Predicting analgesic consumption after minor day surgery

A pilot study

Anne Nikoline Ørstavik

Master of Clinical Psychology

Department of Psychology
University of Oslo

October 2018
Predicting analgesic consumption after minor day surgery

A Pilot study
PREDICTING ANALGESIC CONSUMPTION
Abstract

Background & objective

Previous studies on risk factors for prolonged opioid use or misuse following surgery highlight mental health issues (particularly depression and anxiety) and pain as important risk factors. However, prospective studies are needed to better understand how these factors might increase the probability of problematic use of opioids.

The main objectives of this pilot study were to gather information about the patient group; assess variance in selected measures and test the general set-up of a planned study, and to uncover potential glitches and oversights. Secondary objectives were to assess how pre-operative measures of distress, pain, pain interference, and history of opioid use relate to immediate post-operative use of analgesics, and in particular opiate drugs.

Study design

This was a prospective study. The patients were measured at four different times. T1) a few weeks before surgery, T2) a few hours before surgery, T3) on the operating table three minutes before surgery and T4) the day after surgery. At all time points, we collected measures on negative avert. Pain intensity and pain interference were measured at T1, T2 and T4. At T3 we also measured acute effects of the opioid drug remifentanil, administered for ~3 minutes before the application of anesthesia. Outcome measures were i) whether opioid analgesics were ingested at home after surgery, and ii) the total of analgesic pills (Oxynorm and paracetamol) ingested day one following surgery.

Results

Despite the identification of many necessary improvements to the study protocol, the main result of the pilot study revealed that the study is generally feasible. The interviews at T3 and T4 were successful for both research staff and patients. Further, our preliminary analyses showed levels of pain interference weeks before surgery, and type of operation, to be important predictors for analgesic intake the day after surgery. Higher levels of pain interference were also evident when the group who chose to ingest opioids post-surgery were compared to patients who received opioid analgesics which they did not ingest.

Conclusions

This pilot study suggests that a larger, prospective study including measures before and after surgery, as well as the novel design aspect of including measures of opioid drug effects collected at the operating table, is feasible. I make a series of recommendations for the design of the main study.
Acknowledgements

This pilot has been planned and executed by Siri Leknes, Marie Eikemo, Gernot Ernst and the author. I thank my supervisor Siri Leknes, the P.I., for her support and guidance throughout this entire process. Siri has shared her not only her knowledge, but also her passion and respect for good science. She has welcomed me into her world of research, where ideas flourish and curiosity is valued. I also thank my co-supervisor, Marie Eikemo, for always providing good feedback and input along the way. Marie’s practical approach to both the piloting and writing has made this process doable, and for that I am very grateful.

I also thank Gernot Ernst for our wonderful collaboration, making this project not only possible, but also enjoyable. The data collection for this pilot has been done by the two of us, and Gernot has made it easy for me to see it through, in addition to providing input and answering all my pharmacological questions. I would also like to thank Remy Meir for helping me with the analyses, improving my scientific language and assisting me in many other ways. I am very grateful to the rest of our lab team, who have been endlessly encouraging and supportive along the way. This small community has been a great support. I am thankful to the University of Oslo, Department of Psychology for allowing me to shape this master thesis with them.

Lastly, I would like to thank my wonderful friends and family for always being there and supporting me no matter what. And most of all, I would like to thank Simon, who always believes in me, even when I do not.

Thank you all.
# Table of contents

1 Introduction .................................................................................................................. 1  
  1.1 Opioids and their historical background ................................................................. 1  
  1.2 The opioid epidemic today and the emergence of opioid use disorder .................. 1  
  1.3 Risk factors ............................................................................................................ 3  
  1.3.1 Pain ...................................................................................................................... 3  
  1.3.2 Anxiety ............................................................................................................... 4  
  1.3.3 Sex differences .................................................................................................. 5  
  1.3.4 Drug experience ................................................................................................. 5  
  1.4 The problem – what knowledge do we lack? ......................................................... 6  
  1.5 A possible solution – a prospective study ............................................................... 7  
  1.5.1 Rationale behind the study ............................................................................... 7  
  1.5.2 Pilot study objectives ....................................................................................... 8  

2 Methods ......................................................................................................................... 9  
  2.1 Design ...................................................................................................................... 9  
  2.1.1 Routines for opioid administration at Kongsberg Hospital .............................. 9  
  2.2 Participants ............................................................................................................ 9  
  2.3 Validated measures ................................................................................................ 10  
  2.4 Data collection time-line ...................................................................................... 10  
  2.5 Methodological considerations ............................................................................ 11  
  2.6 Ethical considerations ......................................................................................... 13  
  2.7 Statistical analysis ................................................................................................ 14  

3 Results .......................................................................................................................... 17  
  3.1 Study population .................................................................................................... 17  
  3.2 Pre-operative pain and negative affect .................................................................. 17  
  3.3 Opioid drug responses ......................................................................................... 18  
  3.4 Post-surgery measures ......................................................................................... 18  
  3.5 Comparison of patients who did and did not choose to ingest opioids postoperatively 19  
  3.6 Exploring predictors of post-surgery analgesic consumption .............................. 21  

