hoe een vrouw er eigenlijk bij moet lopen zeg maar. En ja, als dan... Ik had al, naar mijn eigen inziens... Pas ik niet in dat plaatje en dat wil je dan natuurlijk wel...'

'...and the ideal image of what a woman should look like. And yes, if... I already had, in my opinion... I don't fit into that image and naturally you would want that...'

5.3.10 Social Factors

One of the most dominant theoretical domains is Social Factors, as it was frequently mentioned by each participant. Social Factors encompass all interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviours. Social Factors played a significant role in both the using and purchasing behaviour. Specific beliefs

identified within this domain include Social media, Friends, Family, Social Comparison and Social Norms.

Social media

Participants indicated that social media played a significant role in directly influencing their purchasing and using behaviour, as well as their thoughts or feelings associated with GLP-1 RA. All participants mentioned they had come across GLP-1 RAs on different social media platforms. One participant for example mentioned the GLP-1 RA seemed more approachable, because the medicine was widely available on various social media platforms:

P4:

'Ja, best wel, want het is verkrijgbaar via social media, dus dan... Is het ook aantrekkelijker.'

'Yeah, because it was available on social media, so... That makes it more approachable.'

One participant mentioned seeing multiple 'before and after' videos of people using the GLP-1 RA, demonstrating how much weight they had lost through its use. The same participant also shared how they naturally came across social media platforms wherein losing weight with the GLP-1 RA was the main subject, driven by the social media algorithm:

P3:

'Nou, ja, ik denk... Ik denk dat niet per se, maar wel gewoon van die accounts waarbij je dan ja, hoe vaker je het 'likt' of hoe langer je die filmpjes bekijkt, des te meer krijg je zulke content te zien. Dus je rolt er als het ware er een beetje vanzelf in.'

'Well, yes, I think... I don't necessarily think so, but it's just those accounts, the more you 'like' or the longer you watch their content, the more you get such content recommended. So, you kind of naturally end up in it.'

Additionally, the use of GLP-1 RAs has been promoted by various influencers (bron), which directly influenced one participant's decision to use the drug. This can be illustrated by the following quote:

P4:

'We hebben ook een beetje op internet gekeken en toen zagen we dat beroemdheden zoals Kim Kardashian en Kylie Jenner dat ook gebruiken en andere beroemdheden ook, om te af te vallen, om slank te zijn. En toen dachten we van, ja, we kunnen het proberen.'

'We also did some research online, and then we saw that celebrities like Kim Kardashian and Kylie Jenner also use it to lose weight and to be slim, and other celebrities too. And then we thought, yeah, well, we could try it.'

Lastly, one participant indicated they did not seek any help on social media, but they did notice individuals on social media asking them for advice and help associated with both the purchase and the use of GLP-1 RA. Multiple times they were asked questions about the selling environment and advice about the GLP-1 RA use.

Friends

The second specific belief identified in the domain of Social Influences involves the influence of friends within the participants' environment. One participant mentioned that their

confidence in the efficacy of using GLP-1 RA was directly shaped by a friend who claimed to have lost weight through the medication use.

One participant highlighted that their friends and social circle directly influenced their feelings of social comparison and group norms. This contributed to the participant experiencing social pressure to conform the standards set by their group of friends for body image. As a result, they felt motivated to lose weight to fit in. This sentiment can be illustrated by the following quote from the participant:

P1:

'En waar het bij mij mijn sociale kring... In dat opzicht, met name met mijn vriendenkring, heeft daar een rol in gespeeld. Als ik zo naar mijn vriendenkring kijk dan zijn het over het algemeen allemaal mensen die zo in een modeblad kunnen zeg, maar die hebben gewoon de standaarden van... Ja, eigenlijk de sociaal maatschappelijke standaarden die gezet worden voor schoonheid en het ideaalbeeld zeg maar. Ja, ja, en hoe je het wendt of keert, ja... Je gaat jezelf er toch mee vergelijken.'

'And for me, in my social circle... In that sense, especially with my circle of friends, that has played a role in it as well. When I look at my friends, they are generally all persons who could easily be in a fashion magazine, they simply have the standards of... Yeah, just the social standards that are set for beauty and the ideal image. Yeah, and no matter how you look at it... Eventually you're going to compare yourself with them.'

Family

The most mentioned specific belief was family. This belief was identified with all participants and was in total referenced to 26 times. Family played various roles, and the dominant roles will now be discussed.

Two participants mentioned that their parents were strongly opposed to the use of GLP-1 RAs for weight loss. The reasons behind the parents' opposition were not further explored during the interviews. Despite their parents' disapproval, both participants expressed a strong motivation to lose weight, highlighting the decision-making process they underwent when weighing alternatives. As a result of the parents' disapproval, one of the participants mentioned they made the decision not to tell their parents about the illegal purchase and use of the medicine.

P3:

'Nee, eigenlijk niet, want ik kende zelf niemand die het had gebruikt en ik wist ook wel dat mijn ouders er heel erg op tegen waren. Zelfs... Ja, de weg via de huisarts, dus ik had het hen ook helemaal niet verteld.'

[...]

'Want ik woon nog thuis. Dus ik dacht ook van joh, als ik ze dat nou ook nog eens ga uitleggen... En dan ook nog eens dat ik het zelf haal via een Telegram groep [en niet via de huisarts]. Ja, dan gaan ze al helemaal de pan uit schieten.'

'No, actually not, because I didn't know anyone who had used it themselves, and I also knew that my parents were very much against it. Even... Yeah, the route through the general practitioner, so I hadn't told them anything about it.'

[...]

'Because I still live at home. So, I also thought, well, if I explain that to them now... And then also that I got it myself through a Telegram group [and not through the general practitioner]. Yeah, then they would completely freak out.'

In contrast to the disapproving view of the families of the two earlier mentioned participants, three of the participants mentioned their family played a positive influence in using the GLP-1 RA. The participants discussed how they had seen family members use the GLP-1 RA before, directly increasing the participants confidence in the efficacy of the medicine. Two of the three participants mentioned that the family members using the GLP-1 RA also used the medicines aiming to lose weight, and that they had advised them about online purchasing as well. One of the three participants discussed their family members were diagnosed with diabetes and were using the GLP-1 RA after medical prescription. This participant also indicated they did purchase the GLP-1 RA online in accordance with their niece and sister, indicating that she would not maybe have done it individually. These beliefs are all related to group norms, and specifically family norms. This can be exemplified by the following quote:

P4:

'Ik heb Ozempic gekocht omdat in mijn familie er een aantal mensen zijn, onder andere mijn oma en mijn moeder, die diabetes hebben en zij slikken [spuiten] dat ook. Maar dat is echt... Zij hebben dat voorgeschreven gekregen van de huisarts. [...]. En dus, wij hebben... Ik heb het eigenlijk ook niet alleen gedaan. Mijn nicht en mijn zus hebben het ook gedaan. En we hebben het eigenlijk bij hen (familie, moeder en oma) gezien. Toen zagen we dat er een mogelijkheid was om het te kopen. Via Turkije en dan via Turkse mensen in Duitsland. En toen dachten we van ja, waarom niet? En we willen toch afvallen.'

'I bought Ozempic because there are several people in my family, including my grandmother and mother, who have diabetes and they also take [inject] it. But that... It was medically prescribed for them. [...]. And so, we... I didn't do it by myself actually. My niece and sister did it too. And we saw them [family, grandmother and mother] use it. Then there was an opportunity to buy it in Turkey, and then we would receive it through Turkish people in Germany. So, we thought, well, why not? We still wanted to lose weight.'

The last dominant role the family can fulfill is contributing the motivation to lose weight, and not to purchase the GLP-1 RA per se. One participant emphasized the role their family played by commenting on their body, and their problems with the participant's weight. The participant shared this had been like this since they were young, and it had shaped their self-confidence about their body weight. Social pressure and fitting in the social norm are clearly revealed in this specific belief. Because of the feelings of insecurity this specific belief is also related to the domain of Emotions. This sentiment can be illustrated by the following quote:

P3:

'Dus ik had eigenlijk al ja, zo lang als ik me kan herinneren, opmerkingen gekregen van mijn omgeving, ook van familie, over mijn lichaam. Dus dat heeft er wel een soort rol in gespeeld [...].'

'So, for as long as I can remember, I had received comments about my body, from my family as well. That has played some kind of role in it [...].'

Often mentioned was the increased confidence and improved general perception of GLP-1 RA use for weight loss due to the experiences of individuals within participants' close social circles, including friends and family members.

Another factor related to social norms involves familiarity with GLP-1 RAs, which was also discussed in the domain of Knowledge. Participants noted that they were aware that the GLP-1 RAs were primarily intended to treat diabetes patients, thus shaping the social norms surrounding their use.

