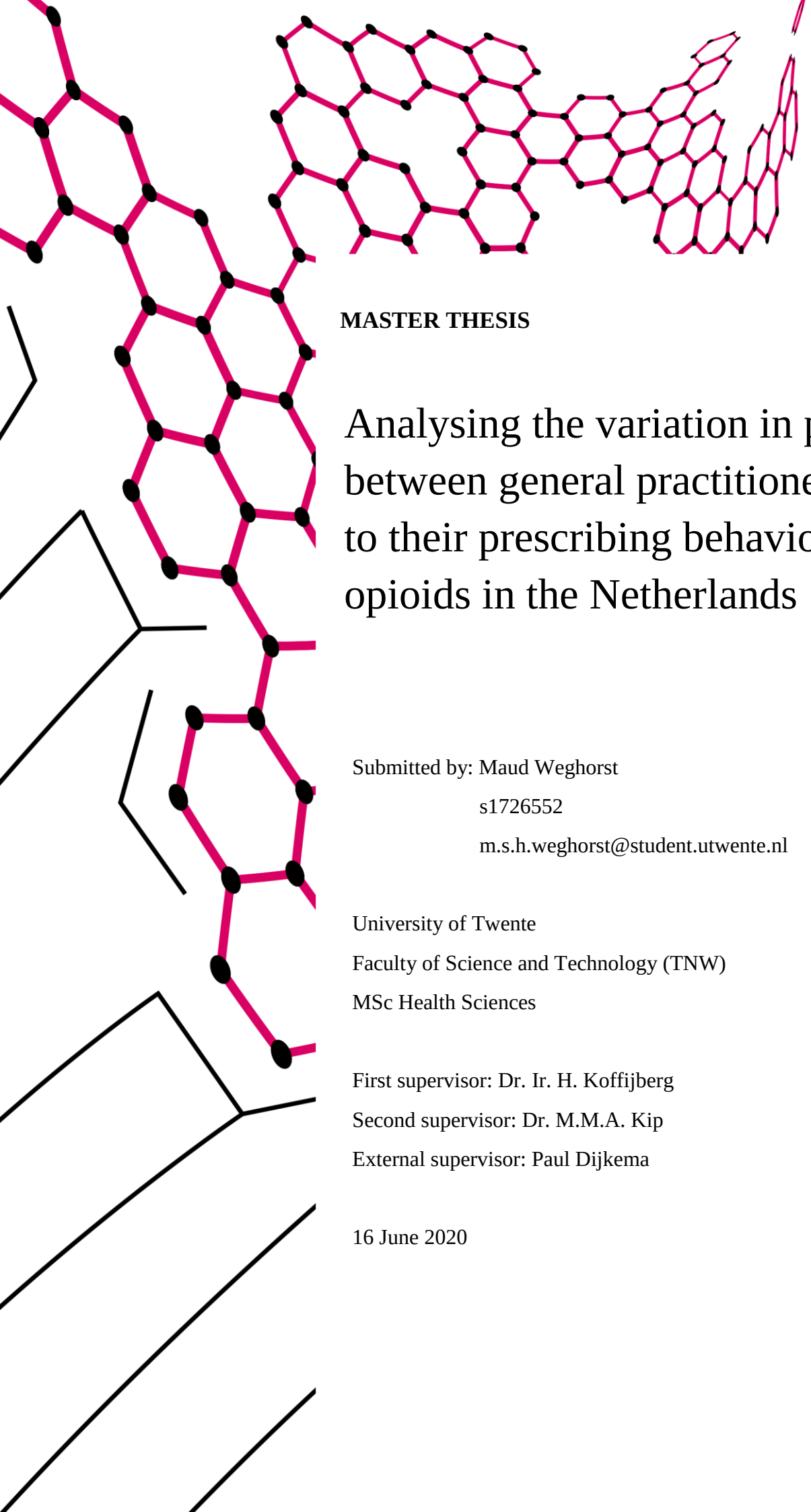

MASTER THESIS

Analysing the variation in practice between general practitioners according to their prescribing behaviour of opioids in the Netherlands

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In front of you lies the master thesis "Analysing the variation in practice between general practitioners according to their prescribing behaviour of opioids in the Netherlands". This thesis is the final product of the master program Health Sciences with the specialization Optimization of Healthcare Processes at the University of Twente. I have written this thesis in the period of the 5th of June 2019 till the 16th of June 2020. In this period I performed two master theses; one for the master Health Sciences and one for the master Business Administration.

Company X already performed a study on the opioid (mis)use in the Netherlands. Since this required further study into this topic, I conducted this follow-up research. During my thesis I have been supported by Paul Dijkema. He created a personalized database in which I was able to perform analyses and give insight in the variation in practice in opioid use of the Company X population. Therefore, I would like to thank him for his time and effort.

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Finally, I would like to thank my friend, family and friends for their interest in my research, their valuable feedback and their support to bring this thesis to a successful end.

I hope you will enjoy reading this thesis.

Maud Weghorst
Almelo, June 2020

Abstract

Introduction Millions of people worldwide are suffering from pain and opioids are prescribed for this problem more and more often. Opioid use in chronic pain treatment is complex, as patients may derive both benefit and harm. Opioids were previously used during and after surgeries and for pain relief for patients with cancer. However, in recent years opioids also have been prescribed to patients with pain that is not related to surgery pain or cancer pain. This has led to an increase in the prescription of opioids such as oxycodone, morphine and fentanyl. The overuse of opioids and the associated consequences, such as addiction, can lead to large healthcare expenditures. Due to differences in socioeconomic status, the opioid use and prescribing patterns of general practitioners varies between municipalities in the Netherlands.

Aim Get insight in the variation in practice between general practitioners according to their prescribing behaviour of opioids in the Netherlands.

Methods This study is a quantitative study whereby descriptive statistics are used to give an overview of the variation in practice between opioid use and opioid prescription behaviour in the Netherlands. The data that is used is retrospective and is available through the declaration database of Company X. To get information about the socioeconomic status of inhabitants in the Netherlands, the database of CBS Statline is used. The data is based on all Dutch persons from all ages who were insured at Company X in 2018. Both the declaration data from Company X and CBS Statline data is imported in Microsoft Excel to perform descriptive statistical analyses.

Results There were in total 774.463 declarations of opioids in 2018, where 487.185 of the declarations (63%) were for women and 287.278 of the declarations (37%) were for men. All these declarations were for 142.605 different users. The age category 95-100 has relatively the highest number of opioid users, since 52.2% of all insured persons in that category is an opioid user. Zip code 4104 (Culemborg) has the highest score of 14.5 times more opioid declarations than expected. Zip code 5709 (Helmond) has the highest increase in prescribed duration of use of opioids per patient than expected, with a factor of 4.82. When combining the number of opioid declarations and the duration of opioid use, the municipalities Aalburg, Sliedrecht and Heerlen have the highest increase in opioid declarations and duration of use compared to expected. No conclusions can be made about the relationship between socioeconomic status and the prescribing patterns of general practitioners with respect to opioids.

Discussion The first limitation of this study is that an assumption is made that the general practitioner is operating in the same four-digit zip code area as the patient. Moreover, the variation is analysed only with declaration data from Company X. Another limitation is that the analyses focused on socioeconomic status is performed on municipality level. Furthermore, the socioeconomic status is expressed in only two variables, namely the percentage high educated people and the average disposable income. Another limitation is that there is no correction for the health status of the opioid users. The last limitation is that there is no data included which includes the experiences of the general practitioners or the opioid users. Recommendations for future research would be that studies should focus more on the data related to the general practitioner, all aspects related to the socioeconomic status should be considered instead of only two variables and that more data with respect to the experiences of the general practitioners and opioid users should be included.

Table of Content

1. Introduction

1.1 Background information and problem formulation

Millions of people worldwide are suffering from pain and opioids and opiates are prescribed for this problem more and more often. Opiates are the substances refined from opium, such as morphine; opioids are synthetic morphine-like substances such as oxycodone and fentanyl (1). In this thesis the term "opioids" will be used for both opiates and opioids. Opioids act on the brain's opiates receptors. These receptors are largely responsible for the sensation of pain and pleasure (2). Opioid use in chronic pain treatment is complex, as patients may derive both benefit and harm. Adequate pain relief has a positive influence on the quality of life, functional recovery, the risk of postoperative complications and the risk of persistent postoperative pain (3). However, the use of opioids can be accompanied by side effects such as drowsiness, constipation, headaches, confusion, depression or breathing problems (4). Prolonged use of opioids can lead to an increase in the sensitivity to pain, physical dependence and sometimes addiction. The reason for an increase in the sensitivity of pain is because opioid abuse can impair the brain's production of natural pain killers and dopamine.

Nowadays, health care expenditures are rising all over the world. In 2015 the healthcare costs in the Netherlands were more than €85 billion, which is more than €5.000 per inhabitant. Besides, healthcare is the largest expenditure item within the government budget, since €80.4 billion was spent on healthcare in 2018. This is around 28% of the total government budget (5). According to the "trend scenario" that Rijksinstituut voor Volksgezondheid en Milieu (RIVM) published in 2018, health care expenditures will rise to €174 billion in 2040. This means that in the period from 2015 till 2040, the health care expenditures will grow with an average of 2.9% per year (6). Opioids are not very expensive drugs. However, the overuse of opioids and the associated consequences, such as addiction, can lead to large healthcare expenditures.

The fact that excessive use of opioids is harmful has become clear from the massive opioid misuse epidemic in the United States (7) (8). In the period from 1999 to 2016, more than 200.000 patients died due to an overdose of opioids. There was a fivefold increase in the number of deaths due to an overdose in the period from 1999 to 2016 (9). This makes it a major public health crisis in the United States. Despite the stricter regulation of the prescription of opioids in Europe compared to the United States, opioid use in Europe is also increasing. The opioid crisis in the United States, whereby the use, misuse and overdosing of opioids is increasing, is expanding towards Europe (10).

In the Netherlands, the past years showed signals of an increase in the prescription of opioids such as oxycodone, morphine and fentanyl (strong opioids) (11). Figure 1 shows that the number of patients who were prescribed a strong opioid increased six-fold in the period from 2005 to 2015 (12).