4 Discussion .................................................................................................................... 25  
  4.1 Suggestions for the main study ............................................................................. 27  

5 Conclusion ................................................................................................................... 33  

References ....................................................................................................................... 34  

Appendix 1 Study Protocol for T1 ................................................................................. 42  
Appendix 2 Study Protocol for T2 ................................................................................. 43  
Appendix 3 Study Protocol for T3 ................................................................................. 44  
Appendix 4 Study Protocol for T4 ................................................................................. 45
1 Introduction

1.1 Opioids and their historical background

There are three main types of opioid receptors, Mu, Kappa and Delta (Kane, Svensson, & Ferguson, 2006). Mu-opioid agonists are the most powerful pain-relieving drugs currently available (Raffa, Ossipov, & Porreca, 2017). Mu-opioids are drugs with morphine-like action; this includes both natural and synthetic compounds. They have several medical uses, including pain relief, treatment of diarrhea and as an antitussive (Bowery, 2007). Originally opiates, such as morphine, were derived from the juice of the opium poppy plant. The first references for opium use dates back to the third century B.C., by the Greek Theophrastus. Since then, there have been many accounts of use of opium for medical and recreational reasons. Some of these descriptions of medical use of opioids also include the problems of withdrawal from opioids (Koob, Arends, & Le Moal, 2014b). Use of opioids is, and has always been, highly addictive (Koob et al., 2014b). Addiction, which is characterized by a compulsion to take the drug in question, an inability to limit intake, and a severe negative emotional state when the drug is withdrawn (Koob, Arends, & Le Moal, 2014a), is a common consequence of excessive opioid use. There are two behavioral domains in which opioids have pronounced effect, and that is pain relief and intoxication, characterized by a feeling of euphoria or “high” (Koob et al., 2014b).

1.2 The opioid epidemic today and the emergence of opioid use disorder

The use of opioids was unlimited and widespread in the U.S. up until 1914 when the Harrison Narcotics Act was enacted. However, excessive heroin use and opioid addiction had already become a substantial medical problem (Koob et al., 2014b), and still is today (Gomes, Tadrous, Mamdani, Paterson, & Juurlink, 2018). Approximately one third of the population in the U.S. report having chronic pain (Gostin, Hodge, Jr, & Noe, 2017) and one fifth of the population in Europa report experiencing chronic pain (Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006). With a letter to the editor from Porter and Jick (1980) stating that opioids used to treat pain did not lead to addiction in their study, over-prescription of opioids for pain escalated. The massive citation of this letter lead to a common belief that pain was protective factor against opioid addiction. In the mid 1990s the American Pain Society lobbied to recognize pain as the fifth vital sign. The society emphasized the importance of patients’ rights to appropriate pain management. As a consequence, the liberalization of prescribing opioids for chronic, non-cancer pain continued (Skolnick, 2017).
The belief that opioid taken for pain relief is not addictive has since been refuted (Chou et al., 2015; Juurlink & Dhalla, 2012; Skolnick, 2017), but not in time to prevent millions of people from developing opioid addiction. Despite great efforts to understand addiction, the number of opioid dependent individuals and opioid overdoses has continued to rise both in the U.S and in Europe (World Drug Report, 2017). Opioids are found in 84% of all fatal overdoses (EMCDDA, 2018). Opioid overdoses increased in the U.S. 156% from 2010 to 2015 (Gostin et al., 2017). Even though the evidence for its efficaciousness gradually diminishes, opioids are still being prescribed massively (Juurlink & Dhalla, 2012). The number of chronic opioid users is growing, and with it the societal burdens of both morbidity and economic costs continue to rise. The Opioid epidemic has now reached a scope that even the President of the U.S. acknowledges it (Davis, 2017). In the U.S., they are now selling less prescription opioids, but this is not reflected in the overdose statistics, where the numbers are still at a peak. Figure 1 illustrates the amount of prescription opioids sold in the U.S. and Europe (Ruchat, Suter, Rodondi, & Berna, 2018). In Europe, the selling rate is still rising. In Norway, there has been an 19.5% increase in registered prescription opioid users (Anatomical Therapeutic Chemical Classification System (ACT)), code N02A) from 2007-2017 (NorPD, 2018). This statistic does not include any illegal use.

One of the main challenges of the opioid epidemic is limiting availability. Since 1990, prescription opioids have quadrupled globally (Tetrault & Butner, 2015). Opioids have become the most prescribed drug class in the U.S. (Deyo, Von Korff, & Duhrkoop, 2015). It is frequently found in house medicine cabinets, and is commonly used during routine medical care, like surgery. The likelihood of being exposed to opioids is high, even though it is now common knowledge that the drugs are highly addictive. However, proper use of opioids can improve quality of life for patients suffering from cancer pain (Swarm et al., 2013). As there are no alternative drugs that have the same analgesic qualities as opioids, prohibiting the class of drugs altogether is not a viable option. Because opioid addiction has become such a pressing problem, the fifth version of the Diagnostic
and Statistical Manual of Mental Disorder (DSM-5) has separated Opioid Use Disorder (OUD) from Substance Use Disorder (SUD) (Webster, 2017).