5.3.11 Environmental conditions

Environmental conditions entail any environmental factors that discourages or encourages the development of skills, abilities, or adaptive behaviour. Two participants mentioned they had seen GLP-1 RAs mentioned on the news, which facilitated their decision to use the medication. One participant indicated that their busy schedule left them with little time to lose weight through conventional methods, encouraging them to use the medication. The selling environment could also facilitate purchasing behaviour by providing the participant with privacy, associated with feelings of shame, as earlier discussed in the domain of Emotions. Another environmental condition facilitating purchasing behaviour is the participants' knowledge of receiving a medical prescription, thereby revealing a direct association with their illegal online purchase. Lastly, some participants also mentioned that GLP-1 RAs were frequently discussed in their environment without specifying the factors. To illustrate this, the following quote is included:

P3:

'Omdat ik er eigenlijk heel veel over had gelezen en over had gehoord. Ja, je zag het ook natuurlijk overal om je heen.'

'Because I actually read a lot about it and heard a lot about it too. Yeah, at some point you saw it everywhere around you.'

As mentioned earlier, some researchers categorize facilitators and barriers under the domain Environmental Conditions. According to the definitions by Table 1, facilitators and barriers are identified in the domain Behavioural Regulation. In reality, it is likely a combination of both.

5.3.12 Intention

Intention encompasses conscious decisions to perform a behaviour. The intention of all participants was to lose weight using the GLP-1 RA, which was already established in the domain of Goals. Purchasing the GLP-1 RA online is used as a means to achieve this goal, due to the lack of a medical prescription.

Identified with multiple participants was the specific belief self-interest. Various statements indicated expressions of self-interest. For example, participants mentioned their awareness of the GLP-1 shortage; however, this was often followed by a narcissistic reaction. Participants expressed it was not their focus at the moment, showing nonchalant behaviour during the interviews. Losing weight was their primary focus and goal, demonstrating feelings of self-interest. This sentiment can be illustrated by the following quote:

P5:

'Ja ja, maar ik zei al, ik dacht daar echt niet aan. Mijn eerste ding was, dat was echt afvallen.'

'Yeah, yeah, but as I had said before, I was not really focused on that. My main thing was losing weight first.'

One participant explicitly mentioned they were unwilling to make the effort to lose weight in a conventional, healthy way, expressing intention not to try it. To illustrate this, a quote from the participant is included.

P4:

'Omdat ik te lui was om het zelf te proberen [afvallen]. Eigenlijk hoort dat echt niet maar... Ja, dat is wel eigenlijk waar het op neer kwam. Ik was gewoon een beetje te lui. Dus ik dacht van, ja, ik wil gewoon afvallen en iedereen doet het. Dus, waarom zou ik het niet doen?'

'Because I was too lazy to make an effort by myself [to lose weight]. And I know that is actually not okay... But, yeah, that is what it came down to. I was just too lazy. So, I thought to myself, I want to lose weight, and everyone is doing it. Why shouldn't I do it then?'

6. Discussion

6.1 Dominant specific beliefs

Framing the determinants of the illegal online GLP-1 RA purchasing behaviour enables a deeper understanding of this phenomenon. Specific beliefs that were frequently emphasized by participants, and their corresponding COM-B domains, will now be discussed.

6.1.1 Psychological capability

Within the Psychological Capability of the COM-B Model, the theoretical domains of Behavioural Regulation and Memory, Attention and Decision processes were frequently identified in the specific beliefs. In this research, Behavioural Regulation encompasses all facilitators and barriers related to the target behaviour. Interestingly, only one barrier was identified during the interviews, while participants mentioned several facilitators that made the online purchasing of GLP-1 RA easier. Highlights of the facilitators include the time and effort saved, the absence of needing a prescription, and the privacy provided by online purchasing. These findings are in line with the results of other research, which had identified similar facilitators in the illegal online purchasing behaviour of consumers of prescription medicines, not specifically GLP-1 RAs (119).

6.1.2 Reflective Motivation

Reflective motivation encompasses several domains within the TDF, including Social/Professional Identity, Intention, Goals, and Beliefs about Consequences. The theoretical domain Beliefs about Consequences includes Perceived Benefits and Risks. These perceived benefits and risks are in line with earlier found determinants in research on online purchasing behaviour of prescription medicines. Benefits that were mentioned, and found in earlier research include Privacy, Bypassing health professionals, Medicines availability, and Being able to purchase prescription medicines (119). Intention and Goals are at the core of the motivation to lose weight. All participants shared the goal of losing weight and demonstrated high motivation to achieve this goal. Conscious decisions were made to work towards this target, as evidenced by the specific beliefs in the domains of Knowledge and Memory, Attention, and Decision Processes.

It's noteworthy that none of the participants mentioned the goal of purchasing the GLP-1 RA online. Instead, this process was seen as means to achieve the overarching goal of weight loss. Despite online purchase not being a specific goal, participants expressed intentionality as they showed self-interest during the decision-making process when purchasing. Additionally, participant acknowledged various serious disadvantages or risks associated with the GLP-1 RA purchase or use but consciously decided to engage in the target behaviour due to their strong motivation to lose weight, which is directly linked to reflective motivation as well.

6.1.3 Social Opportunity

Specific beliefs within the domain of Social Factors were frequently mentioned by all participants, with the dominant specific beliefs revolving around participants' close social environment, including family, friends, and social media platforms. Family was the most frequently mentioned specific belief, referenced a total of 26 times by all participants. For two participants, their families actively disapproved of the GLP-1 RA to lose weight, but these participants indicated that they did not take that into consideration. On the other hand, three participants mentioned that their families facilitated the use and/or purchase of the GLP-1 RA. Similar sentiments were observed regarding friends in participants' close environments,

with friends and family advising or indicating the efficacy or convenience of using or purchasing the GLP-1 RA.

Interestingly, participants who received recommendations from their close social circles typically showed little to no interest in conducting extensive research about the GLP-1 RA themselves, indicating a high level of trust in their social circles. This trust further increased when participants witnessed the weight loss in their friends or family members themselves, reinforcing their confidence in the efficacy of the medication.

6.2 Risks associated with GLP-1 RA use

The contextual framework of this research involved an examination of available online research on the short- and long-term risks associated with using GLP-1 RAs. Despite the potential risks associated with GLP-1 RA use, interestingly, almost none of the participants expressed significant concerns about their health. While some participants mentioned mild worries, only one participant reported conducting extensive research on the short- and long-term effects, which included findings related to intestinal and kidney failures. However, this participant quickly dismissed these side effects and remained optimistic about GLP-1 RA use. This sentiment was also identified with other participants.

Interestingly, the short- and long-term health risks associated with the use of GLP-1 RAs that were identified earlier in this research, were unknown to most of the participants. Additionally, all participants seemed to underestimate the short- and long-term effects, either by deeming them irrelevant and thus not conducting any research about them, and when they had conducted research, they appeared to think the side effects will not affect them.

6.3 Risks associated with purchasing prescription medicines online

The contextual framework also addresses risks associated with purchasing prescription medicines online in general, including concerns about product authenticity, the absence of healthcare practitioners leading to various health hazards, and the risk of consumer fraud.

During the online purchasing process, two out of the five participants questioned the authenticity of the products they were buying. One participant expressed concerns about consumer fraud, scams, and invasion of their personal privacy, particularly due to their use of the social media platform Telegram, which directly contributed to their distrust. However, the other participants did not mention similar concerns or risks associated with purchasing prescription medicines online. Overall, the participants did not express significant concerns associated with illegally purchasing prescription medicines online, indicating they are unfamiliar with the risks associated with this behaviour.

Overall, this optimistic behaviour regarding perceived risks was also seen in earlier research, as the researchers stated consumers might be enticed by the benefits of the online purchase. When perceived benefits outweigh perceived risks, consumers are more likely to make the purchase. The researchers did state that the probability of making the purchase could be increased when consumers have inadequate knowledge about the risks associated with the purchase (119), a phenomenon identified with most participants in this research.

6.4 Shortage of GLP-1 RAs

The mentioned global shortage is linked with considerable health risks for obesity and T2D patients treated with GLP-1 RAs. This research found that all participants were aware of the GLP-1 RA shortage, yet this awareness was tied to a sense of self-interest, as they did not

view the shortage as an obstacle to their own online purchasing behaviours. Public discussions about this shortage, such as in news articles (122), might have adverse consequences.

Earlier research has indicated that shortages might even act as a motivator, leading some patients to seek alternative sources on the internet, regardless of the risks involved (123). Pandemics such as COVID-19 have been pointed out in the media and could facilitate as factors that could cause panic buying of prescription medicines from any available online source, driven by fears of running out or the lack of effective treatments (124). In line with this, a multinational study, which explored consumer behaviour of purchasing medicines from the internet, found that some consumers accepted to take the risks and buy prescription medicines online in the case of emergencies such as the medicine shortages (125).