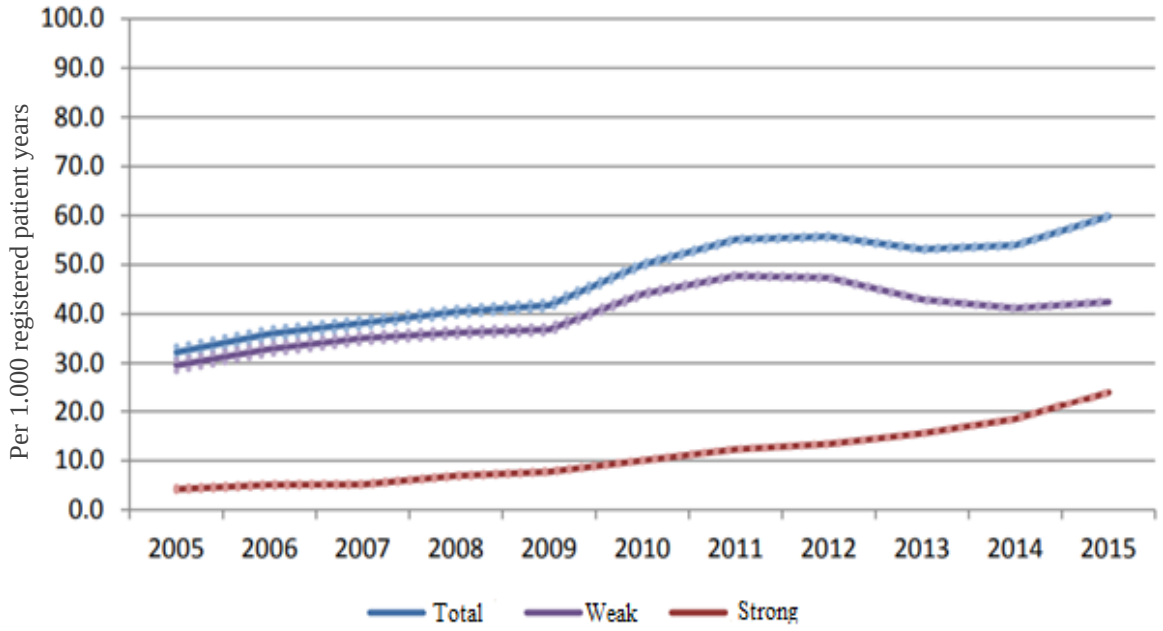


Figure 1: Number of patients with at least one prescription from an opioid in Dutch general practices per 1.000 registered patient years (13)

There are some general reasons that have led to an increase in the number of opioid prescriptions. Some of these explanations are the increase in attention for the treatment of pain, patients tend to ask sooner for adequate and fast working pain medication, opioids can be easily accessed via repeat prescriptions, doctors prescribe opioids sooner after surgery and the number of elderly with chronic conditions seems to increase in the Dutch community (14) (15).

Opioids were previously used during and after surgeries and for pain relief for patients with cancer. However, in recent years opioids also have been prescribed to patients with pain that is not related to surgery pain or cancer pain, such as rheumatism, osteoarthritis or a paraplegia (16). The "Nederlands Instituut voor Onderzoek van de Gezondheidszorg" (NIVEL) conducted a study where they investigated the prescribing behaviour of general practitioners in the period from 2005 to 2015. They found an increase in the number of prescriptions of opioids, which was attributed mostly to pain not associated with cancer (no-cancer pain) (12). There is no consensus in the literature whether the advantages of prescribing opioids on the long term compensate the risks for patients with no-cancer pain. However, there is evidence that the

chance of overdose and misuse of prescribed opioids due to psychological dependency is higher in patients with chronic no-cancer pain than in patients with cancer pain (17).

In the Dutch health care system, health insurance companies are responsible for offering good quality health care at an affordable price. Company X is a health insurance company located in the Netherlands. It is the fourth biggest health insurance company (18). Their market share is mostly located in the north and east of the Netherlands. Together with their members, healthcare providers, patient associations and other partners, Company X is committed to maintain the accessibility and affordability of care. They achieve this by supporting projects and research that improve the quality of healthcare. This support makes the movement possible towards a new organization of care (19). In their mission it is stated that "together we ensure good quality and affordable care and we strengthen the living power of every person" (20). Company X focusses on the care with the best ratio between relevant health outcomes and corresponding costs. This is called value-based healthcare. According to Company X, value-based healthcare is the key for future-proof and better healthcare. It can lead to a better experience of the quality of care, improvement of the health of the customers and a decrease in the costs in order to guarantee accessible and affordable care (21).

1.2 Aim of the study

Since health care expenditures are rising in the Netherlands, Company X aims to decrease healthcare costs but maintain (or improve) the current quality of care. One way to achieve this is by decreasing the unnecessary overuse of opioids in the Netherlands. A lot of research is performed to investigate the prescribing patterns of general practitioners with respect to opioids over the whole world to decrease the unnecessary overuse. However, the socioeconomic status of the patient can have an influence on the prescribing behaviour of general practitioners. The socioeconomic status represents the position of people on the social ladder. That position arises from a combination of material circumstances; skills, abilities and knowledge; and the social network and the status and power of people in that network. There are significant differences in health between people a high socioeconomic status and people with a low socioeconomic status. This difference is partly due to a worse lifestyle and living environment in people with a low socioeconomic status.

Due to these differences in socioeconomic status, the opioid use of people and prescribing patterns of general practitioners is different in the Netherlands. NIVEL (12) and the "Nederlands Tijdschrift voor Geneeskunde" (NTvG) (22) studied the opioid use in an outpatient

setting in the Netherlands. Both found an increase in the use of opioids and agreed on the fact that more research is needed to explain the increase in prescribing opioids in the Netherlands. Therefore, this study aims to get insight in the variation in practice between general practitioners according to their prescribing behaviour of opioids in the Netherlands. When this variation is clearly formulated, Company X has an overview which municipalities can generate cost savings by decreasing the number of unnecessary opioid prescriptions. To get insight in this variation in practice the following research question and sub questions need to be answered:

Research Question: "What is the variation in practice between general practitioners according to their prescribing behaviour of opioids and to what extent is this linked to the socioeconomic status of the patient?"

Sub question 1: "What is the variation in practice between general practitioners according to the number of declarations for opioids per four-digit zip code?"

Sub question 2: "What is the variation in practice between general practitioners according to their prescribed duration of use of opioids per four-digit zip code?"

Sub question 3: "What is the relationship between the number of opioid declarations and the socioeconomic status of the patient per municipality?"

Sub question 4: "What is the relationship between the prescribed duration of use of opioids and the socioeconomic status of the patient per municipality?"

2. Theoretical Framework

2.1 The Agency Theory

The agency theory is a theory that can explain the dual role of a physician as a consumer and intermediary (23). It was first established by Michael and Meckling (24) in academic literature, where they introduced the initial perspective of different objectives for the theory. The agency theory presents a framework that helps analysing relationships between interdependent stakeholders, to identify the problem that exists between parties and mechanisms. An agency relationship occurs when one party (the principal) relies on another party (the agent) to perform actions on behalf of the client (25). Within the context of this topic about prescribing behaviour of general practitioners, there is one important agency relationship applicable. That is the relationship between the patient (principal) and the physician (agent). The patient is as principal dependent on the physician, who acts like an agent, to prescribe the appropriate opioid. This dependence originates from the specialized knowledge and technical skills required to make a decision (26). A patient [1] prefers the most efficient, practical, least invasive treatment (27), [2] may know something about their own condition but does not have knowledge about the effectiveness of alternatives, [3] is less inclined to take unnecessary risks since the patient is the one to whom an intervention is being prescribed, and [4] has little control since the physician's prescription is a function of many variables such as drug characteristics, habit persistence and drug cost/benefit ratio (23). When analysing the variation in practice between general practitioners according to their prescribing behaviour of opioids, there should be paid attention to this principal agent problem in health care, which asserts that health care providers will act to maximize their profits at the expense of the patients' interest.

Effects of the agency can be caused by the influence of standard social pressures, which influences the impact on prescription. Physicians may experience the expectations and requests of the patient for a drug as a social pressure to prescribe a specific drug. When a physician does not prescribe medication that the patient prefers, it might hurt the patient – physician relationship. This reduces the possibility of a therapeutic functional cooperation (28). When the physician listens to the preferences of the patient for a particular opioid through the provision of a prescription, the confidence of the patient that the prescription is right will be enhanced (29).

2.2 Socioeconomic Status

Over the last decades, a lot of evidence has accumulated demonstrating the differences in health between all different socioeconomic statuses, also referred to as the social gradient in health (30). The social determinants of health are key concepts that can be used for explaining the gradient. These include the social and economic factors that are shaping the health outcomes at both individual and population levels (31). In the article of Bartley (32), they refer to four common theories which are used to examine inequalities in health. These four are cultural-behavioural, materialist, psychosocial and life course and will be further explained below.

The *cultural-behavioural approach* argues that the link between socioeconomic status and health is the result of differences between socioeconomic classes. These differences are expressed in terms of their health-related behaviour (32). Unhealthy behaviours may be more culturally acceptable among people with a lower socioeconomic status (33). This account of health inequalities is largely agency-based (34). The *materialist explanation* is focused on what income enables people to buy goods and services and limits the exposure to adverse physical and psychological risk factors. They look beyond the individual-level factors (agency) in favour of the role of public policy and services, such as transport, schools and welfare in the social patterning of inequality (32) (35). *Psychosocial explanations* focus on how people feel about social inequality. Besides, it focuses on the effects of biological consequences of these feelings on their health status. Stress responses can be stimulated by feelings of subordination or inferiority. This can lead to long-term consequences for the mental and physical health, especially when they occur for a prolonged period of time (32). The last theory is the *life-course approach*, which combines aspects of the theories described above and allows different causal mechanisms and processes to explain the social gradient in different sorts of diseases. Inequalities in the accumulation of social, biological and psychological (dis)advantages over time lead to health inequality between people with different socioeconomic status (36).

This thesis will focus only on the materialist explanation. The reason for this is that there is no general data available from the cultural-behavioural approach. This approach is based on data coming from behaviour, something that is not measured and published on a national level. The psychosocial explanation is not suitable for the current analysis, since this is based on feelings and emotions, which is also not available in national databases. This results in the fact that the life-course approach is also not suitable, since this is a combination of all aspects. Therefore, only the materialist explanation of the socioeconomic status is taken into consideration in this thesis.

3. Methods

This chapter provides an overview of all methods used for analysing the research question and sub questions. First the research design will be discussed, then the study population will be described and lastly the data processing is explained per sub question.

3.1 Research design

This study is a quantitative study whereby descriptive statistics are used to give an overview of the variation in practice between opioid use and opioid prescription behaviour in the Netherlands. The data that is used is retrospective and is available through the declaration database of Company X. From this declaration database data was extracted from all insured people who received opioids from a public or outpatient pharmacy in 2018. It concerns extramural opioid use only. Opioid prescriptions were defined as ATC-codes that belong to the therapeutic subgroup N02A (opioids). The opioids named codeine and buprenorphine were excluded from this study, since these opioids are also used for other purposes than pain relief. An opioid user is a patient for whom a prescription of an opioid has been declared at least one time in 2018. To get additional information about the socioeconomic status of inhabitants in the Netherlands, the database of CBS Statline is used. This database provides information about educational attainment and the average disposable income of all inhabitants in the Netherlands in 2017. Since the socioeconomic data from CBS Statline only got data on municipality level, the four-digit zip code from the declaration database is linked to the corresponding municipality. This means that this analysis is performed on municipality level.

3.2 Study population

The data is based on all Dutch persons from all ages who are insured at Company X. The age of the patient was determined by looking at the age of the patient on the date of prescription. Insured persons who died during the study period were included up to and including the month of death. Insured persons who were born or immigrated during the reporting year were included from that month. For the classification by municipalities, the municipality where the person received the prescription is the municipality that was used. This means that when patients moved during the study year, opioids that were prescribed after the date of moving were registered under their new four-digit zip code.

The data with respect to the general practitioners is based on all general practitioners who have their practice located in the Netherlands. Only general practitioners who prescribed opioids to insured persons of Company X were included in the dataset.

3.3 Data processing

Both the declaration data from Company X and CBS Statline data is imported in Microsoft Excel to perform descriptive statistical analyses. To perform these analyses, the declaration data needed to be organized and some data needed to be deleted or calculated. Declarations which had unknown zip codes or zip codes referring to Germany were excluded from the analyses (n = 14, 0.002%). Moreover, all opioids which were prescribed as injection fluid were excluded from the analyses in sub questions 1-4 (n = 19.909, 3.1%). The exact dose which is administered to the patient is unknown when it comes to liquid opioids, which makes the analysis about the average prescribed days of opioids unreliable. Therefore, only opioids which were prescribed as tablet, capsule, suppository or nose spray were included in these analyses. The number of days a patient can use the prescribed opioids is calculated and added to the dataset. In the dataset there was only data available about the number of tablets/capsules/suppositories/nose sprays prescribed and how much milligrams active substances of opioids are in this type of opioid. To calculate the duration of use of opioids, the number of tablets/capsules/suppositories/nose sprays was first multiplied with the number of active substances of opioids in milligrams. Then this number was divided by the Daily Defined Dosage (DDD) for that specific opioid. The DDD is the approximate average maintenance dose for adults when using a drug. This DDD is presented by the WHO Collaborating Centre for Drug Statistics Methodology (37). This study used descriptive statistics to give insight in the variation in practice in opioid declarations and opioid duration of use. The next three paragraphs will discuss which methods are used to analyse the demographical data and sub questions 1-4.