For some patients, OUD may subsequently develop in parallel with pain disorders following surgery. This is a common route to OUD. Pain is a biopsychosocial experience, and for some individuals, post-operative pain may never subside, but instead develops into chronic pain. The duration and intensity of post-operative pain is variable. Opioid analgesics are commonly given to surgical patients to treat acute post-operative pain. Patients who have pain that does not subside, may take opioids for a longer period of time. This can create an iatrogenic opioid addiction and is an important contributor to the opioid epidemic.

1.3 Risk factors

The literature identifies several important risk factors for developing prescription opioid misuse. The most common are mental health issues (particularly depression and anxiety), alcohol- and substance abuse, pain disorders, tobacco use, prior opioid use, some somatic comorbidities, and parallel use of benzodiazepines (Clarke, Soneji, Ko, Yun, & Wijeysundera, 2014; Goesling et al., 2016; Inacio, Hansen, Pratt, Graves, & Roughead, 2016). The study of risk factors for OUD is important because the population, the behavior, and the route to addiction may differ from what we already know from studies on substance abuse disorder (SUD) (Webster, 2017). Many of the behaviors associated with illegal drug use in SUD do not need be present in OUD patients and vice versa. For example, seeking prescriptions from multiple prescribers and “losing prescriptions” is typical behavior associated with OUD. This is different from abuse of illegal drugs, where prescription drugs are more often seen as a way for many to finance their addiction to illicit drugs.

1.3.1 Pain

The research on predictors for prolonged opioid use highlight pain as an important risk factor (Bedard, DeMik, Dowdle, & Callaghan, 2018; Brummett et al., 2017; Goesling et al., 2016; Inacio et al., 2016). Because opioids are primarily used as analgesics, it is reasonable to assume that higher levels of pain could be a predictor for persistent opioid use (Rosenbloom, McCartney, Canzian, Kreder, & Katz, 2017), i.e. that patients with higher levels of pain receive and take more opioids. However, the reasons for initiated use and continued use may not be the same. The field has not reached any consensus regarding the reasons for continued use of opioids, i.e. use of opioids to treat persistent pain. The continued use of opioids may not be dependent on the level of pain, or on the reduction of pain that is attributed to the opioid medication (Goesling et al., 2016). A study on
patients seeking treatment for prescription opioid dependence, showed that the reason for maintaining opioid use is primarily to avoid the discomfort associated with withdrawal (Weiss et al., 2014). This applied to both chronic pain patients seeking treatment, as well as non-chronic pain users. In this study, both groups claimed that the reasons for initial use was pain relief, although the chronic pain patients were more likely to report this. For the chronic pain group, the second most important reason for maintaining misuse was pain relief. However, another study highlighted pain severity as the most important predictor for continued opioid use (Rosenbloom et al., 2017). While the exact role of pain as a risk factor for addiction to opioids is not entirely clear, it is clearly important.

The term pain interference, while not precisely defined in the scientific literature on pain (Wilson, 2014), is a measure of the patients’ experienced consequences of pain in different aspects of life. This includes how pain interferes with social, emotional, vocational, cognitive and physical activities. Validated measures of pain interference include both Patient-Reported Outcome Information Systems (PROMIS) (Schuller et al., 2018) and the Brief Pain Inventory (BPI) (Holen, Lydersen, Klestad, Loge, & Kaasa, 2008). Back pain is associated with high pain interference, and a study by Inacio et al. (2016) showed that patients with a back pain diagnosis prior to total hip arthroplasty have up to four times higher risk of developing chronic opioid use following surgery, compared to those without prior pain diagnosis. Pain interference may be more predictive of prolonged opioid use than pain intensity (Adams et al., 2018; Rosenbloom et al., 2017), possibly due to patients’ desire to use opioids to cope with the consequences of chronic pain. High consumption of analgesics may also be partly explained by high pain interference, and less by pain reduction, as commonly assumed.

1.3.2 Anxiety

The experience of pain is in large part dependent on one’s mental and emotional state. People with a known affective disorder, such as depression and anxiety, are more likely to experience high pain severity than people without (Lumley et al., 2011). The literature on risk factors for prolonged opioid use also highlights anxiety and pain catastrophizing. Pain catastrophizing, expecting and imagining worst case scenarios regarding pain experience and healing, is one of the most important predictors for development of chronic post-surgical pain (Burns et al., 2015). Large retrospective studies have shown that having a diagnosed anxiety disorder correlates with prolonged opioid misuse and is therefore a potential risk factor (Bateman et al., 2016; Brummett et al., 2017; Inacio et al., 2016). Pain catastrophizing has also been shown to be particularly common among patients.
receiving prescription opioids. In a study by Valdes et al. (2015) it was found that pain catastrophizing was strongly associated with opioid consumption, but not with non-steroidal anti-inflammatory drugs (NSAIDs) and other non-prescription analgesics. Pain catastrophizing was associated with opioid misuse even when controlling for anxiety (Martel, Wasan, Jamison, & Edwards, 2013). Moreover, anxiety, depression and pain catastrophizing are closely associated with experiencing negative affect, which is in turn a risk factor for prescription opioid misuse (Martel, Dolman, Edwards, Jamison, & Wasan, 2014a).