The result of this research aligns with the aforementioned literature, highlighting that during the interviews one participant specifically mentioned that the shortages significantly influenced their decision to purchase GLP-1 RAs online. In this research the news was also mentioned multiple times, identified as an Environmental Condition. It is possible that the news articles regarding GLP-1 RA shortages are associated with a form of panic buying, that was seen during the pandemic. Further investigation is necessary to fully understand how awareness of shortages affects the online GLP-1 RA purchasing behaviours of consumers.

6.5 Integration of TDF and COM-B Model

The twelve identified domains, along with their respective subdomains, have been mapped onto the COM-B Model. Relying on this theoretical framework, the study presents a comprehensive conceptual framework outlining the determinants influencing the decision to purchase GLP-1 RAs online without a medical prescription. Figure 8 provides an illustration of this comprehensive framework, showing the interactions between the determinants and how they are able to influence behaviour. When the TDF domains are mapped onto the domains of the COM-B Model, intervention functions, strategies, and Behaviour Change Techniques (BCTs) can be systematically selected, using the earlier discussed Behaviour Change Wheel (BCW). Selecting strategies is implemented in this research as this was not included in this research project, but the results form the groundwork for eventual future research.

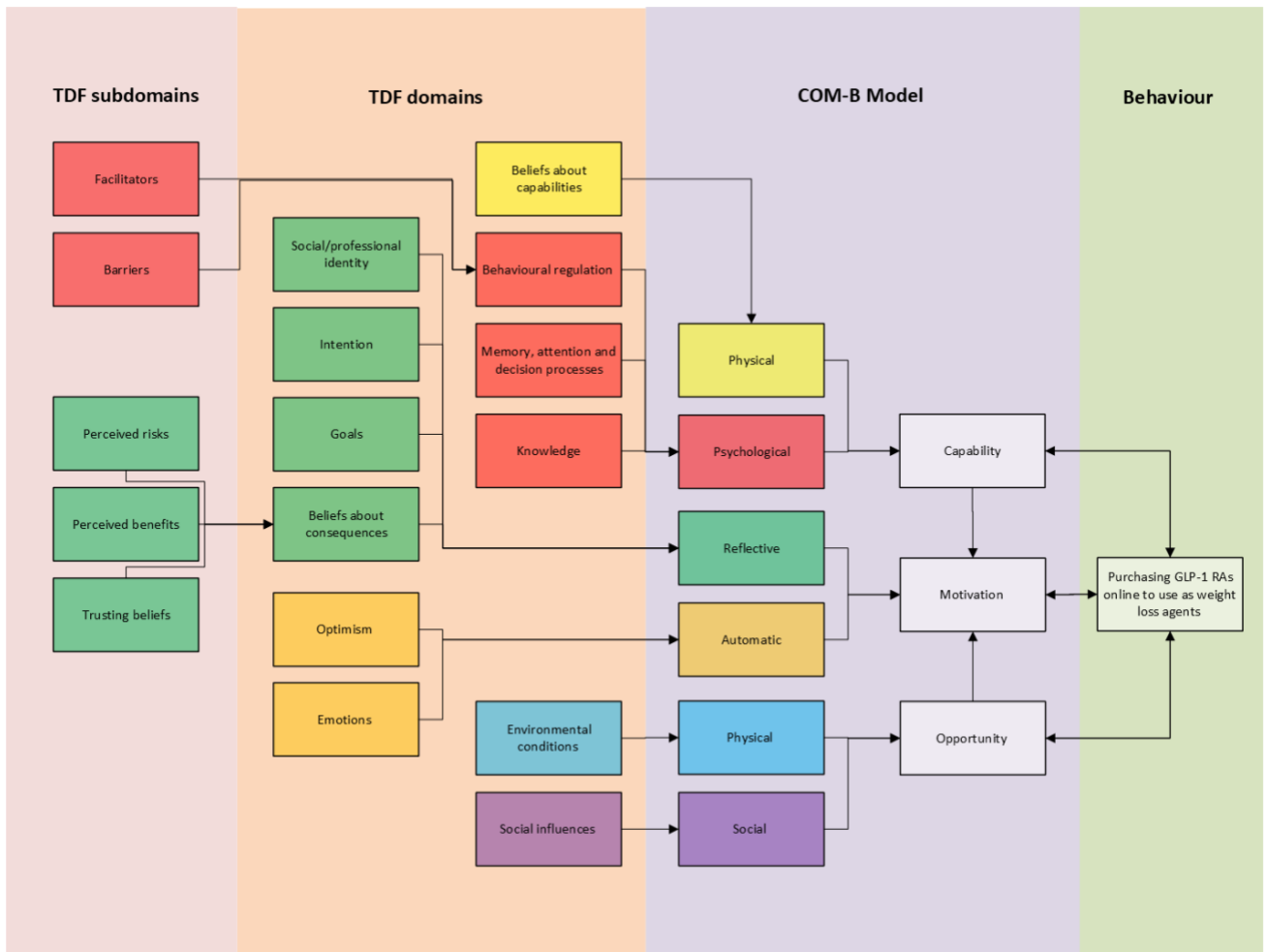


Figure 8. Integration model of TDF and COM-B Model, with the identified domains.

6.6 Strengths and limitations

Strengths

This study is the first study to date that explores the consumers behaviour of purchasing GLP-1 RAs online, without medical prescription. The research offers a comprehensive perspective on the various factors influencing individuals to purchase GLP-1 RAs online. Additionally, the study was guided by the COM-B Model and TDF, validated behavioural theories that enhance the validity and credibility of the research findings. Using behavioural science leads this research to be one of the few that research the behaviour of illegal online purchasing of pharmaceuticals with theoretical underpinning.

Limitations

Firstly, the potential stigma linked to the illegal purchase of prescription medicines online posed challenges in recruiting participants willing to discuss their experiences openly. Consequently, the study involved a limited number of participants, necessitating careful consideration as these individuals may represent only a fraction of views on the illegal purchase of GLP-1 RAs online. Furthermore, participants may have provided inaccurate answers during the interviews, possibly not reflecting their true opinions due to apprehension about potential consequences. Therefore, the findings of this study may not entirely mirror the broader perspective of consumers acquiring GLP-1 RAs online.

Secondly, while thematic analysis was utilized in this research, it is essential to acknowledge the interpretive nature of the COM-B Model and the TDF. This introduces subjectivity in categorizing specific beliefs into theoretical domains, as evidenced by discussions between the researcher and HW. Different opinions arose regarding the categorization of specific beliefs, which are outlined in the Results section.

This brings attention to the third and final limitation; the absence of a second researcher to code the interview transcriptions. This was due to the relatively short duration of the research. Although a second researcher did not code the interviews, HW also categorized the coded specific beliefs into corresponding theoretical domains of the TDF and provided feedback, which was considered by the researcher.

7. Conclusion

In conclusion, the integration of the COM-B Model and TDF, alongside the BCW approach, as provided a comprehensive understanding of the determinants influencing the online purchase of GLP-1 RAs without medical prescription. This research presents a conceptual framework illustrating the interactions between these determinants and their influence on the target behaviour, as depicted in Figure 8. By mapping the TDF domains onto the COM-B Model, intervention functions and strategies using the BCW approach can be systematically selected, offering a theoretical-based approach to intervention design.

Dominant specific beliefs and their corresponding domains of the COM-B Model, shed light on the psychological, motivational, and social factors driving individuals' decisions regarding online GLP-1 RA purchases. Psychological capability, reflective motivation, and social opportunity emerged as dominant domains in the COM-B Model.

Regarding the risks associated with GLP-1 RA use and online purchasing of prescription medicines, participants expressed a notable lack of concern despite potential health hazards. This optimism towards perceived risks aligns with earlier research findings, suggesting that consumers may be enticed by the benefits of online medicine purchases, especially in the face of shortages of these medicines.

Speaking of shortages, awareness of the global shortage of GLP-1 RAs did not inhibit participants from engaging in online purchasing behaviours. Instead, shortages were potentially perceived as a motivating factor, driving some individuals to seek alternative sources online instead of medical prescription, as observed in previous studies researching other groups of medicines.

In this research is found that the consumer behaviour or purchasing GLP-1 RAs online is a complex and multi-dimensional phenomenon that is influenced by various internal and external factors. This complexity arises from the multiple determinants that interfere with the eventual purchasing decision including cognitive processes, social factors, environmental factors, financial determinants, and emotions, which significantly increases the complexity of understanding the decision. The overarching interpretation of the behaviour of online buying GLP-1 RAs without medical prescription enables a deeper understanding, but it remains a complex phenomenon.

Strengths of this study lie in its pioneering exploration of consumer behaviour in purchasing GLP-1 RAs online, guided by the utilization of validated behavioural theories. However, limitations such as recruitment challenges and the subjective nature of theoretical domain categorization, must be acknowledged. Future research should acknowledge these limitations and aim to address them to further explore the complex dynamics underlying the behaviour of online purchasing prescription medicines.

In summary, this study contributes valuable insights into the multifaced determinants shaping the online purchasing behaviour of GLP-1 RAs, laying the groundwork for the development of targeted interventions and communication strategies to address this emerging public health concern.