3.3.1 Demographical data of the study population

To get insight in the demographical data of the study population, a graph is made in which the number of opioid users was plotted against age categories, divided into groups of 5 years. Since the number of people are unequally distributed among all age categories, a ratio is calculated whereby the number of opioid users is divided by the number of insured persons in that age category. This ratio was plotted against all age categories. This same analysis is performed separately for men and women, whereby the number of opioid users is divided by the number of insured men and insured women. Thereafter, all declarations were plotted against the medical specialties to see which specialty prescribed opioids the most.

3.3.2 Sub question 1

To answer sub question 1, the number of opioid declarations of Company X members was analysed at four-digit zip code level corrected for case-mix. The total number of insured persons in 2018 was divided by the total number of declarations in 2018. This was done for each age category for men and women. Then this number was multiplied with the number of declarations in the relevant age category for men and women. These expected declarations were added up and the number of actual declarations was divided with the number of expected declarations. The mean of all these numbers was calculated and then the difference between these numbers and the mean was calculated. This gives a factor that represents the increase in the expected number of opioid declarations per four-digit zip code. With the tool Map Charts from Microsoft Excel 2019 the opioid use is graphically visualized on the map of the Netherlands. All four-digit zip codes which had less than 100 declarations in 2018 were excluded from the analysis and were not marked in the graphs. In this way, four-digit zip codes which had only a few declarations were not unfairly seen as low opioid consuming zip code or high opioid consuming zip code due to a small sample size.

3.3.3 Sub question 2

To answer sub question 2, the average prescribed duration of use in days was analysed at four-digit zip code level corrected for case-mix. The average duration of use in days was calculated by dividing the total number of days per age category for men and women with the total number of declarations in that age category for men and women. Then for each four-digit zip codes the number of declarations was multiplied with the average duration of use in days per age category for men and women. These days were added up and then this number was divided with the actual duration of use in days. The mean of all these numbers was calculated and then the difference between the numbers and the mean was calculated. This gives a factor that represents the increase in the expected prescribed duration of use in days. With the tool Map Charts from Microsoft Excel 2019 the average prescribed duration of use of opioids in days was plotted on the map of the Netherlands. All four-digit zip codes which had less than 100 declarations in 2018 were excluded from the analysis and were not marked in the graphs. In this way four-digit zip codes who had only a few declarations were not unfairly seen as low opioid consuming zip code or high opioid consuming zip code due to a small sample size.

3.3.4 Sub questions 3 and 4

To answer sub questions 3 and 4, the data was linked to the socioeconomic data from CBS Statline. For each municipality, the percentage of high educated persons and the average

disposable income were plotted against the factor standing for the increase in the number of opioid declarations compared to expected (sub question 3) and plotted against the increase in the duration of use of opioids in days compared to expected (sub question 4). High educated persons are people with a degree in “Hoger Beroepsonderwijs” (HBO) or “Wetenschappelijk Onderwijs” (WO) level, or when they are studying at HBO or WO level. Municipalities with less than 10.000 inhabitants in 2017 were excluded from the analyses. In this way municipalities who had not many inhabitants were not unfairly seen as low opioid consuming municipality or high opioid consuming municipality due to a small sample size. A trendline shows what influence these two determinants of socioeconomic status have on the number of opioid declarations and the prescribed duration of use per municipality.

4. Results

In this chapter, first all results with respect to demographical data will be presented. Secondly, the analyses about the number of declarations of opioids per four-digit zip code and the duration of use of opioids per four-digit zip code will discussed. Then these results are linked to the socioeconomic status of the patients on municipality level. Lastly, a combined factor score will be presented on municipality level to give an answer to the research question.

4.1 Demographical data

There were in total 774.463 declarations of opioids in 2018, where 487.185 of the declarations (63%) were for women and 287.278 of the declarations (37%) were for men. All these declarations were for 142.605 different users. From all these users, there were 84.237 women (59%) and 58.368 (41%) men. The age of the opioid users ranges between 0 and 108 years old. Figure 2 shows the number of opioid users per age category. As can be seen from this figure, the age category 71 years old has the highest number of opioid users, namely 3.220 opioid users in total.

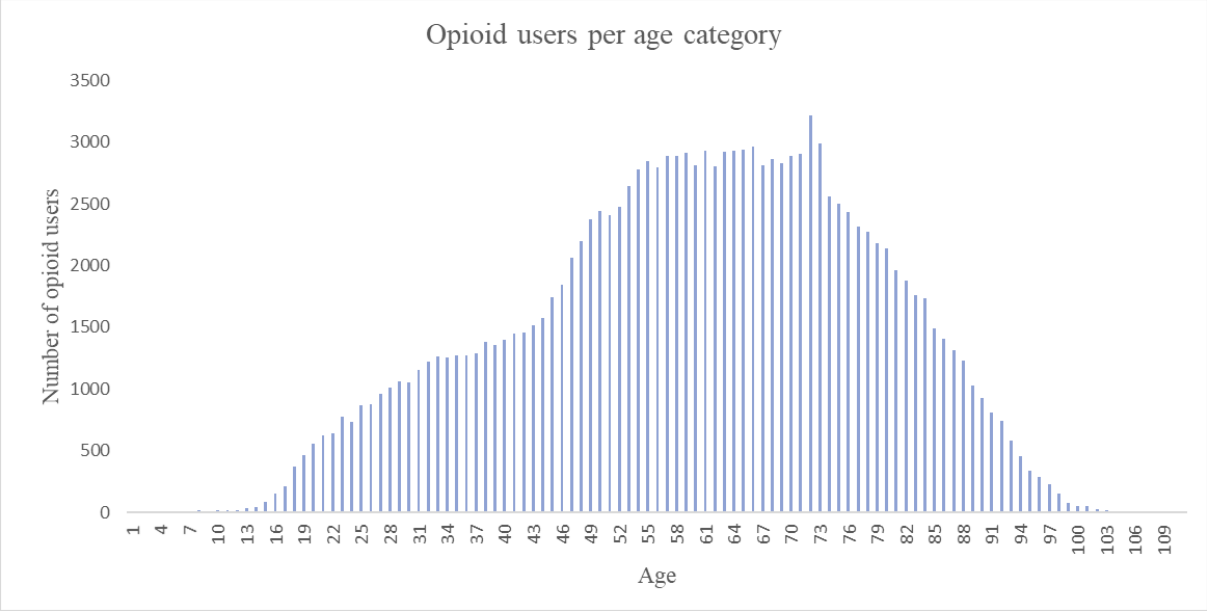


Figure 2: Number of opioid users per age year

Not every age category has the same number of insured persons. Therefore, figure 3 shows the number of opioid users per age category corrected for the number of insured persons per age category. This figure shows that the age category 95-100 has relatively the highest number of opioid users, since 52.2% of all insured persons in that category is an opioid user. The same analysis is done for the variable gender. For both men and women, the number of opioid users

was corrected for the number of insured persons per men and women. This shows that from all insured men, there were 5.1% opioid users and from all insured women there were 7.5% opioid users. Appendix 1 shows the number of opioid users divided by the number of insured persons per age category for both men and women separately.

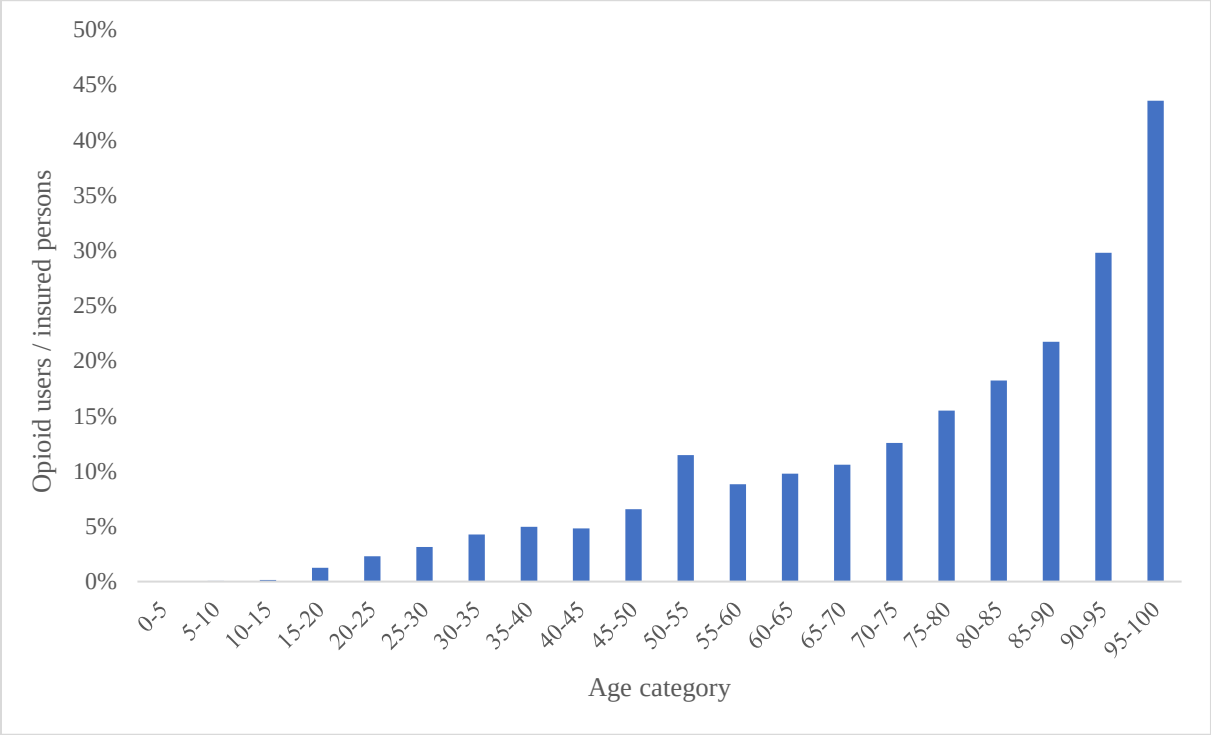


Figure 3: Percentage opioid users per age category

The 774.460 declarations of opioids in 2018 were prescribed by 124 different specialties. Figure 4 shows per specialty how many opioids were prescribed. As can be seen in this figure, almost 650.000 declarations were prescribed by general practitioners. This means that this is the biggest group of specialists that prescribe opioids. There were in total 8.516 general practitioners included in the dataset. All general practitioners are located in the Netherlands. The category “unknown” stands for declarations that were prescribed by a medical specialism that is unknown in the declaration dataset of Company X. The category “other” represents another medical specialism than one of the six medical specialties in figure 4. This can be all medical specialities who prescribed a declaration for opioids other than the explicitly incorporated specialties.