1.3.3 Sex differences
Most articles highlight women as being more at risk to misuse of opioids, but there are also some large studies showing men as the more vulnerable sex (Cochran et al., 2014; Sun, Darnall, Baker, & Mackey, 2016). In a commentary, Darnall and Stacey (2012) highlight that women are more vulnerable to chronic pain and that women on average experience higher levels of pain intensity than men. As pain severity is an important indicator for prescribing opioids, it is not surprising that epidemiological studies on pharmacy claims also find that women receive more opioids (Brummett et al., 2017). However, in a study on gender differences among opioid addicted patients, men were significantly more likely to receive alcohol and drug treatment, and exhibited more OUD related behavior such as receiving opioids from other people’s prescriptions after having consumed their own (Back, Payne, Simpson, & Brady, 2010). Women are also more likely to experience depression and anxiety, two major predictors of opioid addiction (Brummett et al., 2017; Inacio et al., 2016; Sun et al., 2016). Other studies have shown that women suffer from more psychological distress as a consequence of chronic pain and therefore have other reasons to misuse opioids than men (Darnall & Stacey, 2012; Jamison, Butler, Budman, Edwards, & Wasan, 2010)

1.3.4 Drug experience
Patients who suffer from both SUDs and anxiety- and mood disorders often use substances to self-medicate (Bizzarri et al., 2007; Khantzian, 1997). Having a positive subjective experience of drug effects is predictive of continued use (de Wit & Phillips, 2012). Studies of abuse liability for prescription opioids also highlight likeability. In a study by Wightman, Perrone, Portelli, and Nelson (2012), higher drug liking was associated with higher scores on SOAPP-R (Screener and Opioid Assessment for Patients with Pain- Revised). SOAPP-R is an instrument used to predict increased risk of opioid misuse in chronic pain patients (Butler, Fernandez, Benoit, Budman, & Jamison, 2008). Higher scores on SOAPP-R have also been associated with higher analgesic effect (Bruehl et al., 2015). This suggests that the individuals who are at high risk of misuse maybe the
ones who also receive sufficient and appropriate analgesia from the opioids. This indicates that the subjective experience of opioids may be of central importance for future use and potential misuse, both in terms of analgesic effect and in terms of liking and positive affective experience. However, most of these studies are retrospective, i.e. based on patients’ recall of their initial drug experience prior to addiction. When asked to describe their first “opiate experience”, patients who misuse their opiates describe their first encounter with opiates as much more pleasant than those in chronic opioid treatment who adhere to treatment (Bieber et al., 2008; Skala et al., 2013). This increase in reports of drug high and euphoria may however be due to memory bias, a cognitive bias that can either impair or enhance the recollection of a memory. Prospective data is needed to resolve the predictive power of early drug responses for subsequent drug use. In addition to this, prior opioid experience is also a risk factor associated with prolonged use of opioids following surgery (Bedard et al., 2018; Brummett et al., 2017; Inacio et al., 2016). This was measured through having prescribed opioids prior to surgery. However, these prescriptions usually followed diagnosis, which indicated prescription opioids, like myalgia and chronic back pain.

1.4 The problem – what knowledge do we lack?

The majority of studies on risk factors for prolonged opioid use- and misuse are retrospective insurance claims analyses investigating opioid consumption following surgery. These studies are a good source of information regarding the demographic characteristics associated with problematic and prolonged opioid use; however, there are several methodological considerations that need to be addressed. In these studies, mental health diagnoses are commonly associated with prolonged opioid use. However, the mental health status is usually operationalized through the prescription claims of antidepressants and other psychopharmacologic drugs, which means that people who suffer from mental health problems, but do not use such drugs are not included in the sample. Furthermore, these studies often do not differentiate between reasons for prescribing. Indications for psychopharmacologic drugs include, but are not limited to, psychopathology. For instance, they are commonly used to treat headaches and migraines (Smitherman, Walters, Maizels, & Penzien, 2011), neuropathic allodynia (Kremer et al., 2018) as well as chronic non-cancer pain (Giladi et al., 2015).

In a review on risk factors associated with opioid misuse, Pergolizzi et al. (2012) caution against the interpretation of mental health diagnoses as a risk factor for opioid misuse. This category of diagnoses is highly stigmatized and may in many cases be concealed. Some patients may even choose to self-medicate co-occurring mental disorders with opioids rather than with the
appropriate psychopharmacologic medication. This suggests that the statistical associations between mental health disorders and opioid misuse may be confounded. While retrospective analyses have provided valuable information about patient characteristics, how and why these characteristics are related to opioid misuse is still unknown, and prospective studies are needed to address these questions.