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9. Appendix

Appendix 1

Semi gestructureerd interview schema

Introductie

Bedankt voor uw deelname aan het onderzoek.

Tijdens het vorige telefoongesprek hebben we de praktische zaken besproken en heeft u uw deelname bevestigd.

Ik zal nogmaals het doel van het interview benoemen. Ik doe onderzoek naar de motivatie om een afslankmiddel online te kopen, en wil daarom graag weten wat de invloeden zijn op de beslissing om uiteindelijk het medicijn online te kopen. De medicijnen waar ik geïnteresseerd in ben zijn bekend onder de merknamen Ozempic, Wegovy, Victoza, Saxenda.

Ter herhaling deelname is te allen tijde vrijwillig. U kunt altijd terugtrekken, ook al is het interview begonnen. Het interview zal ongeveer 20-30 minuten duren.

Na afronding van het interview noteer ik uw mailadres waarnaar ik de vergoeding op zal sturen. De vergoeding is een 15 euro VVV-cadeaubon.

Tenslotte worden alle antwoorden geanonimiseerd, uw naam wordt niet bekend gemaakt en niks is herleidbaar naar u als persoon.

Heeft u nog vragen voor mij?

Vervang GLP-1 RA door merknaam

Vragen

Bevestiging oneigenlijk gebruik GLP-1 RAs door illegaal online kopen

- Welk afslankmiddel heeft u online gekocht? Wat was uw ervaring met dit middel, wat vond u ervan? (bevestiging en diepgang over online aankoop GLP-1RA)

Motivatie (motivation) GLP-1 RA online kopen

- Waarom heeft u de GLP-1 RA gekocht? (reflective and automatic motivation)
- En waarom heeft u de GLP-1 RA online gekocht? (reflective and automatic

Uit literatuur blijkt dat mensen ook wel eens een GLP-1 RA online kopen omdat zij zich hopeloos of wanhopig voelen, omdat zij het niet voorgeschreven krijgen van de arts, of omdat er weinig van het middel beschikbaar is bijvoorbeeld.

motivation)

- In hoeverre herkent u het bovenstaande? Speelden er andere emoties een rol in de beslissing om de GLP-1 RA online te kopen? (automatic motivation)
- Wat waren de voordelen voor u om de GLP-1RA online te kopen? (reflective motivation)
- En wat waren de risico's voor u om het online te kopen? (reflective motivation)
 - En risico's met betrekking tot het gebruik van de GLP-1 RA? (bijwerkingen) (reflective motivation)
 - En eventueel de toedieningsvorm? (injectie) (reflective motivation)

Vermogen (capability)

- Hoe wist u van het bestaan van online verkoop van de GLP-1 RA? (psychological capability, social opportunity)
- Wat vond u van de website waar u de GLP-1 RA heeft gekocht? In hoeverre vertrouwde u de website, en waar kwam dit door? (mogelijk eerdere ervaringen of door hoe de website eruit zag) (psychological capability and reflective motivation)
- Waarom heeft u de keuze gemaakt om de GLP-1 RA online te kopen, in plaats van het te laten voorschrijven door een dokter? (psychological capability)
 - Wat maakt het online kopen van de GLP-1 RA voor u makkelijker dan het te laten voorschrijven door een dokter? (makkelijk om online te kopen, medicijnen thuis bezorgd, geen recept nodig) (facilitators, psychological capability)
 - Wat maakt het online kopen moeilijk voor u, zijn er barrières? (kost veel geld, moeilijke website, vertrouwde de website niet) (barriers, psychological capability)

Kans (opportunity)

- In hoeverre heeft uw omgeving een rol gespeeld in het kopen of de beslissing om te kopen van de GLP-1 RA online? (denk aan vrienden en/of kennissen die ervaring hiermee hadden) (social and physical opportunity)
 - Heeft u online gebruik gemaakt van hulp over het gebruik of het kopen van de GLP-1 RA online? (social opportunity)

Afsluiting

Geslacht en leeftijd:

Emailadres voor vergoeding (online VVV-cadeaubon):

Hartstikke bedankt voor uw deelname aan dit onderzoek. Het wordt gewaardeerd dat u de tijd heeft genomen om de vragen te beantwoorden. Ter herhaling, alle antwoorden worden anoniem verwerkt en de antwoorden zijn dus in geen enkele manier traceerbaar naar de persoon, u. Prettige dag verder.

Appendix 2

Oproeptekst versie 1

Koop jij online weleens een medicijn om af te vallen? En wil jij meedoen aan mijn onderzoek?

Uit onderzoek blijkt dat mensen steeds vaker online geneesmiddelen bestellen zonder recept van een arts. Zo ook met het doel om af te vallen. Denk dan bijvoorbeeld aan Ozempic, Wegovy, Victoza of Saxenda. Doe jij dat ook of ben jij dat van plan? Dan zoek ik jou voor mijn onderzoek.

Ik ben Ivy, een studente aan de Universiteit Utrecht, en ik ben bezig met de master Farmacie. Op dit moment ben ik bezig met mijn onderzoek aan de universiteit, over medicijnen die worden gebruikt om af te vallen. Ik wil graag weten waarom iemand ervoor kiest om online zonder recept van de arts een afslankmiddel te kopen. Als deze informatie bekend is, kan de communicatie over het veilig gebruik van deze medicijnen verbeterd worden. Daarom wil ik graag bij mensen die deze medicijnen online kopen een interview afnemen. Het is een telefonisch gesprek van ongeveer 20-30 minuten. Alle gegevens blijven anoniem en je kan je op elk moment terugtrekken uit het onderzoek. Heb je vragen over het onderzoek of interesse om mee te doen, stuur mij dan een privé-bericht of mail naar: ivy.onderzoek@gmail.com.

Alvast bedankt!

Appendix 3

Oproeptekst versie 2

Beste groepsleden,

Voor mijn opleiding Farmacie ben ik dringend op zoek naar mensen die weleens Ozempic, Saxenda, Victoza etc. online kopen, zonder recept van de arts. Als je van plan bent om de middelen online te kopen is dat ook goed. Ik wil graag telefonisch een interview van ongeveer een halfuur afnemen en als compensatie ontvang je een €15 VVV-cadeaubon!
emoji

Ben jij of ken jij iemand? Neem dan contact met me op en help mij met afstuderen! *emoji*

Appendix 4

Table 2

Theoretical domain	Subdomain	Specific belief	Sample quote Nederlands Translated to English	References
1. Skills	-	-	-	-
2. Memory, attention and decision processes	-	Hesitation beforehand about GLP-1 RA-use	-	3
		Individually conducting online research prior to GLP-1 RA-use	P2: <i>'Ik zou het eerst even zelf proberen, ik zou eerst... Even mijn eigen zoekvaardigheden gebruiken.'</i> <i>'I would first try it myself, I would first... Use my own searching skills.'</i>	2
		Self-financing the GLP-1 RA (1)	P3: <i>'Maar ja, ik zat er niet heel erg mee dat er tekorten aan [GLP-1 RAs] waren. Ik dacht vooral van, joh, als ik er zelf voor betaal is het toch prima.'</i> <i>'Well, I wasn't very bothered about the shortages [of GLP-1 RAs]. I mainly thought, if I pay for it myself, it's fine.'</i>	7
		Social identity associated with GLP-1 RA-use (2)	P1: <i>'Ik had wel op een gegeven moment dat ik wel even dacht van, oké, nee, moet ik hier wel aan beginnen? Is het wel wijsheid, kom ik wel niet over als een persoon die heel lui is?'</i> <i>'At some point I did start thinking, okay, do I really want to start this? Is it wise? Am I not going to come across as someone who is just very lazy?'</i>	3
		Rethinking the risks on physical health associated with GLP-1 RA-use (3)	P4: <i>'Ja, ik was er wel een beetje sceptisch erover. En ik dacht wel van ja, stel nou, het beïnvloedt mijn gezondheid heel erg. [...] Maar ja, als je het zo bekijkt... Voeding die we eten... Ja, dat is ook niet bepaald echt goed voor je.'</i> <i>'Yeah, I was a bit skeptical about it. And I did think, what if it really affects my health. [...] But if you look at it that way... The food we</i>	1