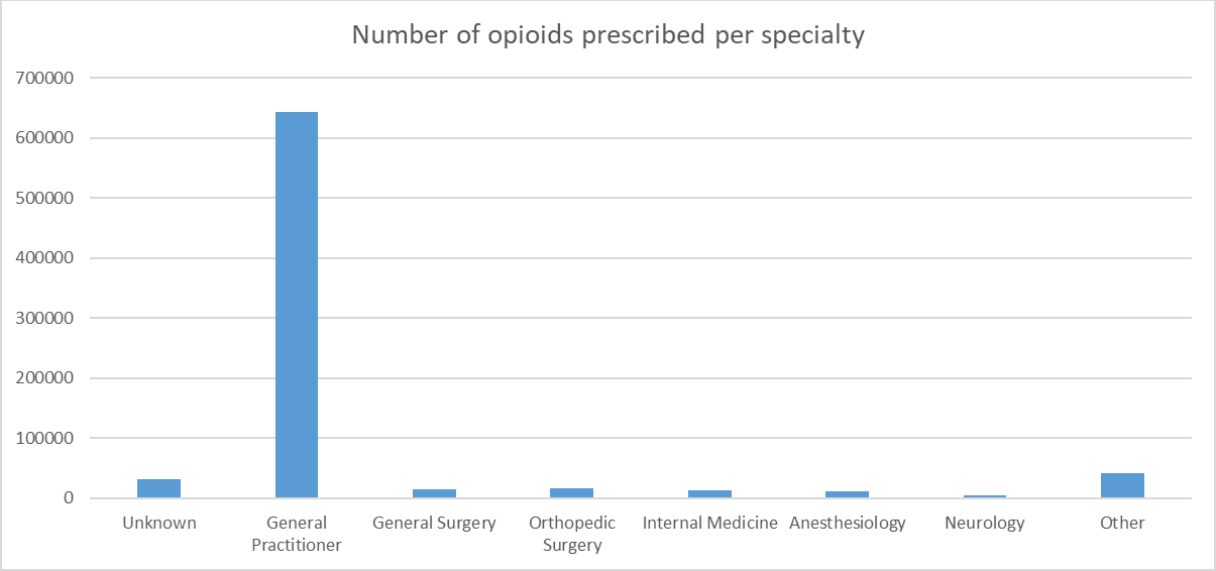


Figure 4: The number of opioids prescribed per specialty

4.2 Sub question 1

To answer sub question 1: "What is the variation in practice between general practitioners according to the number of declarations for opioids per four-digit zip code?", the data needed to be corrected for case mix. This is done by calculating the average number of declarations per person for each age category and gender per year. Table 1 provides an overview of these average number of declarations per person for each age category and gender per year.

Age Category	Man	Woman
0-5	0,00012	0,00002
5-10	0,00012	0,00007
10-15	0,00115	0,00059
15-20	0,00749	0,01679
20-25	0,02351	0,05152
25-30	0,04779	0,09379
30-35	0,07432	0,15214
35-40	0,10095	0,20588
40-45	0,16308	0,29156
45-50	0,22858	0,33971
50-55	0,27530	0,39869
55-60	0,33231	0,45700
60-65	0,36618	0,50664
65-70	0,36324	0,53502
70-75	0,43118	0,67202
75-80	0,57346	0,96783
80-85	0,74032	1,35500
85-90	0,92762	1,85733
90-95	1,41942	2,42005
95-100	1,76812	2,98788

Table 1: The average number of declarations per person in the relevant age category per year

For each four-digit zip code a factor is calculated that represents the increase or decrease in the number of opioid declarations compared to what is expected for this municipality when looking at the distribution of the inhabitants over the age categories for men and women. Figure 5 shows this factor on the map of the Netherlands. Zip codes which are not marked on the map had less than 100 declarations. Table 2 shows the ten zip codes with the highest increase in number of opioid declarations compared to expected.

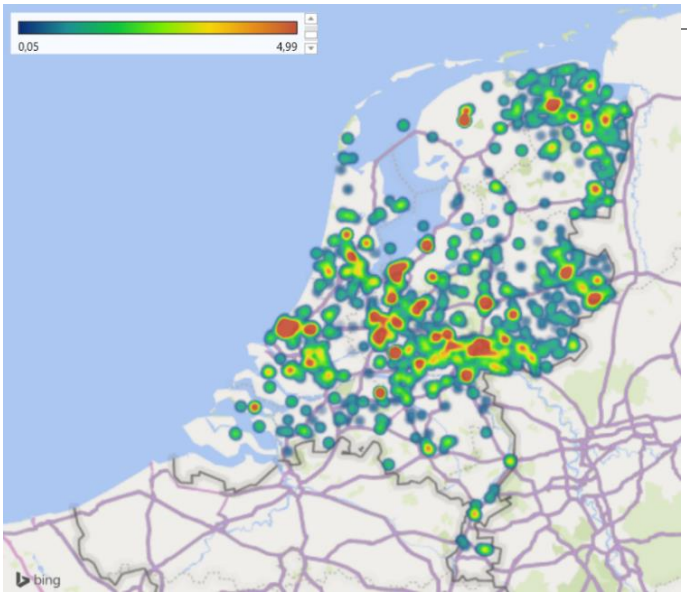


Figure 5: Heatmap with factors per zip code

Municipality	Zip code	Factor1
Culemborg	4104	14.87
Leeuwarden	9088	12.00
Aalburg	4265	8.77
Lelystad	8233	6.82
Schouwen-Duiveland	4307	5.65
Alkmaar	1486	5.18
Nijmegen	6534	4.70
Leeuwarden	8933	4.39
Amersfoort	3826	3.38
Apeldoorn	7329	2.94

Table 2: Top 10 highest increase in opioid declarations than expected

As can be seen from figure 5, there are a couple of zip codes that have more opioid declarations than is expected for these zip codes. One red dot represents one zip code with a higher factor than expected for this zip code. When the red dots are larger, this means that there are more zip codes in the same municipality with a higher number of opioid declarations than expected. As can be seen from this figure, the five municipalities with multiple high factors in opioid declarations are Den Haag, Almere, Arnhem, Apeldoorn and Groningen.

Table 2 shows the four-digit zip codes with the highest factors. Since some municipalities do not have multiple zip codes scoring very high, they do not represent a big red dot in figure 5. The municipality Culemborg with zip code 4104 has the highest score of 14.5 times more opioid declarations than expected. Appendix 2 shows the top 10 lowest increase in opioid declarations compared to expected. Appendix 3 shows the absolute differences in opioid declarations compared to expected.

4.3 Sub question 2

To answer sub question 2: “What is the variation in practice between general practitioners according to their prescribed duration of use of opioids per four-digit zip code?”, the data needed to be corrected for case mix. This is done by calculating the average duration of use in days per declaration for each age category and gender per year. Table 3 provides an overview of the average duration of use in days per declaration for each age category and gender.

Age Category	Man	Woman
0-5	14	1
5-10	7	2
10-15	10	19
15-20	11	11
20-25	10	12
25-30	10	15
30-35	13	14
35-40	16	17
40-45	14	18
45-50	15	20
50-55	17	21
55-60	18	21
60-65	20	22
65-70	21	22
70-75	20	22
75-80	19	19
80-85	17	17
85-90	15	16
90-95	14	14
95-100	14	15

Table 3: The average duration of use for opioids (expressed in number of days a patient can take the opioids) for each age category and gender

For each four-digit zip code a factor is calculated that represents the increase in the prescribed duration of opioid use compared to what is expected. Figure 6 shows this factor on the map of the Netherlands. Zip codes which are not marked on the map had less than 100 declarations. Table 4 shows the ten zip codes with the highest increase in the prescribed duration of use of opioids compared to expected.

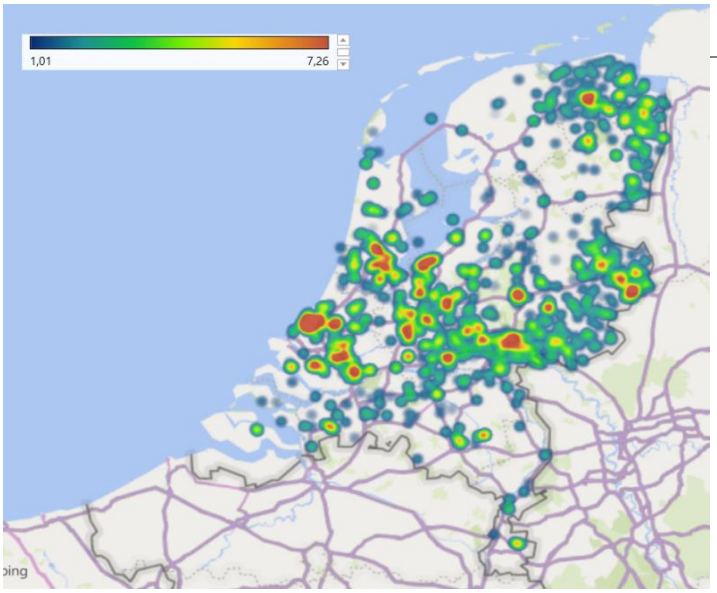


Figure 6: Heatmap with factors per zip code

Municipality	Zip code	Factor2
Helmond	5709	4.82
Vlagtwedde	9545	3.30
Gorinchem	4207	3.14
Zeist	3703	3.03
Stadskanaal	9661	3.02
Wassenaar	2242	3.01
Leerdam	4141	2.91
Tiel	4013	2.87
Sliedrecht	3362	2.72
's Hertogenbosch	5213	2.72

Table 4: Top 10 highest increase in duration of opioid use prescribed

Figure 6 represents the factors standing for the increase in the prescribed duration of use of opioids than expected. As can be seen from figure 6, the five municipalities with the highest increase in the prescribed duration of use than expected are Den Haag, Amsterdam, Almere, Groningen and Rotterdam. As can be seen from table 4, zip code 5709 in the municipality Helmond has the highest increase in prescribed duration of use per patient than expected. In this zip code, there was a 4.82 times higher duration of use of opioids prescribed than expected. Appendix 2 shows the top 10 lowest increase in opioid duration of use compared to expected. Appendix 3 shows the absolute differences in duration of opioid use compared to expected.

4.3 Sub question 3

To answer sub question 3: "What is the relationship between the number of opioid declarations and the socioeconomic status of the patient per municipality?" the increase in the expected number of opioid declarations is plotted against the percentage high educated people and the average disposable income (figure 7&8). The blue points represent all municipalities with more than 10.000 inhabitants in the Netherlands, whereby only zip codes with more than 100 declarations are included. There are four different sizes of blue points, dependent on the number of inhabitants per municipality. Size one represents less than 20.000 inhabitants, size two represents between 20.000 and 50.000 inhabitants, size three represents between 50.000 and 100.000 inhabitants and size four represents more than 100.000 inhabitants. When looking at figure 7, the seven municipalities with 50% or more high educated persons are all between 0.5-

and 1.5-times more opioid declarations than expected. The municipalities Delft, Leiden, Utrecht and Diemen had fewer opioid declarations than expected and Wageningen, Groningen and Nijmegen had more opioid declarations than expected. The outliers (>50% high educated people) have a strong effect on the trend line. Moreover, the outliers are all municipalities with a high number of inhabitants. Therefore, it is not possible to make conclusions about the relationship between high educated people and the number of opioid declarations according to this analysis.