We are still a long way from understanding the processes that make opioid drugs so addictive. However, clinical studies have started to address the causes of opioid misuse in chronic pain patients. This group of patients is particularly vulnerable to opioid misuse, with misuse estimates of 25-50% (Vowles et al., 2015). New clinical data shows that the misuse of prescription opioids in chronic pain is driven more by emotional distress than by a desire for pain relief (Martel, Dolman, Edwards, Jamison, & Wasan, 2014b; McHugh et al., 2016). These results are in line with previous epidemiological studies, where vulnerability to addiction is increased by negative affect, presence of stressors, and poor social support networks (Stone, Becker, Huber, & Catalano, 2012). While the associations between pain, affective state, and risk for misuse are already established, more research on how these factors interact and change will provide us with a unique understanding as to how they work as risk factors. Because pain and mental health are a crucial part of the opioid epidemic, the link between them deserves a closer look.

1.5 A possible solution – a prospective study

1.5.1 Rationale behind the study

Prescription opioids remain the gold standard treatment for acute postoperative pain, both in Norway and the U.S. It is now clear that the presence of pain does not protect against the addictive properties of opioids, as was previously assumed (Portenoy & Foley, 1986; Porter & Jick, 1980). Very little is currently known about the risk of opioid misuse after surgery and prescription opioid exposure in Norway, as most of existing studies use data from the U.S. and Canada. However, the many differences between Norway and the U.S., (e.g. in prescription rates for opioid drugs, see Figure 1) mean that new, local data is needed for assessment and possible improvement of Norwegian clinical practices.

Through a collaboration with an anesthetist at Kongsberg Hospital, a local Norwegian hospital, we have had access to a group of patients undergoing minor day surgery. We planned a prospective pilot study, to assess pre-operative distress-, opioid drug effects-, several pain measures and post-operative analgesic consumption. A novel feature of our study design was that we measured how patients felt before surgery (e.g. feeling distressed, happy, nervous), and also
measured their affective responses to pre-surgery opioid analgesia. In Kongsberg, as in many hospital departments in Norway, remifentanil is administered 3 minutes before anesthesia to reduce the discomfort associated with general anesthesia. Remifentanil is a highly potent mu-opioid receptor agonist drug, commonly used adjunct to anesthesia (Patel & Spencer, 1996). During this time, we collected verbal ratings of drug high, positive and negative feelings, and side effects. Prospective data obtained in the current project may enable a more unbiased test of whether early positive drug experiences are actually predictive of subsequent risk of misuse. We also wanted to explore associations between relevant variables in this population on measures such as pain, pain interference, negative affect, and history of opioid use with post-operative consumption of analgesics and opioids immediately following surgery (the following day), after 6 months and after 12 months. The pilot is, however, not longitudinal, and only includes follow-up one day after surgery.

1.5.2 Pilot study objectives
The primary aim of the pilot study was to collect detailed information on pre- peri- and post-operative variables in a sample of day surgery patients at Kongsberg Hospital, variables of probable relevance for further studies on risk factors for drug abuse. This was considered essential for a proper design of a full-scale, prospective study. Secondary objectives were to assess how pre-operative measures of negative affect, pain, pain interference, and history of opioid use relate to immediate post-operative use of analgesics, and in particular opiate drugs. Another secondary objective was to assess and compare psychological characteristics of patients who chose to use opioid drugs following surgery and those who did not.
2 Methods

2.1 Design

This was a prospective, exploratory observational pilot study. The study was designed to ensure minimal inconvenience for participants. Participants received surgical treatment as usual. By not having any interventions, we were able to keep the ecological validity the study high. The participants answered questions at four different time points: Weeks before surgery, twice on the day of surgery and once on the day following the procedure. The participants were asked to report their level of anxiety, distress, pain, and pain interference at several time points. The amount of analgesics consumed at day one post-surgery was recorded as the main outcome variable for data analysis.

2.1.1 Routines for opioid administration at Kongsberg Hospital

The combination of opioids and benzodiazepines (BZD) is standard anesthetic procedure for surgical treatments at Kongsberg Hospital. To minimize risk of opioid misuse, physicians administer pain management plans that favor NSAIDs and paracetamol for post-surgical pain and only prescribe a limited number of opioid pills (1-5 pills of Oxynorm 5 mg). Patients are not given an opioid pill supply or prescription to last long term, but are instead given a few single doses to use as needed during the first few days following surgery. Patients are encouraged to only take opioids to reduce pain flares, a period when pain is markedly more severe than usual (Suri, Saunders, & Von Korff, 2012), and not as an ongoing solution for pain reduction. This is a very different culture concerning opioid use and prescription as compared to the U.S. and Canada, where 30 or more prescription opioid pills are often prescribed by default following surgery (Chiu et al., 2018).