			<i>eat... Well, that's not exactly good for you either.'</i>	
3. Knowledge	-	Knowledge of possibilities about purchasing GLP-1 RAs through social media	<p>P3: <i>'Ik ging er eigenlijk zelf een beetje van uit dat ik dat wel kon vinden op Telegram. Ik heb zelf nog nooit eerder in mijn leven Telegram gebruikt, maar ik wist dus wel dat je er, ja, eigenlijk van alles kan kopen. Dat er een hele zwarte markt is.'</i></p> <p><i>'I assumed I could find it on Telegram myself. I have never used Telegram before in my life, but I did know that you can buy pretty much anything on there. There is a whole black market.'</i></p>	4
		Knowledge of reduced availability of GLP-1 RAs	<p>P2: <i>'Ja, mijn huisarts die zei van, van ja, omdat er ook wel een groot tekort aan is. Ook om die redenen hoor, dat was het dat ik op gegeven moment ook verder ben gaan zoeken.'</i></p> <p><i>'Yeah, my general practitioner said, well, because of the big shortage of it. It is also for those reasons, why I eventually started searching for other options.'</i></p>	3
		Familiarity with GLP-1 RAs, recognizing their use as diabetes treatment, and not primarily intended for the participant (10)	<p>P3: <i>'Nou, ja, ik klink misschien een beetje narcistisch, maar ik wist zelf ook heel goed dat het eigenlijk een medicijn is wat voor diabetes wordt gebruikt.'</i></p> <p><i>'Well, I might sound a bit narcissistic now, but I knew very well that it is actually a medicine used for the treatment of diabetes.'</i></p>	4
		Knowledge about the options to purchase GLP-1 RAs in countries beside the Netherlands	<p>P2: <i>'Maar hij kreeg het dus mee in België of Duitsland... Ik weet het niet. Uit één van die twee [landen] had hij het al meegekregen.'</i></p> <p><i>'He got it in Belgium or Germany... I'm not sure. He had already gotten it from one of those two [countries].'</i></p> <p>P3: <i>'Of ik kwam op van die Chinese websites terecht via onder andere TikTok, waar je het dan zou kunnen kopen.'</i></p>	5

			<i>'Or I ended up on those Chinese websites through TikTok or other platforms, where you could supposedly buy it.'</i>	
		Knowledge of not receiving medical prescription of the GLP-1 RA, without visiting a doctor. Basic knowledge of overweight or obesity diagnoses (4)	P4: <i>'Omdat ik dat via de huisarts eigenlijk absoluut niet zou meekrijgen, want ik heb geen obesitas. Ik had een beetje over[gewicht].'</i> <i>'Because I would absolutely not get it through my general practitioner, because I am not obese. I was only a bit over[weight].'</i>	1
		Knowledge of not receiving medical prescription of the GLP-1 RA after visiting a doctor (4)	P2: <i>'Ik vond het een beetje jammer dat ik het niet via de huisarts kreeg omdat ze daar echt benadrukte dat er een tekort aan is en dat ik geen diabetes heb.'</i> ... <i>'Ja, want je krijgt het gewoon niet via de huisarts, al zou je zeg maar om smeken, zeg maar.'</i> <i>'I was a bit disappointed that I couldn't get it through the general practitioner because they really emphasized the shortage and that I don't have diabetes.'</i> ... <i>'Yeah, because you just won't get it through the general practitioner, even if you were to beg for it.'</i>	8
		Knowledge about injecting the GLP-1 RA (5)	P5: <i>'Ik had dat gewoon van mijn vader gezien en ook in mijn familie... Was gewoon een spuitje.'</i> <i>'I had seen it from my father and also the rest of my family... It was just an injection.'</i>	6
4. Behavioural regulation	Facilitators	Receiving guidance of healthcare providers on GLP-1 RA-use	P2: <i>'Ik had liever gehoopt via mijn huisarts was, dan ging het nog makkelijker in die zin. Toch wel, maar als het ook begeleid kan worden via een andere weg, waarom niet?'</i> <i>'I would have preferred it was through my general practitioner, it would have been easier in that sense. But still, if it can be guided in another way, why not?'</i>	4

		Convenience purchasing GLP-1 RA online, saving effort	<p>P1: <i>'...en ik denk ook wel een stukje gemak want je hoeft in feite, maar op twee knoppen te drukken.'</i></p> <p><i>'...and I also think it's a bit of convenience because, basically, you only have to press two buttons.'</i></p> <p>P5: <i>'Ik bestel echt alles online, kleertjes en van alles. Ja, het is praktischer en handiger eigenlijk.'</i></p> <p><i>'I order everything online, clothes and everything. It's more practical and convenient, actually.'</i></p>	7
		Convenience purchasing GLP-1 RA online, saving time	<p>P4: <i>'Ja, je krijgt het gewoon snel in handen eigenlijk. Je bestelt het en... En dan wordt het geregeld en het wordt opgestuurd, zeg maar.'</i></p> <p><i>'Yeah, you just receive it quickly. You order it and... And it is taken care of, and it is sent your way.'</i></p>	4
		Easier to lose weight using the GLP-1RA than other healthy ways	<p>P4: <i>'Het is wel makkelijk om zo af te vallen, dan hoef je minder moeite te doen...'</i></p> <p><i>'It is easy to lose weight this way, you don't have to put in as much effort...'</i></p>	2
		Purchasing online provides security of GLP-1 RAs availability for the purchaser	<p>P2: <i>'Het enige voordeel is dus dat je het kan kopen, en dan kan krijgen. Dat is het enige voordeel; dat als het beschikbaar is, dat je het kan krijgen.'</i></p> <p><i>'The only benefit is that you can buy it, and then receive it. That is the only benefit; that if it's available, you can expect to get it.'</i></p>	6
		No need to show self when purchasing GLP-1 RA online. Not wanting to show self because of shame for appearance (6)	-	1
		No need for prescription because of the knowledge they	<p>P2: <i>'Ja, je krijgt geen nee. Het is niet alsof een online dokter tegen je zegt, ja, heb nu wel echt diabetes?'</i></p>	9

		did not or would not get the GLP-1 RAs prescribed (4)	<p><i>Of wat dan ook. Dat is het dus niet.'</i></p> <p><i>'Yeah, you don't get a 'no'. It's not like an online doctor is asking you, do you really have diabetes? Or anything like that. That's not how it is.'</i></p>	
	Barriers	Self-financing the GLP-1 RA (1)	<p>P2:</p> <p><i>'Het is duurder, je krijgt het niet vergoed. Ja, dat is het voornaamste waar ik nu een beetje tegenaan hik.'</i></p> <p><i>'It is more expensive, and you have to pay for it yourself. Yeah, that's my main issue that I'm currently struggling with.'</i></p>	7
5. Beliefs about capabilities	-	Injecting the GLP-1 RA (5)	<p>P3:</p> <p><i>'Klopt, inderdaad ja, want het was inderdaad een injectie en ik dacht van joh, stel dat ik het nou op een verkeerde plek toedien of dat ik niet diep genoeg ga met die naald of juist te diep, of ja... Ja, daar zat ik ook wel een beetje aan te denken steeds.'</i></p> <p><i>'Exactly, indeed. Because it was indeed an injection, and I thought, what if I inject it in the wrong place, or if I don't go deep enough with the needle, or too deep, or... Yeah, I was thinking about that all the time.'</i></p> <p>P5:</p> <p><i>'Ik had dat gewoon van mijn vader gezien en ook in mijn familie... Was gewoon een spuitje. [...]. Dus ik heb dat gewoon ingespoten in mijn buik.'</i></p> <p><i>'I had seen it from my father, and also the rest of my family... It was just an injection. [...]. So, I just injected it into my abdomen.'</i></p>	6
		Lack of belief of their ability to lose weight by themselves	<p>P3:</p> <p><i>'Maar ja, toen had ik ook van, joh, het is me al zo vaak niet gelukt [om zelf af te vallen]. Waarom zou het me nu wel zelf lukken?'</i></p> <p><i>'But well, then I also thought, I have failed so many times [trying to lose weight] on my own. Why would I succeed this time?'</i></p>	1

6. Optimism	-	Optimistic about purchasing the GLP-1 RA online	<p>Researcher: <i>'Waren er dingen die het online kopen juist moeilijk voor je maakten?'</i></p> <p><i>'Were there any things that made online purchasing difficult for you?'</i></p> <p>P5: <i>'Nee eigenlijk niet, want ik ben nog jong en ik koop vaak online zoals ik zei. Online kopen is echt iets voor mij, ik doe dat graag.'</i></p> <p><i>'Not really, because I am still young and I often buy something online, as I have said before. Online shopping is really my thing, I enjoy doing it.'</i></p>	1
		Optimistic about the side effects associated with GLP-1-RA-use	<p>P3: <i>'En wat ik het meeste kon vinden is dat je allerlei darm- en nierfalen kon krijgen. Maar zelfs dat nam ik voor lief en ik dacht van joh, de kans dat dat gebeurt na één keer is vast niet zo groot.'</i></p> <p><i>'And what I mostly found is that you could get all sorts of intestinal and kidney failures. But even that I took for granted, and I thought, the chances of that happening after just one use are probably not that high.'</i></p> <p>P4: <i>'Maar ik ben eigenlijk wel van nature een persoon met een hele hoge pijngrens. Dus ik dacht van, oh, ik kan het [de bijwerkingen] wel aan, zal vast niet zo erg zijn. Dus ik had het een beetje onderschat.'</i></p> <p><i>'But naturally, I am a person with a very high pain threshold. So, I thought, oh, I can handle it [the side effects], it cannot be that bad. So, I had underestimated that a bit.'</i></p>	3
		Optimistic about efficacy of GLP-1 RAs	<p>P1: <i>'Maar ja, uiteindelijk, ja, ben je er zo van overtuigd dat het helpt en dat je dus er iets aan hebt, waardoor je uiteindelijk toch een keuze maakt om de producten uit te proberen en dus te kopen.'</i></p>	2