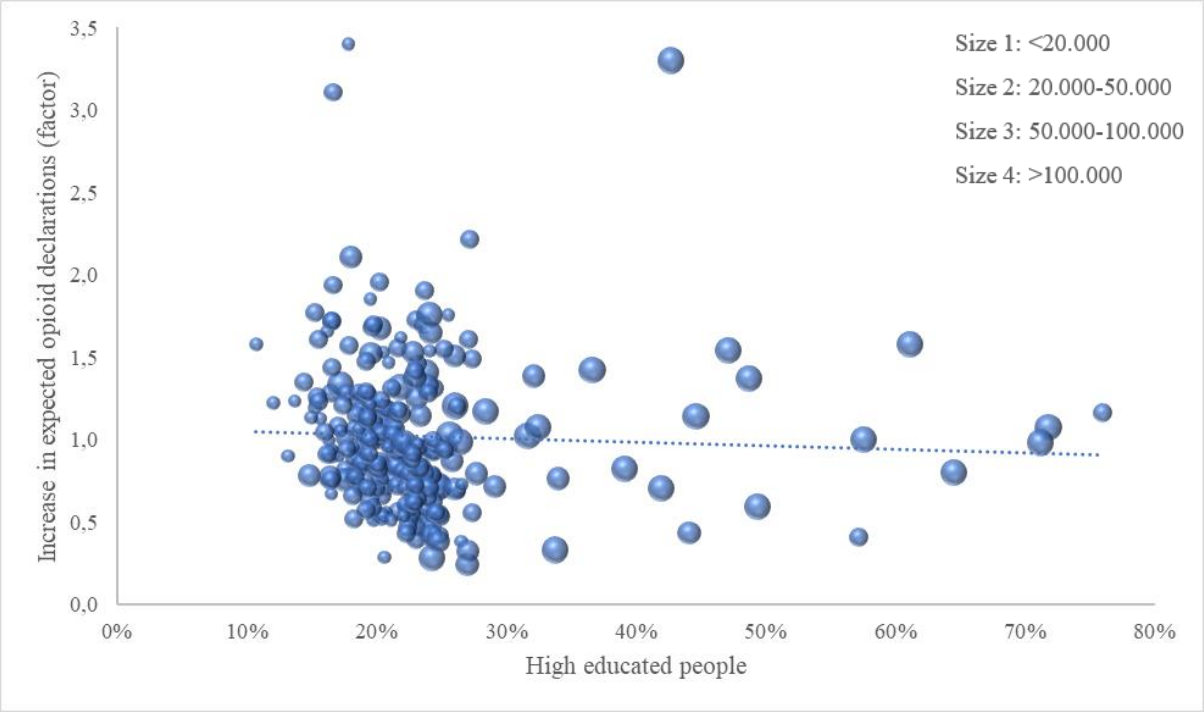


Figure 7: Percentage high educated people plotted against the increase in expected opioid declarations

When looking at figure 8, the municipalities with an average disposable income of €70.000 and more are all between 0.5- and 1.0-times opioids declarations than expected. The municipalities Laren, Blaricum and Wassenaar had fewer opioid declarations than expected and Bloemendaal had the same number of declarations for opioids as expected. The trend line is influenced by outliers, there is only a small number of municipalities on the right side of the graph. Therefore, it is not possible to say something about the relationship between average disposable income and the number of opioid declarations according to this analysis.

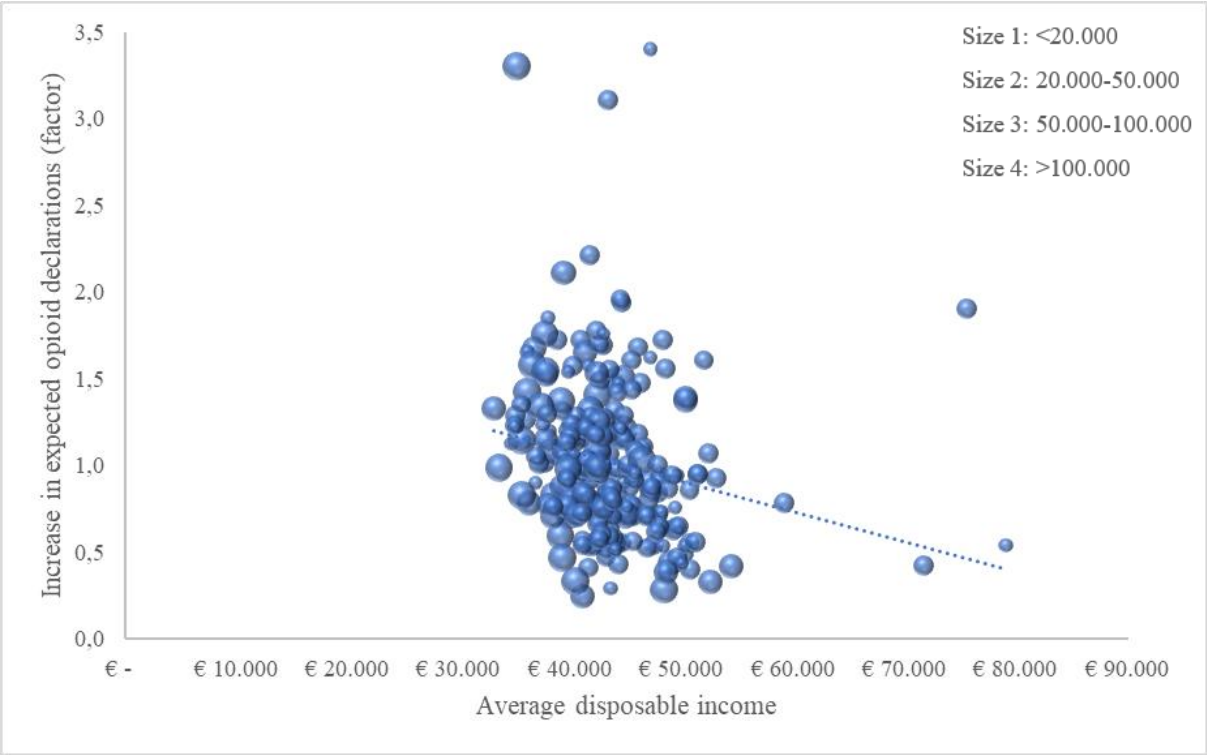


Figure 8: Average disposable income plotted against the increase in expected opioid declarations

4.4 Sub question 4

To answer sub question 4: "What is the relationship between the prescribed duration of use of opioids and the socioeconomic status of the patient per municipality?" the increase in the expected prescribed days of opioids is plotted against the percentage high educated people and the average disposable income (figure 9&10). The blue points represent all municipalities with more than 10.000 inhabitants in the Netherlands, whereby only zip codes with more than 100 declarations are included. There are four different sizes of blue points, dependent on the number of inhabitants per municipality. The sizes go from small to large, whereby size one represents less than 20.000 inhabitants, size two represents between 20.000 and 50.000 inhabitants, size three represents between 50.000 and 100.000 inhabitants and size four represents more than 100.000 inhabitants. Figure 9 shows no effect in the duration of use of opioids when there are more high educated people in the municipality. The outliers in figure 10 have a strong effect on the trend line. Therefore, it is not possible to make conclusions about the relationship between average disposable income and the duration of opioid use. Appendix 4 shows the increase or decrease in the expected number of opioid declarations and duration of use against the percentage high educated people and the average disposable income, whereby not the relative differences but the absolute differences are analysed.

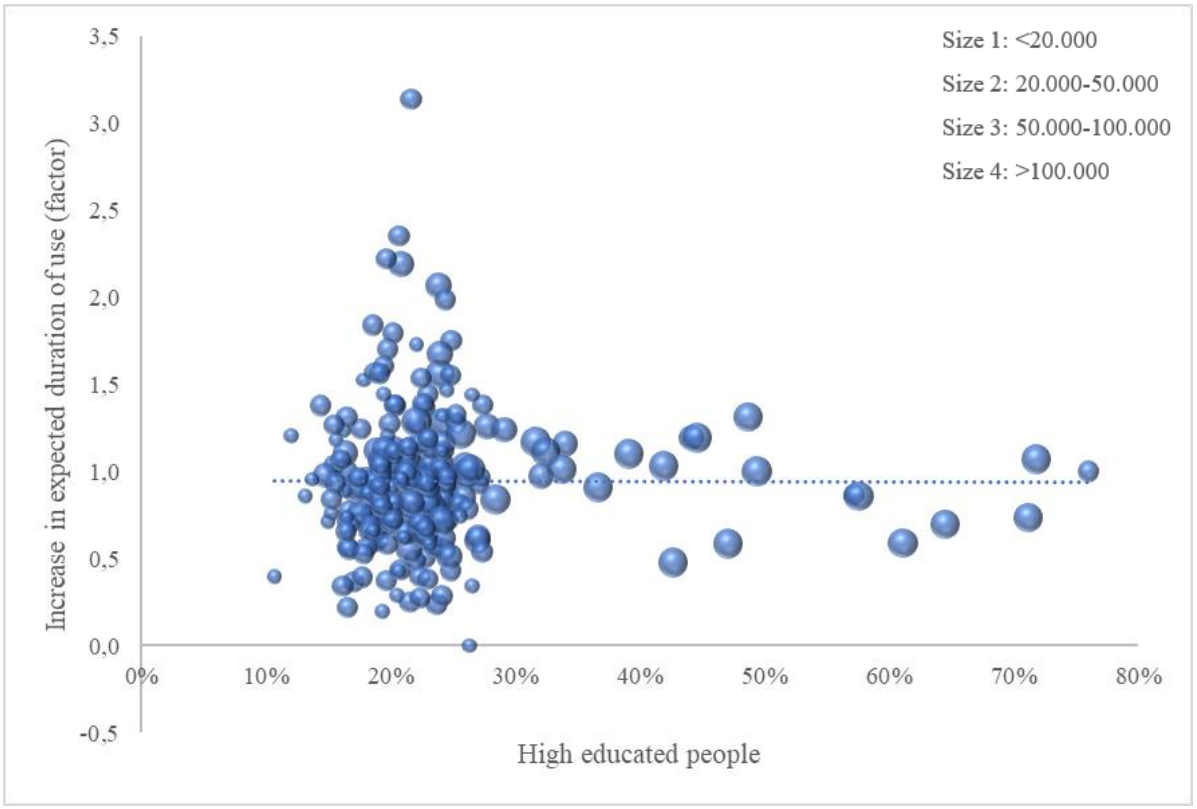


Figure 9: Percentage high educated people plotted against the difference in expected duration of use