2.2 Participants

We recruited patients scheduled for minor day surgery at Kongsberg Hospital. The participants consisted of a general population healthy enough to undergo minor day surgery. All participants where above 18 years of age. Any exclusion criteria for undergoing surgery also excluded participation in the study (obesity, serious psychopathology etc.). Participants were invited to join the study when they arrived at the hospital. Written consent forms were signed by all who agreed to participate. The surgical categories consisted of colorectal, gynecological, minor abdominal, otorhinolaryngology and other surgeries. Other surgeries were mostly different diagnostic biopsies.
2.3 Validated measures

To facilitate comparison with other studies, we chose to use standardized measures wherever possible. Our most important constructs to gauge was anxiety and pain. Parts of the Brief Pain Inventory (BPI) (Holen et al., 2008) were considered suitable for our study. We used a validated Norwegian translation (Klepstad et al., 2002). This was preferable not only because the items were validated but also because the response form was in a numeric rating scale (NRS). This was convenient as the patients could comfortably use the NRS when being interviewed orally in the minutes before surgery and on the day following surgery (as opposed to using a visual analogue scale (VAS)). When interviewing the participants about their experience of opioids we used items from the well-established Drug Effects Questionnaire (DEQ) (Morean et al., 2013). This questionnaire is not validated in Norwegian. We used an in-house translation that has been used in several previous experiments.

2.4 Data collection time-line

T1: 2-3 weeks prior to surgery. Patients accepting to participate, gave their permission for us to gather information about how nervous they were beforehand, several demographic characteristics, and their levels of pain and pain interference. This information came from a form the hospital sends out weeks in advance as a routine leading up to surgery (treatment as usual).

T2: on arrival at the hospital the day of their surgery. Patients were asked to participate in the study on the day they arrived for surgery. The participants consented to the information collected by the hospital during the consultation session. After signing informed consent, the patients completed a new questionnaire recording their mood, pain, pain interference, and previous experience with opioids.

T3: on the operation table. The participants were asked a set of questions relating to their mood, drug liking and drug effects of remifentanil.

T4: the day after surgery. The participants were called by the author the following day and asked specific questions about their mood and their subjective experience of pain, pain interference, analgesics consumption, and whether they had applied other pain relief strategies. This telephone interview proved to be an excellent source of qualitative and quantitative information on how the patients have experienced the pre- and post-surgery periods. Figure 2 illustrates the data collection time line.
2.5 Methodological considerations

When planning the pilot emphasis was placed on balancing the inconvenience to the participants and acquisition of the most important information relevant for the study. Our pilot was characterized as a quality assurance study at the hospital, as there were no interventions, only systematic documentation and information gathering along the way to and after surgery. By choosing a non-interventional design we were able to quickly obtain approval by the ethics committee. This would not have been the case for a pilot involving an experimental variable in the treatment procedures.

**The T1 questionnaire**: We added items on pain and nervousness to an existing questionnaire, that every surgical patient is required to complete and return to the hospital prior to the surgeries. This 2-page questionnaire has not typically been used for research purposes, but by clinicians to assess potential risks. We also changed the rating scale of nervousness about the operation from a visual analogue scale (VAS scale) to a numerical rating scale (NRS). This was done to avoid confusion, since all subsequent measures were collected on NRS scales. The number of items added was limited by the desire to keep the length of the questionnaire to a single A4 sheet (two-sided) for convenience of the patients. See appendix 1 for the T1 questionnaire.

**The T2 questionnaire**: When designing the questionnaire for T2, we chose to limit the questionnaire to a single sheet, printed on both sides. This was necessary to ensure that the participants would be able to complete the form in time for surgery and to limit the effort associated

---

*Figure 2. Data collection time line. The figure gives a brief overview of the measures collected at the different time points.*
with participating in the pilot. Furthermore, we made an effort to avoid fatigue effects sometimes associated with invalid answers on questionnaires. As T2 occurs in the hours right before surgery, we also made sure the majority of questions were of positive or neutral affective denomination, to avoid any unintentional negative priming of the affective state right before surgery. When the patients were completing the T2 questionnaire, they had not eaten since the day before. Moreover, as instructed by the medical personnel, patients had also ingested 1.5-2 g paracetamol and 500 mg naproxen. The effects of fasting and analgesics therefore needs to be considered when investigating pain and mood states at this time point. At T2, the patients rated their current state of several mood measurements, including nervousness. The questionnaire does not specify that the nervousness must be attributed to the surgery, however, as T2 is set only hours before surgery it is not an unreasonable assumption. The nervousness measure at T1 specified that the nervousness is attributed to surgery (“How nervous are you about having surgery/anesthesia). When discussing the results from the study we have chosen to assume that their nervousness measured on T2 is result of the expected surgery. See appendix for T2 questionnaire.

The T3 measure: The established procedures for administration of remifentanil during the minutes leading up to general anesthesia with Propofol placed restrictions on the number of items that could be included in this assessment. Remifentanil was administered 3 minutes before Propofol. The anesthetist estimated that we would have time to pose two questions before remifentanil administration and another 5 questions before the patient would be administered propofol. Following Propofol administration we tentatively added one question, how well they felt. These questions were adapted from the Norwegian translation of the Drug Effects Questionnaire (DEQ). We also included an item measuring their levels of distress. See appendix 3 for the questionnaire.