			<i>'Well, in the end, yeah, you're so convinced that it helps and that you'll benefit from it, which eventually leads you to make the choice to try and buy the products.'</i>	
7. Beliefs about consequences	Perceived risks	Risks on physical health after using the GLP-1RAs (3)	<p>P4: <i>'Ja, ik was er wel een beetje sceptisch erover. En ik dacht wel van ja, stel nou, het beïnvloedt mijn gezondheid heel erg... En dat kan nog steeds. Kijk, we kunnen niet in ons lichaam kijken. Ik weet niet wat voor dingen het heeft gedaan met mijn lichaam.'</i></p> <p><i>'Yeah, I was a bit skeptical about it. And I did think, what if it really affects my health... And that can still happen. Look, we can't look inside our bodies. I don't know how it exactly affected my body.'</i></p>	1
		Side effects of the GLP-1RA	-	7
		Risks associated with not receiving an original product when purchased online	<p>P3: <i>'En natuurlijk ook... Ik dacht, van ja, iedereen kan zeggen dat het juiste medicijn is, maar voor hetzelfde geld zit er heel wat anders in.'</i></p> <p><i>'And of course... I thought, well, anyone can claim that it is the right medicine, but for all you know, it can contain something completely different.'</i></p> <p>P4: <i>'Ja, kijk, ik wist niet zeker of het een echt origineel product was. Dus dat kan ook natuurlijk uit China of namaak of iets zijn.'</i></p> <p><i>'Yeah, you see, I wasn't sure if it was the original product. So, it could be from China or a counterfeit or something.'</i></p>	2
		Risks associated with the usage of medication in general	<p>P2: <i>'Anders had ik het denk ik niet gedaan, hoor. Nee, zeker niet nee. Want het blijft, uhm, het blijft een medicijn, of hoe je het kan noemen.'</i></p> <p><i>'Otherwise, I would not have done it. No, definitely not. Because it is, uhm, it is still a medicine, or however you want to call it.'</i></p>	1

		Not foreseeing risks purchasing GLP-1 RA online	<p>Researcher: <i>'Oké, en zijn er voor jou risico's om het online te kopen?'</i></p> <p><i>'Okay, and were there any risks for you to purchase it online?'</i></p> <p>P2: <i>'Nee, niet zo zeer. Omdat mijn omgeving het heeft gedaan, denk ik dat ik daar geen risico's in zie.'</i></p> <p><i>'No, not really. Because people in my close surroundings have done it, I think I don't see any risks in it.'</i></p>	4
	Perceived benefits	Ability to choose type of GLP-1 RA	<p>P3: <i>'Ook was ik helemaal gefixeerd op Ozempic en dat zou dus niet worden vergoed. Het ging echt om Wegovy, dus ik dacht van, nou ja, ik kan dat [levensstijl interventie programma] dan wel een jaar doen, maar dan krijg ik nog niet wat ik wil. Dus ik dacht van... Ik, ik neem het lot in eigen handen.'</i></p> <p>...</p> <p><i>'De arts met wie ik had gesproken van de huisartsenpost vertelde me ook echt van, joh, Wegovy doet echt hetzelfde als Ozempic, het is gewoon een ander merk. Maar goed, als je zo gefixeerd bent op een bepaald iets en daar zoveel informatie over binnenkrijgt... Ja, dan wil je ook niet meer anders horen.'</i></p> <p><i>'Also, I was fully focused on Ozempic, and I would have to pay for that myself anyway. It was really about Wegovy, and I thought, well, I can follow that [lifestyle intervention program] for a year, but after that I still won't get what I really want. So, I thought... I, I'll take matters into my own hands.'</i></p> <p>...</p> <p><i>'The general practitioner I spoke in the general practice center told me Wegovy does the exact same thing as Ozempic does, just with a different brand name. But well, if you're so fixated on a specific thing and you receive so much information about that... Yeah, then you don't really want to hear anything else.'</i></p>	4

		Online purchasing provides privacy (11)	<p>P5: <i>'Dus als ik bijvoorbeeld naar de huisarts ging voor de Ozempic, en stel dat dat werd genoteerd in mijn dossier en zo, dat wou ik ook niet eigenlijk. Dus ik ging het gewoon online bestellen en... Dan weet ik het enkel zelf.'</i></p> <p><i>'So, if for example, I went to the general practitioner for Ozempic, and he would note that down in my dossier or something, I did not want that to happen. So, I just ordered it online and... I am the only one that knows.'</i></p>	3
		Possibility to start using the GLP1-RA immediately	<p>Researcher: <i>'En zag je op tegen de leefstijlinterventie [programma] of omdat het zo lang duurde?'</i></p> <p>P3: <i>'Ik was niet per se tegen dat leefstijlprogramma, maar wel het besteden van de tijd die het zou kosten.'</i></p> <p><i>And were you dreading the lifestyle intervention [program] or the time it would take?'</i></p> <p>-</p> <p><i>'I wasn't against the lifestyle program per se, but I was against spending the time it would take.'</i></p> <p>P4: <i>'Het ging waarschijnlijk, voor mijn gevoel, ging het ook veel sneller, want als je het via de huisarts doet moest je door een controle.'</i></p> <p><i>'It probably, in my opinion, went much faster, because if you get it through the general practitioner, you would have to go through a check.'</i></p>	6
		No need for following a lifestyle-intervention program before GLP-1 RA-use (which is mandated when medically prescribed)	-	2

		Losing weight using the GLP-1RA is faster than following other methods	<p>P5: <i>'En ik wou toen ook afvallen en we gingen op vakantie. En ik weet dat je van bepaalde diëten minder snel kan afvallen in plaats van Ozempic.'</i></p> <p><i>'And then I also wanted to lose weight and we were going on holiday. And I knew that you could lose weight faster using Ozempic instead of following various diets.'</i></p>	1
	Trusting beliefs	Increased confidence about GLP-1 RAs efficacy based on use in close environment (7)	<p>P2: <i>'En hij [een vriend] zei dat hij zelf ook iets van 10 kilo ervan was afgevallen, toen dacht ik, nou, weet je, ja, het werkt dus echt wel. Tenminste het kan echt werken. Ik kan me niet voorstellen dat het bij hen werkt en dan dat ik de enige persoon ben waarbij het niet werkt.'</i></p> <p><i>'And he [a friend] told me he himself lost about 10 kilograms with it, and so I thought, well, you know, it really works. At least, there's a possibility it really works. I can't imagine that it works for them and I'm the only person for whom it does not work.'</i></p>	4
		Secure payment option	<p>P3: <i>'Er werd me ook, en dat hielp eraan mee dat ik het helemaal niet vertrouwde, er werd me meerdere malen gevraagd of ik via Bitcoin kon betalen.'</i></p> <p><i>'At one point, I was asked several times if I could pay with Bitcoin, and that facilitated in me not trusting it at all.'</i></p>	2
		Trust seller of the GLP-1RA	<p>P3: <i>'Ja, ik vertrouwde het eigenlijk helemaal niet. Ik vond het bizar sketchy. Het was allemaal anoniem. Ik wilde ook eigenlijk niet dat zij mijn adres wisten, want ik dacht van joh, weet jij veel wat voor gekken daarop zitten. Maar ik mocht het ook absoluut niet ergens afhalen of wat dan ook. Ik mocht het ook niet komen ophalen bij hen thuis.'</i></p> <p><i>'Yeah, I didn't trust it at all. I thought it was extremely sketchy. It was all anonymous also. I actually</i></p>	4

			<p><i>didn't want them to know my address, because I thought, well, you never know what kind of crazy people use this platform. But I was definitely not allowed to pick it up somewhere or something. I wasn't allowed to come pick it up at their house either.'</i></p> <p>Researcher: <i>'Zag je risico's in het online kopen?'</i></p> <p>P4: <i>'Ik was er niet echt bang voor omdat het wel, zeg maar, via een bekend persoon, bekende influencer-achtig iets was.'</i></p> <p><i>'Did you think about the risks of purchasing online?'</i> - <i>'I wasn't really nervous about that because, you know, it was through a well-known person, some kind of famous influencer-person.'</i></p>	
		Trust purchasing environment	<p>P5: <i>'Op school hebben we geleerd van, als dat bijvoorbeeld begint met HTTP... En ik had zo'n extensie gedownload en als dat zo niet een beveiligde website ofzo is... [...]. Ik heb zo dat voorgevoel wel en ik dacht van, het is een betrouwbare site. En het was een betrouwbare site.'</i></p> <p><i>'At school we learned that if a website for example starts with HTTP... And I had downloaded some kind of extension, and if it didn't was a safe website... [...]. I just have some kind of feeling for that and I thought, this is a safe website. And it was a safe website.'</i></p>	5
8. Goals	-	Using GLP-1 RA to lose weight (8)	-	4
9. Social/professional identity	-	Social identity of using the GLP-1 RAs (2)	<p>P2: <i>'Wat het online kopen moeilijker maakt? Nou ja, ik denk dat dat vooral een sociaal psychologische kwestie is, in mijn geval. Ik had wel op een gegeven moment voordat ik die pillen ging halen dat ik wel even dacht van, oké, nee, moet ik hier wel aan beginnen? Is het wel wijsheid, kom ik wel niet</i></p>	3