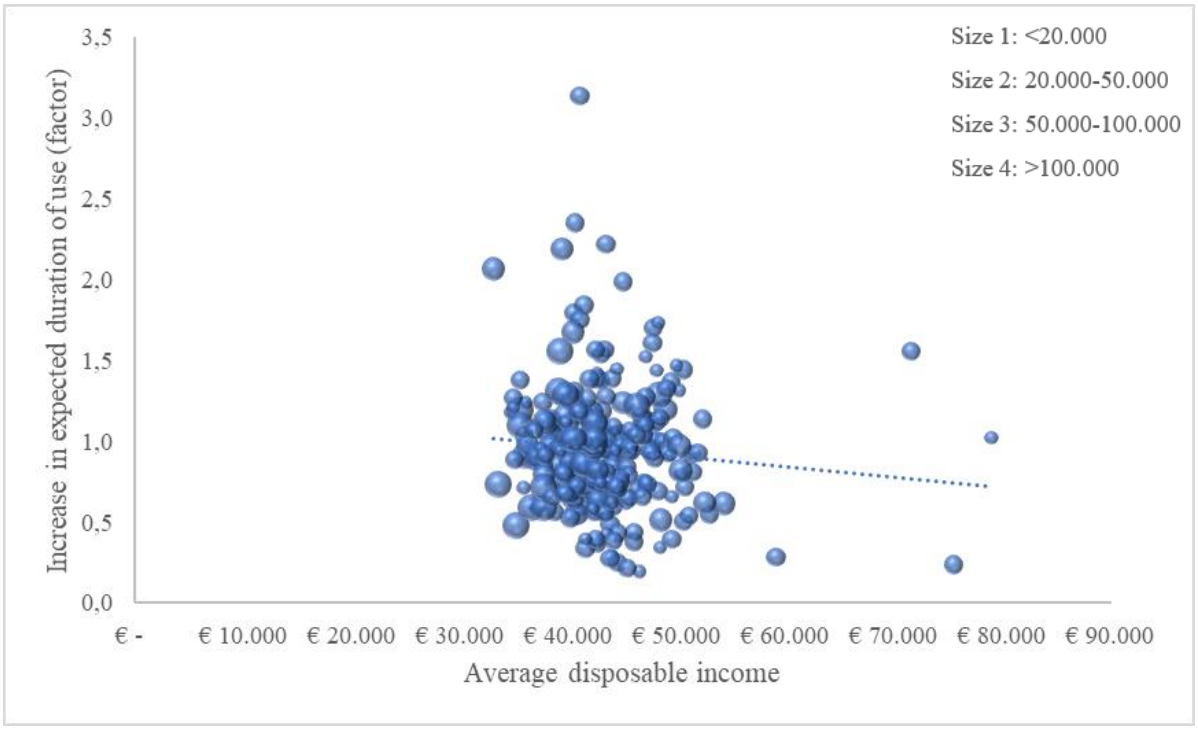


Figure 10: Average disposable income plotted against the difference in expected duration of use

4.5 Comparison of sub question 1 and sub question 2

To get an overview in which municipalities opioids were more often prescribed than expected, the factors of the number of opioid declarations (factor1) and the factors of the opioid duration of use (factor2) were multiplied with each other. Table 5 shows the twenty municipalities with the highest factor. Aalburg is the municipality with the highest multiplied factor, namely 5.18. Appendix 5 shows the twenty municipalities with the lowest factor, whereby also the factor of sub question 1 is multiplied with the factor of sub question 2 per municipality. This represents the best scoring municipalities who prescribed less opioids than expected for this municipality.

Municipality	**Factor 1**	**Factor 2**	**Factor 1*Factor 2**
Aalburg	3.40	1.52	5.18
Sliedrecht	1.19	2.35	2.79
Heerlen	1.33	2.07	2.75
Helmond	1.07	2.19	2.35
Echt-Susteren	2.21	0.97	2.14
Dronten	1.49	1.38	2.06
Harlingen	1.66	1.24	2.05
Goes	1.13	1.79	2.04
Lelystad	2.11	0.95	2.01
Maasgouw	1.55	1.28	1.98
Waddinxveen	1.00	1.99	1.98
Nieuwegein	1.65	1.16	1.92
Stadskanaal	1.35	1.38	1.86
Hellevoetsluis	1.18	1.57	1.85
Eindhoven	1.37	1.31	1.80
IJsselstein	1.56	1.14	1.78
Gorinchem	0.56	3.14	1.77
Leerdam	0.95	1.84	1.75
Vianen	1.21	1.44	1.75
Schouwen-Duiveland	3.11	0.55	1.72

Table 5: Highest 20 factors representing the increase in opioid declarations compared to expected of all municipalities

5. Discussion

In this chapter, the main results of the analyses will be discussed. Thereafter, the implications in this study will be mentioned and recommendations for future research will be presented.

5.1 Main results

This research tried to answer the following research question: "What is the variation in practice between general practitioners according to their prescribing behaviour of opioids and to what extent is this linked to the socioeconomic status of the patient?". To give answer to this research question, four different sub questions needed to be answered. The first sub question analysed the variation in practice between general practitioners with respect to the number of declarations of opioids. This analysis found that the variation is scattered over the map, but with bigger red dots in the regions Den Haag, Almere, Arnhem, Apeldoorn and Groningen. The second sub question analysed the variation in practice between general practitioners with respect to the prescribed duration of use of opioids. This analysis found also that the variation is scattered over the map, with bigger red dots in the regions Den Haag, Amsterdam, Almere, Groningen and Rotterdam. Sub questions 3 and 4 analysed the relationship between socioeconomic status and the number of declarations of opioids (sub question 3) and the prescribed duration of use of opioids (sub question 4). In both the analyses, the trend line is largely influenced by outliers. Therefore, it is not possible to say something about these relationships due to the data and outliers in the graph. To give an answer to the research question, factor1 (sub question 1) and factor2 (sub question 2) were multiplied with each other. Then the twenty municipalities with the highest factor were presented in a table. This table represents the municipalities with the highest factor with respect to the number of opioid declarations and duration of use of opioids. The municipality Aalburg has the highest factor of 5.18.

5.2 Limitations of the study

There are some limitations in this study due to a limited dataset. The first limitation is that an assumption is made that the general practitioner is operating in the same four-digit zip code area as the patient. Since this study performed the analyses based on the four-digit zip code of the patient, it might be possible that the general practitioner who prescribed the opioids is not located in this same zip code. However, in most of the situations the patient has a general practitioner who is located nearby. According to Centraal Bureau voor Statistiek (CBS), the average distance to a general practitioner in the Netherlands is 1 kilometre (38). This suggests that the general practitioner might not always be located in the same four-digit zip code but is

most of the time located in the same municipality. This makes the analyses performed on municipality level more reliable with respect to this assumption.

The second limitation of this study is that the variation is analysed only with declaration data from Company X. Since Company X is a popular health insurance company in a specific couple of areas, the data is not equally distributed throughout the Netherlands. Therefore, the analysis is not representative for the whole country. Moreover, there can be a difference in characteristics of members of Company X and characteristics of members from other health insurance companies. Only popular regions of Company X were included, so it might be possible that these regions have a different socioeconomic status than other regions in the Netherlands. This could have an influence on the analyses performed with respect to socioeconomic status on the number of opioid declarations and duration of opioid use. It might be possible that when looking from the perspective of another health insurance company, other four-digit zip codes will have a high factor compared to the analyses performed with the data from Company X.

The third limitation of this study is that the analyses where the relationship between socioeconomic status and opioid consumption is investigated, is performed on municipality level. The reason why this is analysed on municipality level is because there is no socioeconomic status data available on four-digit zip code level. Therefore, opioid related data from the declaration database of Company X needed to be adjusted from four-digit zip code level to municipality level. This means that for each municipality the weighted average factor of all four-digit zip codes was calculated, by multiplying the factors per zip code with the number of declarations of that zip code. These factors were summed up for all municipalities and divided by the number of declarations per municipality. A disadvantage that occurs when calculating with the mean is that the mean can be influenced by outliers. In these analyses, it can be possible that in one municipality there were four-digit zip codes with a high factor and four-digit zip codes with a low factor. This makes the mean of this number not very high and not very low, while there are big differences between these four-digit zip codes.

The fourth limitation related to the analyses performed with socioeconomic status is that in this study, the socioeconomic status is expressed in two variables. Historically, the Sociaal Cultureel Planbureau (SCP) published each year the socioeconomic status per municipality, but due to unknown considerations they do not provide this information anymore. Only the percentage high educated people and the average disposable income are considered in the analyses. The educational level and average disposable income are two of the most important variables of

socioeconomic status, but the indicator profession is also an important variable to measure the socioeconomic status. The two variables used in this study can give an indication what effect they have on the opioid consumption in the Netherlands, but these results might change when more variables of the socioeconomic status are taken into consideration.

The fifth limitation is that there is no correction for the health status of the opioid users. Sometimes it is necessary for patients to use opioids, for example after a major surgery or when the patient is having chronic pain due to cancer. In this case, it is logical that these patients receive opioids. However, there are also patients that received opioids when it was not necessary. Since there was no insight in the health status of the patient in the dataset, it was not possible to correct for health status.

The last limitation has to do with the results of the analyses and the agency theory. This study used data coming from the database of Company X. This means that there is no data included which considers the experiences of the general practitioners or the opioid users. When looking at the agency theory, it might be possible that the prescribing behaviour of the general practitioner was influenced by the relationship between the general practitioner and the opioid user. This has not been considered in this study.

5.3 Recommendations for future research

This study gave insight in the variation in practice between general practitioners according to their prescribing behaviour of opioids in the Netherlands. However, some assumptions are made and not all data from the Netherlands is analysed in this report. Therefore, some recommendations will be suggested for future research.

The first recommendation is that future research should focus on the data related to the general practitioner. In this study the analyses were performed on four-digit zip code level from the members of Company X. However, when performing these analyses on four-digit zip code level from the general practitioners, the results will give more insight in the relation between the number of opioid prescriptions and the general practitioners. In this way no assumptions should be made about the location of the general practitioner relative to the four-digit zip code of the patient. However, an assumption should be made that the general practitioner only prescribed opioids to inhabitants of that same four-digit zip code.

The second recommendation is related to the socioeconomic status data. In order to state that socioeconomic status does have an influence on the opioid consumption in the Netherlands, all aspects related to the socioeconomic status should be considered in the analysis. This can be

done by calculating a score that represents all variables related to the socioeconomic status. When performing analyses with this score, a more reliable conclusion can be made what influence socioeconomic status has on the opioid prescription in the Netherlands.

The third recommendation is that more data with respect to the experiences of the general practitioner and opioid user should be analysed in future research. This information can be gathered by conducting interviews with both the general practitioner as well as with the opioid user to get more insight in their experiences. In this way the underlying reasons for the variation in practice between general practitioners can be discovered. When these motives are clearly formulated, health insurance companies can take this into account when discussing the overuse of opioids in the Netherlands with the general practitioners.

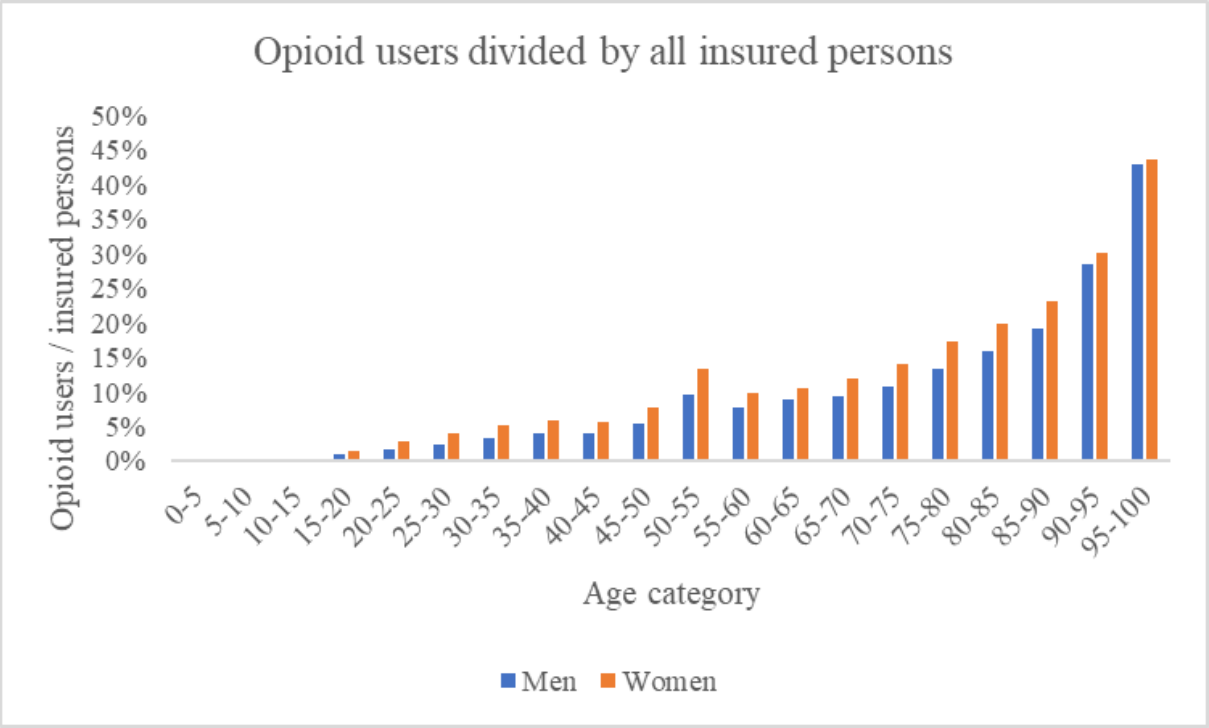
This study found that there is variation in practice between general practitioners with respect to their prescribing behaviour of opioids in the Netherlands. When looking at both the number of opioid declarations and duration of opioid use, the municipalities Aalburg, Sliedrecht and Heerlen have the highest increase in opioid declarations and duration of use compared to expected. When discussing this variation with the highest scoring municipalities and give recommendations for the future on how to change this prescribing pattern, the unnecessary overuse of opioids can be reduced.