The original and validated form of the DEQ separates “like” and “dislike” in two different items, using a unipolar scale for each item (Morean et al., 2013). Using a bipolar scale to investigate liking and disliking means losing some potentially valuable information. However, during the pre-pilot our anesthesiologist reported that patients seemed unable to respond adequately to questions using unipolar scales. For example, the wording of the DEQ ‘liking’ and ‘disliking’ items originally ask how much you “like the effects of the drug” first, and second how much you “dislike the effects of the drug”. However, this seemed to confuse the patients as they reported to like and dislike remifentanil at equal values. We therefore altered our items in T3 to only assess how much they liked the drug effects of remifentanil on a bipolar scale. These answers were given on the NRS scale, where 0 indicated that they did not like the effects, and 10 indicating that they liked the effects very much.
The T4 interview: When designing the questionnaire to be used on the day after surgery, we used a collection of items related to subjective state and pain, some of which matched questions from the previous questionnaires to enable statistical comparison over time. We also asked which analgesics the participants had self-administered for pain relief. The doctors at the hospital had provided the patients with a pain management plan, but not all had adhered to it. Obtaining self-reports about which and how much analgesics patients used provides additional valuable information to just looking at which and how much analgesics has been prescribed in a prescription database. T4 was also the only time where the patients were in actual conversation with a researcher (the author). Some of the questions are open-ended, and the responses are consequently qualitative in nature. We asked about their other pain relieving strategies, apart from medication. We also asked the patients about their pain levels as well as if, and how, they experienced any pain interference. Even though we used validated measurements for both pain and pain interference, the semi-structured interview opens up for a more qualitative and possibly better understanding of their psychology concerning postsurgical pain, healing, and expectations.

At T4, we specifically asked whether or not they had taken opioid analgesics, but not all patients received opioids from the hospital. This information was gathered from two different sources. The anesthesiologist reported what he had provided to them, but the participants were also asked directly about this during the phone conversation. Usually there were no discrepancies, but some of the participants claimed that the analgesics were never provided. The reason for these discrepancies is unclear.

2.6 Ethical considerations

The pilot study protocol was reviewed and accepted by the internal review board at Kongsberg Hospital. As this was conducted as a quality assurance study and there were no interventions, there were few ethical concerns and we received approval from the ethics board quickly. All our documentation is in line with the Helsinki declaration. All patient information was treated with the utmost care. Without any interventions, the ecological validity of the study was high. We observed treatment as usual and documented patients’ status along the way. The patients’ experience of important measures such as pain and nervousness were without interference or manipulation. The pilot was also designed to ensure that there would be no negative impact for either participants nor staff at Kongsberg Hospital. All patients agreeing to participate in the study received a follow-up phone call the day after operation, whereas non-participating patients did not. This phone call can be described as a support call and may be psychologically beneficial for some patients. Apart from
this, there were no benefits from agreeing to participate. This phone call did not affect any other parts of the treatment. However, if patients were to report very high levels of distress or pain, or other serious concerns during the phone call, the interviewer would have advised them to call the clinic during working hours or to call 113. This did not happen during the pilot study. As described below, we made some minor alterations to the study design during the pilot, but these were within the scope of our ethics approval.

2.7 Statistical analysis

All analyses were performed using SPSS statistic software (version 25). Data analyses consisted of exploratory descriptive analyses, t-tests, correlations, and regressions. In addition to this, graphs were made to illustrate characteristics of the group who used opioids post-operatively versus those who received opioids to take home, but did not use them. Descriptive analyses (mean, SD, range, frequencies) and t-tests were used to describe the study sample, and to compare groups (i.e. took opioids or not, operation category) or drug effects.

To assess possible differences between the group who chose to take opioids in the post-operative period and those who refrained, independent samples t-tests were used on relevant measures from the day after surgery (T4), such as pain intensity and experience of analgesic efficacy.

A Spearman’s Rho correlation matrix was used to explore the correlation between the outcome variable, amount of analgesia consumed one day post-surgery, and predictor variables from T1 to T3, as well as to determine significant correlations among the predictive variables. To avoid problems with multicollinearity, when two variables were strongly correlated, only one was included in further analyses; for example, repeated measures of nervousness and pain. Poisson regression analysis was used to investigate the predictive value of risk factors associated with analgesic consumption.

Variables were considered for inclusion in the model selection based on theoretical reasoning and statistical correlations with the outcome (primarily to avoid problems with multicollinearity). The outcome variable, the amount of analgesia consumed one day post-surgery, was based on the patient’s self-report during the follow-up phone call the day after the operation (T4). The outcome variable consisted of the patient’s total consumption of paracetamol and Oxynorm. The NSAID Vimovo was excluded as patients were encouraged to take Vimovo regardless of pain due to its anti-inflammatory qualities. Because the regression is predictive, only variables preceding the outcome where considered for variable selection, i.e. no variables from T4.
were considered for the regression. Based on the literature on predictors for problematic or prolonged opioid use, variables of theoretical interest included key demographic information (operation category, patient sex), substance-related factors (prior opioid use, tobacco use, mood change during acute opioids), presence of pain, pain interference and measures of affect. Based on the strength of individual correlations, pain intensity right before surgery (T2) and pain interference weeks before surgery (T1) were selected for subsequent regression analyses, as these variables had significant correlations with the outcome variable.