			<p><i>over als een persoon die heel lui is?’</i></p> <p><i>‘What made purchasing online more difficult? Well, I think in my case that is mainly a social psychological issue. At some point I did start thinking, okay, do I really want to start this? Is it wise? Am I not going to come across as someone who is just very lazy?’</i></p>	
10. Emotions	-	No emotions	-	1
		Shame	<p>P1: <i>‘Nee, ik denk dat bij mij echt wel de schaamte was, waardoor ik het, waardoor ik uiteindelijk heb gekozen om het online te bestellen.’</i></p> <p><i>‘No, for me, I think it was really the shame that eventually led me to purchase it online.’</i></p>	2
		Determination	<p>P5: <i>‘Quote?’</i></p> <p><i>‘I was scared in the beginning, but I just had to try it. I had to go on this holiday, and I just had to try it.’</i></p>	11
		Desperation to lose weight	<p>P3: <i>‘...dat heeft er wel een soort rol in gespeeld, dat ik eigenlijk altijd al heel graag iets aan mezelf wilde veranderen, maar gewoon niet wist hoe.’</i></p> <p><i>‘...that has played a role in it, that I have always wanted to change something about myself, but I just didn’t know how.’</i></p>	3
		Self-image (9)	<p>P2: <i>‘...en het ideaalbeeld van hoe een vrouw er eigenlijk bij moet lopen zeg maar. En ja, als dan... Ik had al, naar mijn eigen inziens... Pas ik niet in dat plaatje en dat wil je dan natuurlijk wel...’</i></p> <p><i>‘...and the ideal image of what a woman should look like. And yes, if... I already had, in my opinion... I don’t fit into that image and naturally you would want that...’</i></p> <p>P3: <i>‘Ik heb heel lang eigenlijk ‘gestruggled’ met mijn zelfbeeld, over mijn lichaam. Ik ben nooit</i></p>	6

			<p><i>echt heel slank geweest, of wat dan ook.'</i></p> <p><i>'I actually struggled with my self-image for a long time, about my body. I have never been very slim, or anything.'</i></p>	
		No need to show self. Not wanting to show self because of shame for appearance (6)	-	1
11. Reinforcement	-	-	-	-
12. Social factors	-	Social media	<p>P3:</p> <p><i>'Op social media het meeste. Daar zag ik 'before and after' filmpjes van mensen die het van de huisarts hadden gekregen.'</i></p> <p><i>'On social media the most. On there I saw 'before and after' videos of users that had it medically prescribed.'</i></p> <p>P4:</p> <p><i>'Het ging een tijdje heel erg viral hoor, want helemaal op social media ontplofte het met mensen die het verkochten. En toen dachten we van ja, weet je, wat doen het gewoon.'</i></p> <p>...</p> <p><i>'Ja best wel, want het is verkrijgbaar via social media, dus dan... Is het ook aantrekkelijker.'</i></p> <p><i>'For some time, it went really viral, it exploded all over social media with people selling it. And then we thought, you know what, let's just do it.'</i></p> <p>...</p> <p><i>'Yeah, because it was available on social media, so... That makes it more approachable.'</i></p>	20
		Mentioned by influencers	<p>P4:</p> <p><i>'We hebben ook een beetje op internet gekeken en toen zagen we dat beroemdheden zoals Kim Kardashian en Kylie Jenner dat ook gebruiken en andere beroemdheden ook, om te af te vallen, om slank te zijn. En toen dachten we van, ja, we kunnen het proberen.'</i></p> <p><i>'We also did some research online, and then we saw that</i></p>	5

			<p><i>celebrities like Kim Kardashian and Kylie Jenner also use it to lose weight and to be slim, and other celebrities too. And then we thought, yeah, we could try it.'</i></p>	
		Friends	<p>P1: <i>'En waar het bij mij mijn sociale kring... In dat opzicht, met name met mijn vriendenkring, heeft daar een rol in gespeeld. Als ik zo naar mijn vriendenkring kijk dan zijn het over het algemeen allemaal mensen die zo in een modeblad kunnen zeg, maar die hebben gewoon de standaarden van... Ja, eigenlijk de sociaal maatschappelijke standaarden die gezet worden voor schoonheid en het ideaalbeeld zeg maar. Ja, ja, en hoe je het wendt of keert, ja... Je gaat jezelf er toch mee vergelijken.'</i></p> <p><i>'And for me, in my social circle... In that sense, especially with my circle of friends, that has played a role in it as well. When I look at my friends, they are generally all persons who could easily be in a fashion magazine, they simply have the standards of... Yeah, just the social standards that are set for beauty and the ideal image. Yeah, and no matter how you look at it... Eventually you're going to compare yourself with them.'</i></p> <p>P2: <i>'En hij [een vriend] zei dat hij zelf ook iets van 10 kilo ervan was afgevallen.'</i></p> <p>... <i>'...dat heeft er ook wel voor doen zorgen dat... [...] Dat hij ook met zijn resultaten mij weer wat meer positief heeft beïnvloed.'</i></p> <p><i>'And he [a friend] said he himself had lost about 10 kilograms.'</i></p> <p>... <i>'...that also influenced... [...] That also influenced me to be more positive, through his results.'</i></p>	4
		Family	<p>P1: <i>'Mijn familie en dan met name mijn moeder, die wist ervan en die die wilde eigenlijk absoluut niet dat ik</i></p>	26

			<p><i>dat ging doen, maar goed. Ja, je kon me natuurlijk niet tegenhouden in die zin.'</i></p> <p><i>'My family, and especially my mother, knew about it, and absolutely did not want me to use it, but well, yeah. Naturally she couldn't stop me.'</i></p> <p>P2: <i>'Ik heb het naar aanleiding van mijn nicht gedaan, want mijn nicht die had het dus aangeraden, want zij is zelf 5 kilo ermee afgevallen. Toen zei ze tegen mij van, ja, waarom kan je dit dan niet proberen? Als je dan toch [wil afvallen]. Dus zodoende ben ik er wel echt gewoon naar gaan zoeken.'</i></p> <p><i>'I did it, influenced by my niece, because she recommended it, because she herself lost 5 kilograms with it. Then she said to me, why don't you try this as well? If you want [to lose weight]. That lead me to really start my search.'</i></p> <p>P3: <i>'Dus ik had eigenlijk al ja, zo lang als ik me kan herinneren, opmerkingen gekregen van mijn omgeving, ook van familie, over mijn lichaam. Dus dat heeft er wel een soort rol in gespeeld [...].'</i></p> <p><i>'So, for as long as I can remember, I had received comments about my body, from my family as well. That has played some kind of role in it [...].'</i></p> <p>P4: <i>'Ik heb Ozempic gekocht omdat in mijn familie er een aantal mensen zijn, onder andere mijn oma en mijn moeder, die diabetes hebben en zij slikken [spuiten] dat ook. Maar dat is echt... Zij hebben dat voorgeschreven gekregen van de huisarts. [...]. En dus, wij hebben... Ik heb het eigenlijk ook niet alleen gedaan. Mijn nicht en mijn zus hebben het ook gedaan. En we hebben het eigenlijk bij hen (familie, moeder en oma) gezien.'</i></p>
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			<p><i>Toen zagen we dat er een mogelijkheid was om het te kopen. Via Turkije en dan via Turkse mensen in Duitsland. En toen dachten we van ja, waarom niet? En we willen toch afvallen.'</i></p> <p><i>'I bought Ozempic because there are several people in my family, including my grandmother and mother, who have diabetes and they also take [inject] it. But that... It was medically prescribed for them. [...]. And so, we... I didn't do it by myself actually. My niece and sister did it too. And we saw them [family, grandmother and mother] use it. Then there was an opportunity to buy it in Turkey, and then we would receive it through Turkish people in Germany. So, we thought, well, why not? We still wanted to lose weight.'</i></p> <p>P5: <i>'Echt veel, ja, want ik hoorde echt veel positieve verhalen. Van vrouwen meestal, die waren afgevallen en ook positief. En ik zag dat ook want het is mijn familie, en ik ken hen sowieso. Ik zag dan ook dat die kilo 's echt weg waren. Daarom heb ik het ook geprobeerd.'</i></p> <p><i>'A lot, because I heard a lot of positive stories. Mostly from women, who had lost weight with it, who were also positive. And I could see it too, because they are my family, and naturally I know them. I could see the kilograms were really gone. That's why I decided to try it too.'</i></p>	
		<p>Increased confidence about GLP-1 RAs efficacy based on use in close environment (7)</p>	<p>P2: <i>'En hij [een vriend] zei dat hij zelf ook iets van 10 kilo ervan was afgevallen, toen dacht ik nou weet je weet, ja. Ja, het werkt dus echt wel. Tenminste het kan echt werken. Ik kan me niet voorstellen dat het bij hen werkt en dan dat ik de enige persoon ben waarbij het niet werkt.'</i></p> <p><i>'And he [a friend] told me he himself lost about 10 kilograms from it, and so I thought, well, you</i></p>	<p>4</p>