6. References

1. Koob GF. The neurobiology of addiction: a neuroadaptational view relevant for diagnosis. Addiction. 2006;101:23-30.
2. Psychemedics. Opiates/Opioids hard drug testing 2019 [Available from: https://www.psychemedics.com/opiates/.
3. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. The lancet. 2006;367(9522):1618-25.
4. NHG-werkgroep Pijn. NHG-Standaard Pijn. 2018.
5. Volksgezondheid en zorg. Kosten van ziekten 2019 [Available from: https://www.volksgezondheidenzorg.info/kosten-van-ziekten#node-zorgkosten-nederland.
6. Rijksinstituut voor Volksgezondheid en Milieu. Zorguitgaven: Hoe ontwikkelen zich de zorguitgaven in de toekomst? 2018 [Available from: https://www.vtv2018.nl/zorguitgaven.
7. Vashishtha D, Mittal ML, Werb D. The North American opioid epidemic: current challenges and a call for treatment as prevention. Harm reduction journal. 2017;14(1):7.
8. Rigg KK, Monnat SM, Chavez MN. Opioid-related mortality in rural America: geographic heterogeneity and intervention strategies. International Journal of Drug Policy. 2018;57:119-29.
9. Seth P, Rudd RA, Noonan RK, Haegerich TM. Quantifying the epidemic of prescription opioid overdose deaths. American Public Health Association; 2018.
10. Helmerhorst G, Teunis T, Janssen S, Ring D. An epidemic of the use, misuse and overdose of opioids and deaths due to overdose, in the United States and Canada: is Europe next? The bone & joint journal. 2017;99(7):856-64.
11. van Amsterdam J, van den Brink W. The misuse of prescription opioids: A threat for Europe? Current drug abuse reviews. 2015;8(1):3-14.
12. Weesie Y, Dijk, L. van, Nielen, M., Flinterman, L., Hek, K. Voorschrijven van opioïden in de huisartsenpraktijk.; 2016.
13. Nivel. Opioïden 2019 [Available from: https://www.nivel.nl/nl/uitgelicht/opioiden.
14. Dahan A, Kramers K, Schellekens A, M. N. Pijnbestrijding: geef opiaten slechts een bijrol 2018 [Available from: https://www.medischcontact.nl/nieuws/laatste-nieuws/artikel/pijnbestrijding-geef-opiaten-slechts-een-bijrol.htm.
15. Van der Lugt P. Een miljoen Nederlanders gebruikt zware pijnstillers. Wat nu? Follow the Money. 2017 [Available from: www.ftm.nl/artikelen/miljoen-nederlanders-gebruikt-zware-pijnstillers.
16. OptimalCare pijnklinieken. Medicijnen: Opiaten 2018 [Available from: https://www.optimalcare.nl/pijnbehandelingen/medicijnen.
17. Vowles KE, McEntee ML, Julnes PS, Frohe T, Ney JP, van der Goes DN. Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. Pain. 2015;156(4):569-76.
18. De Nederlandsche Bank. Visie op de toekomst van de Nederlandse zorgverzekeraars. 2017.
19. Menzis. Zorgvernieuwing (fonds RVVZ) 2019 [Available from: https://www.Menzis.nl/over-Menzis/zorg-voor-de-toekomst/zorgvernieuwing-fonds-rvvz.
20. Menzis (B). Missie en Profiel 2019 [Available from: https://www.Menzis.nl/over-Menzis/over-de-cooperatie-Menzis/profiel.
21. Menzis (C). Jaarverslag 2018, Waardegerichte zorginkoop 2019 [Available from: https://jaarverslag.Menzis.nl/mj2018/voor-mens--maatschappij-in-2018/goede-en-betaalbare-zorg/waardegerichte-zorginkoop.

22. Maike H.J. Schepens, Maarten Leusink, Sytske E. de Vries, Judith A. van Erkelens, Henk Eleveld, Anneke Prenger, et al. Toename in extramuraal opioïdgebruik in Nederland; Gebruik en voorschrijfgedrag onderzocht op basis van declaraties. 2019.
23. Groves KE. The influence of pharmaceutical marketing activity, practice characteristics and physician profile on physician prescribing behaviour. 2006.
24. Michael J, Meckling W. Theory of the firm: Managerial behavior, agency costs and ownership structure. Journal of Financial Economics. 1976;3(4):305-60.
25. Mott DA, Schommer JC, Doucette WR, Kreling DH. Agency theory, drug formularies, and drug product selection: implications for public policy. Journal of Public Policy & Marketing. 1998;17(2):287-95.
26. Schommer JC, Hansen RA. The study of direct-to-consumer advertising for prescription drugs☆. Research in Social and Administrative Pharmacy. 2005;1(2):348-68.
27. Wyszewianski L. Defining, measuring, and improving quality of care. Clinics in Family Practice. 2003;5(4):807-25.
28. Knight A. Patient-centred prescribing. Aust Prescrib. 2013;6:199-201.
29. Murshid MA, Mohaidin Z. Models and theories of prescribing decisions: A review and suggested a new model. Pharmacy Practice (Granada). 2017;15(2).
30. Marmot M. Social determinants of health inequalities. The lancet. 2005;365(9464):1099-104.
31. Braveman P, Gottlieb L. The social determinants of health: it's time to consider the causes of the causes. Public health reports. 2014;129(1_suppl2):19-31.
32. Bartley M. Health Inequalities: An Introduction to Theories, Concepts. Methods. 2004.
33. Macintyre S. The black report and beyond what are the issues? Social science & medicine. 1997;44(6):723-45.
34. Øversveen E, Rydland HT, Bambra C, Eikemo TA. Rethinking the relationship between socioeconomic status and health: Making the case for sociological theory in health inequality research. Scandinavian journal of public health. 2017;45(2):103-12.
35. Skalická V, Van Lenthe F, Bambra C, Krokstad S, Mackenbach J. Material, psychosocial, behavioural and biomedical factors in the explanation of relative socioeconomic inequalities in mortality: evidence from the HUNT study. International journal of epidemiology. 2009;38(5):1272-84.
36. Bambra C. Work, worklessness, and the political economy of health: Oxford University Press; 2011.
37. WHO Collaborating Centre for Drug Statistics Methodology. ATC/DDD index 2020 [Available from: https://www.whocc.no/atc_ddd_index/?code=N02AB&showdescription=no.
38. Centraal Buraeu voor de Statistiek. Huisarts in 2019 gemiddeld op 1 kilometer afstand 2019 [Available from: https://www.cbs.nl/nl-nl/nieuws/2020/17/huisarts-in-2019-gemiddeld-op-1-kilometer-afstand.

Appendix 1


Opioid users divided by all insured persons
Opioid users / insured persons
50%
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
0-5
5-10
10-15
15-20
20-25
25-30
30-35
35-40
40-45
45-50
50-55
55-60
60-65
65-70
70-75
75-80
80-85
85-90
90-95
95-100
Age category
Men
Women

Appendix 2

Municipality	Zip code	Factor1
Haarlemmermeer	2134	0.16
Amsterdam	1019	0.17
Amstelveen	1181	0.17
Amstelveen	1187	0.19
Arnhem	6814	0.20
Schoonhoven	2871	0.21
Enschede	7524	0.21
Eemsmond	9999	0.24
Bodegraven-Reeuwijk	2411	0.24
Gouda	2804	0.24

Table 1: Top 10 lowest increase in opioid declarations than expected

Municipality	Zip code	Factor2
Leeuwarden	9088	0.12
Graft-De Rijp	1486	0.16
Hattem	8051	0.19
Nijmegen	6534	0.21
Enkhuizen	1601	0.21
Smallingerland	9203	0.21
Zwartewaterland	8281	0.22
Elburg	8081	0.23
Bloemendaal	2051	0.24
Hof van Twente	7496	0.25

Table 2: Top 10 lowest increase in duration of use of opioids than expected

Appendix 3

Municipality	Zip code	Absolute difference (declarations)
Culemborg	4104	111
Leeuwarden	9088	101
Aalburg	4265	167
Lelystad	8233	246
Schouwen-Duiveland	4307	122
Alkmaar	1486	85
Nijmegen	6534	174
Leeuwarden	8933	141
Amersfoort	3826	346
Apeldoorn	7329	404

Table 1: Absolute difference in declarations compared to expected

Municipality	Zip code	Absolute difference (days)
Helmond	5709	9340
Vlagtwedde	9545	5631
Gorinchem	4207	4777
Zeist	3703	4770
Stadskanaal	9661	10070
Wassenaar	2242	3939
Leerdam	4141	3873
Tiel	4013	3684
Sliedrecht	3362	7521
's Hertogenbosch	5213	3370

Table 2: Absolute difference in days compared to expected

Appendix 4

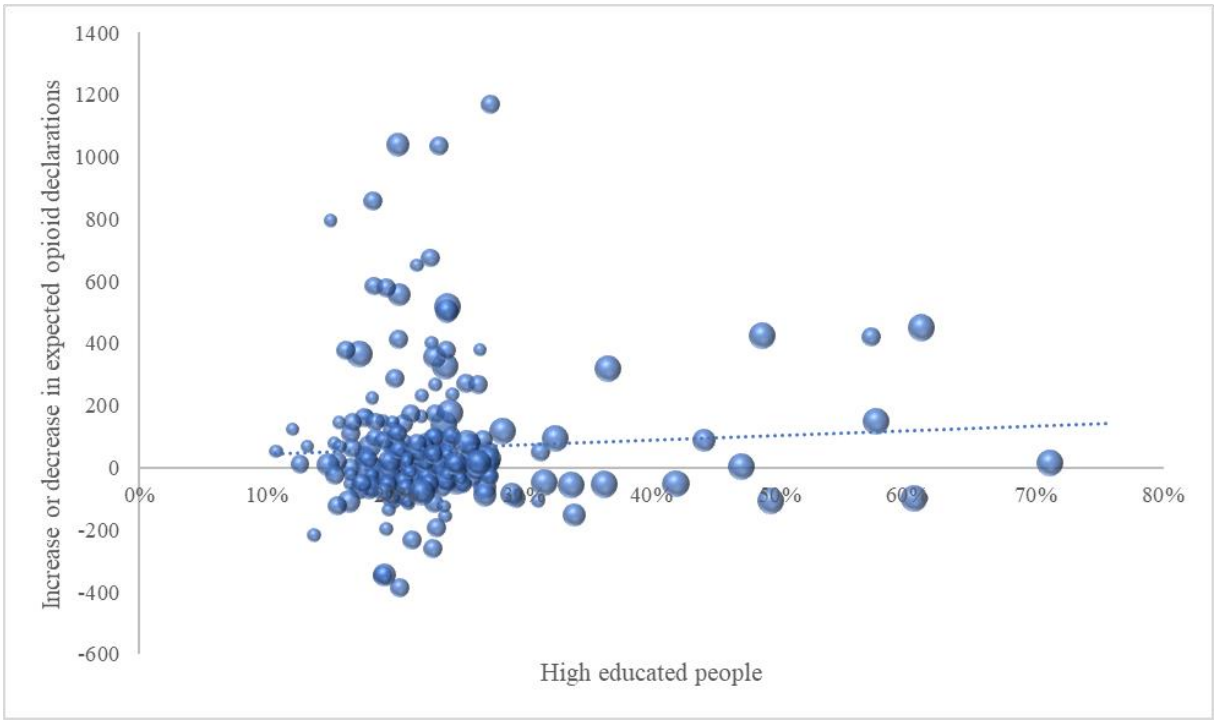


Figure 1: High educated people plotted against the absolute increase or decrease in expected opioid declarations

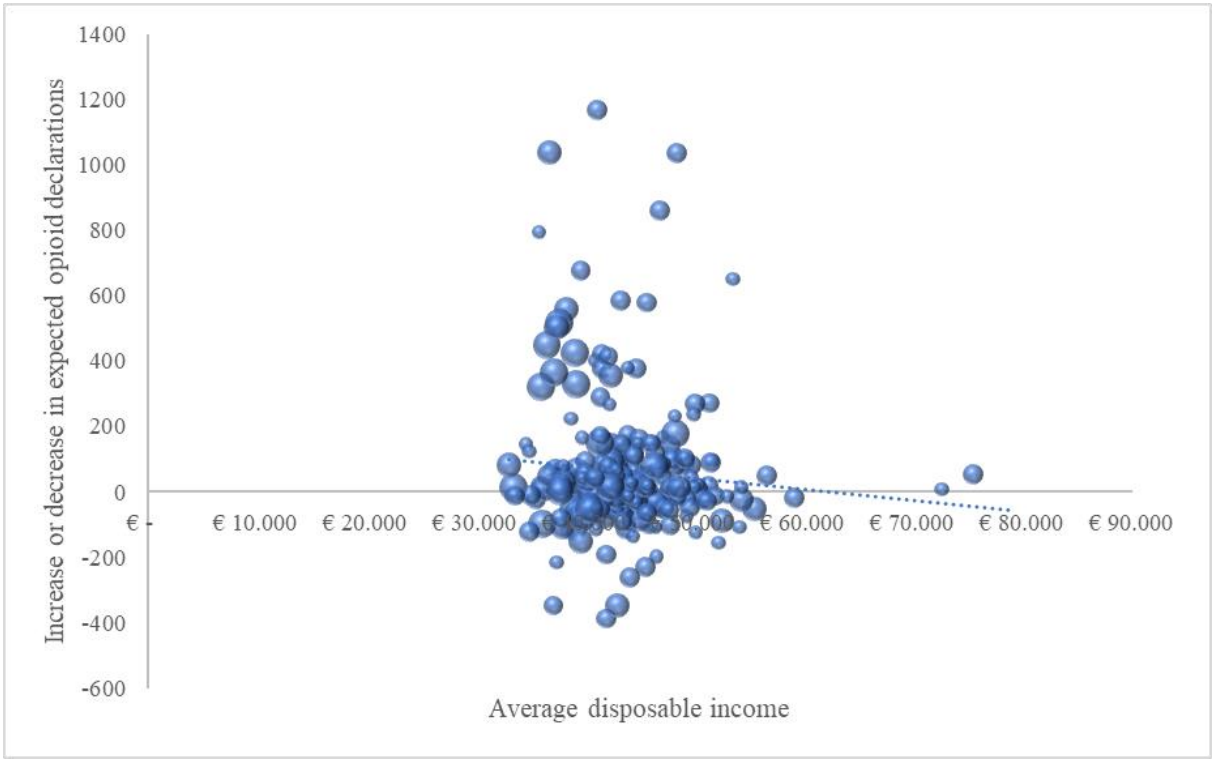


Figure 2: Average disposable income plotted against the absolute increase in expected opioid declarations

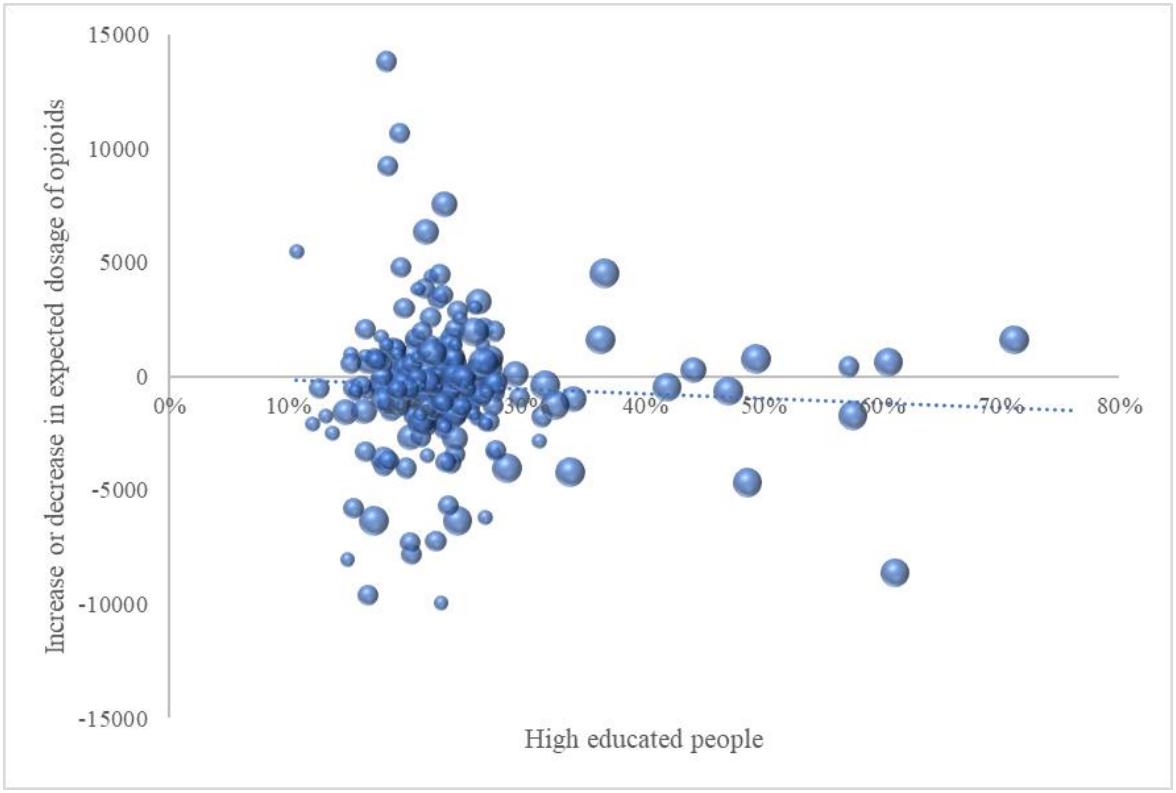


Figure 3: High educated people plotted against the absolute increase or decrease in the expected duration of use of opioids

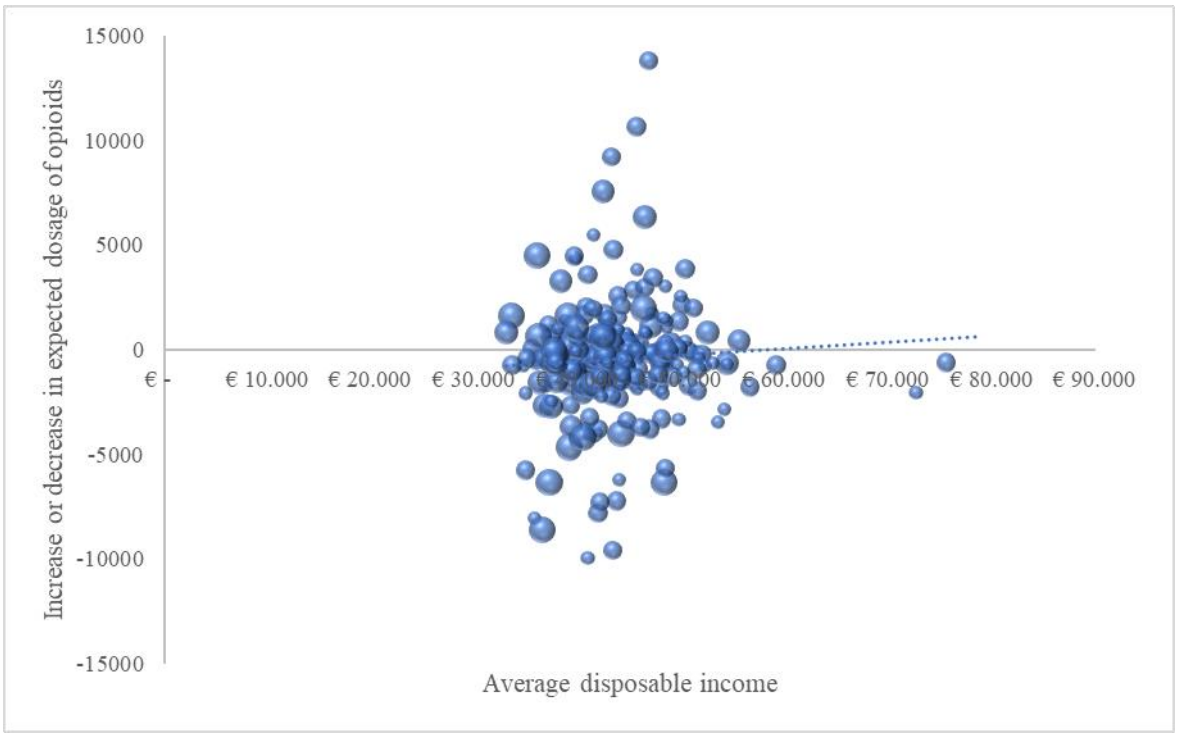


Figure 4: Average disposable income plotted against the absolute increase or decrease in the expected duration of use of opioids

Appendix 5

Municipality	Factor 1	Factor 2	Factor 1*Factor 2
Schoonhoven	0.21	0.53	0.11
Ommen	0.29	0.43	0.12
Heumen	0.38	0.34	0.13
Gouda	0.24	0.60	0.15
Raalte	0.58	0.27	0.16
Krimpen aan den IJssel	0.72	0.25	0.18
Sint-Michielsgestel	0.47	0.39	0.18
Woerden	0.38	0.51	0.20
Pijnacker-Nootdorp	0.32	0.62	0.20
Schijndel	0.67	0.30	0.20
Hattem	1.10	0.19	0.21
Heemstede	0.78	0.29	0.22
Lisse	0.55	0.43	0.24
Lansingerland	0.42	0.62	0.26
Barendrecht	0.40	0.72	0.28
Voorschoten	0.56	0.54	0.30
Wijchen	0.43	0.70	0.30
Noordoostpolder	0.91	0.34	0.31
Zwartewaterland	1.44	0.22	0.31
Zuidhorn	0.51	0.62	0.32

Table 1: Lowest 20 factors representing the increase in opioid declarations compared to expected of all municipalities