			<i>know, it really works. At least, there's a possibility it really works. I can't imagine that it works for them and I'm the only person for whom it does not work.'</i>	
		Self-image (9)	<p>P2: <i>'...en het ideaalbeeld van hoe een vrouw er eigenlijk bij moet lopen zeg maar. En ja, als dan... Ik had al, naar mijn eigen inziens... Pas ik niet in dat plaatje en dat wil je dan natuurlijk wel...'</i></p> <p><i>'...and the ideal image of what a woman should look like. And yes, if... I already had, in my opinion... I don't fit into that image and naturally you would want that...'</i></p> <p>P3: <i>'Ik heb heel lang eigenlijk 'gestruggled' met mijn zelfbeeld, over mijn lichaam. Ik ben nooit echt heel slank geweest, of wat dan ook.'</i></p> <p><i>'I actually struggled with my self-image for a long time, about my body. I have never been very slim, or anything.'</i></p>	6
		Purchasing GLP-1RAs with someone together	-	1
		Logarithm on social media	<p>P3: <i>'Nou, ja, ik denk... Ik denk dat niet per se, maar wel gewoon van die accounts waarbij je dan ja, hoe vaker je het 'likt' of hoe langer je die filmpjes bekijkt, des te meer krijg je zulke content te zien. Dus je rolt er als het ware er een beetje vanzelf in.'</i></p> <p><i>'Well, yes, I think... I don't necessarily think so, but it's just those accounts, the more you 'like' or the longer you watch their content, the more you get such content recommended. So, you kind of naturally end up in it.'</i></p>	1
		Increased insecurity by comparison with others in social groups	-	3
		The need for more information about	<p>P2: <i>'Maar ook toen ik zei van, je mag mijn PM, privébericht, sturen [voor</i></p>	4

		use of GLP-1RAs on social media	<p><i>het interview], was jij niet de enige die gelijk mij een privébericht had gestuurd. Er waren ook gelijk andere meiden die mij een privébericht hadden gestuurd. [...] Dat gaat heel snel. En ja, en met de vraag van, oh, waar heb jij dan vandaan en kan je mij dan helpen? Et cetera, et cetera, dus... Nee, ik heb zelf geen hulp gezocht via sociale media, of wat dan ook. Maar er wordt wel hulp aan mij gevraagd heb ik meteen gemerkt.'</i></p> <p><i>'Even when I said, you can send me a PM, private message [for the interview], you were not the only one to immediately sent me a private message. There were also other girls who had sent me a message. [...] That goes very quickly like that. Yeah, with questions asking where I purchased it and if I could help them, et cetera, et cetera, so... No, I did not seek any help myself on social media platforms, or something. But I did notice that people immediately were asking me for help.'</i></p>	
		There have been no social influences in the decision to purchase the GLP-1 RA	<p>P5: <i>'Niemand heeft me echt gemotiveerd om het online te kopen. Ik heb het gewoon gehoord en ik heb dat gewoon gedaan.'</i></p> <p><i>'Nobody motivated me to purchase it online. I just heard it and then I just bought it.'</i></p>	5
		Familiarity with GLP-1 RAs, recognizing their use as diabetes treatment, and not primarily intended for the participant, recognizing social norms (10)	<p>P5: <i>'Aan de ene kant begrijp ik wel dat niet iedereen dat eigenlijk moet gebruiken, want het is vooral eigenlijk voor de diabetespatiënten en zij krijgen sowieso als eerste voorkeur. Ik snap het volledig, dat dat niet aan iedereen wordt uitgedeeld eigenlijk.'</i></p> <p><i>'On the one hand, I do understand that not everyone should use it, because it is mainly for diabetes patients, and they naturally receive priority. I fully understand that it is not distributed to everyone just like that.'</i></p>	4
13. Environmental conditions	-	Mentioning on the news	P3:	3

			<p><i>'Het is wekelijks wel weer in het nieuws, dus daardoor dacht ik eigenlijk van, oh, dat is echt gewoon... 'The way to go.'</i></p> <p><i>'It was on the news weekly, leading me to think that this was really... The way to go.'</i></p> <p>P5: <i>'Maar wel via het nieuws. En ook van, via Ozempic zijn heel veel mensen afgevallen.'</i></p> <p><i>'On the news a lot. In the sense of, many people have lost weight by using Ozempic.'</i></p>	
		Tight schedule, no time to lose weight in a healthy way	<p>P1: <i>'Ik was de afgelopen tijd bezig om een aantal kilo's kwijt te raken, en met mijn drukke schema die ik heb met werk en met studeren en het sociaal leven eromheen, heb ik niet altijd tijd om te sporten. Dus toen had ik dat ook besloten, om aan die pillen te beginnen.'</i></p> <p><i>'I have been trying to lose a few kilograms lately, and with my busy schedule with work and studying, and my social life, I don't always have the time to exercise. So that's when I decided to start taking those pills.'</i></p>	2
		Mentioning in environment (not specified)	<p>P3: <i>'Omdat ik er eigenlijk heel veel over had gelezen en over had gehoord. Ja, je zag het ook natuurlijk overal om je heen.'</i></p> <p><i>'Because I actually read a lot about it and heard a lot about it too. Yeah, at some point you saw it everywhere around you.'</i></p>	9
		Knowledge of not receiving medical prescription of the GLP-1 RA, with or without visiting a doctor (4)	<p>P2: <i>'Ik vond het een beetje jammer dat ik het niet via de huisarts kreeg omdat ze daar echt benadrukte dat er een tekort aan is en dat ik geen diabetes heb.'</i></p> <p>...</p> <p><i>'Ja, want je krijgt het gewoon niet via de huisarts, al zou je zeg maar om smeken, zeg maar.'</i></p> <p><i>'I was a bit disappointed that I couldn't get it through the general practitioner because they really</i></p>	9

			<p><i>emphasized the shortage and that I don't have diabetes.'</i></p> <p>...</p> <p><i>'Yeah, because you just won't get it through the general practitioner, even if you were to beg for it.'</i></p>	
		Online purchasing provides privacy (11)	<p>P1:</p> <p><i>'En ik dacht ja, als ik het online bestel is het heel discreet. Ja, ziet niemand het. En dan hoef ik mijn gezicht ook nergens te laten zien, zeg maar.'</i></p> <p><i>'And I thought, well, if I order it online, it can be done discretely. Nobody can see it. And I don't have to show my face anywhere.'</i></p>	3
14. Intention	-	Using GLP-1 RA to lose weight (8)	-	4
		Self-regard	<p>P3:</p> <p><i>'Nou, ja, ik klink misschien een beetje narcistisch, maar ik wist zelf ook heel goed dat het eigenlijk een medicijn is wat voor diabetes wordt gebruikt. Maar ja, ik zat er niet heel erg mee dat er tekorten aan waren. Ik dacht vooral van, joh, als ik er zelf voor betaal is het toch prima.'</i></p> <p><i>"Well, I might sound a bit narcissistic now, but I knew very well that it is actually a medicine used for the treatment of diabetes. Yeah, it didn't really bother me that there were shortages of it. I mainly thought, well, if I pay for it myself, it's fine.'</i></p> <p>P5:</p> <p><i>'Ja ja, maar ik zei al, ik dacht daar echt niet aan. Mijn eerste ding was, dat was echt afvallen.'</i></p> <p><i>'Yeah, yeah, but as I had said before, I was not really focused on that. My main thing was losing weight first.'</i></p>	4
		Unwilling to make the effort for healthy weight loss	<p>P4:</p> <p><i>'Omdat ik te lui was om het zelf te proberen [afvallen]. Eigenlijk hoort dat echt niet maar... Ja, dat is wel eigenlijk waar het op neer kwam. Ik was gewoon een beetje te lui. Dus ik dacht van, ja, ik wil gewoon afvallen en iedereen doet het. Dus, waarom zou ik het niet doen?'</i></p>	1

			<p><i>'Because I was too lazy to make an effort by myself [to lose weight]. And I know that is actually not okay... But, yeah, that is what it came down to. I was just too lazy. So, I thought to myself, I want to lose weight, and everyone is doing it. Why shouldn't I do it then?'</i></p>	
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