In addition, the predictive value of two measures of nervousness on analgesic consumption was tested. First, the level of nervousness weeks before surgery (T1) was considered, as this variable may be a proxy for a general tendency for nervousness related to personality traits. Second, the patients’ levels of nervousness right before surgery (T2), which may reflect acute nervousness and therefore act as a state measure, was also taken into account. Both these measures where included for further analyses, but they were not placed in the same regression model due to the high correlation between them (r=0.621). Patients’ mood changes during acute opioids was included because of theoretical significance. See Table 1 for the complete list of variables selected for regression analyses (model selection).

<table>
<thead>
<tr>
<th>Demographic variables</th>
<th>Pain variables</th>
<th>Affect variables</th>
<th>Substance abuse variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation category</td>
<td>Pain interference weeks before surgery*</td>
<td>Nervousness weeks before surgery (trait measure)</td>
<td>Prior opioid exposure</td>
</tr>
<tr>
<td>Participant sex</td>
<td>Pain levels approximately three hours before surgery*</td>
<td>Nervousness right before surgery (state measure)</td>
<td>Tobacco use</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mood improvement during acute opioids</td>
</tr>
</tbody>
</table>

* chosen because of significant correlation with the outcome

I conducted Poisson as the outcome variable is a count variable. One of the statistical assumptions of a Poisson regression analysis is that the mean and standard deviation are equal. Our data were to some degree over-dispersed. Accordingly, I used robust estimation of covariance in all Poisson regressions to correct for over-dispersion (Field, 2013). Bivariate regressions were first
applied for the selected predictors. Based on BIC (Bayesian Information Criterion)- and p-values, the most significant variable was first entered in the regression, followed by the other significant (theoretically or statistically) variables, one at the time. The BIC value is a criterion for model selection, used to compare models. The model with lowest BIC value is preferred (Neath & Cavanaugh, 2012). These models were also evaluated by BIC value and p-value comparison. In addition to this, gender information was used as a covariate in one regression model assessing the potential bias of unequal spread of men and women in the different operation categories.
3 Results

3.1 Study population

Thirty-eight patients were recruited for this pilot study. We were able to contact 34 participants post-surgery for the T4 interview; thus, the final sample size was 34. Women made up the majority of the sample, with 61.8%. The mean age for all participants was 48.7 years. Table 2 describes the patient’s sex, age, operation category, tobacco use, their previous experience with opioids as well as the number of chronic pain patients. Seven participants reported using tobacco. The largest operation category was the colorectal surgeries (21/34). Nineteen (55%) participants reported having chronic pain. Seventeen reported having previous experience with opioids. Table 2 displays patient characteristics.

Table 2. Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>21 (61.8%)</td>
<td>13 (38.2%)</td>
<td>34</td>
</tr>
<tr>
<td>Age</td>
<td>49.2± 12.7</td>
<td>49.2± 17.0</td>
<td>48.7±14.3</td>
</tr>
<tr>
<td>Age range</td>
<td>49</td>
<td>47</td>
<td>53</td>
</tr>
<tr>
<td>Operation type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colorectal</td>
<td>8</td>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>Gynecological</td>
<td>7</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Otorh.</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Min. abdominal</td>
<td>4</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Tobacco</td>
<td>6</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Pain more than 3 months</td>
<td>12 (35.3 %)</td>
<td>7 (20.6%)</td>
<td>19 (55.9 %)</td>
</tr>
<tr>
<td>Pain duration, months</td>
<td>25.5±40.3</td>
<td>13.70±32.43</td>
<td>20.97±37.41</td>
</tr>
<tr>
<td>Prior opioids</td>
<td>12 (35.3%)</td>
<td>5 (14.7%)</td>
<td>17 (50%)</td>
</tr>
</tbody>
</table>

N = number of participants, Mean±Standard Deviation. Otorh. = otorhinolaryngology, Min. abdominal = minor abdominal surgery.

3.2 Pre-operative pain and negative affect

Table 3 displays descriptive statistics for the continuous variables included in the regression models. The average reported nervousness a) weeks before and b) right before surgery were 3.5 and
3.6 respectively, measured on a 11-point numeric rating scale (NRS). As expected, patients displayed a range of nervousness levels, supporting the feasibility of exploring the role of these feelings in a larger observational study. A wide range of responses were also found for other key variables (Table 3). Pain interference levels weeks before surgery was on average 2.79 on the NRS, whereas reported pain levels right before surgery were on average only 0.55 on the NRS. The low pain reports before surgery likely reflect patients’ intake of paracetamol and NSAIDs during the hours leading up to surgery (1-2 g paracetamol ingested in the morning, followed by 500 mg naproxen on arrival at the hospital).

### Table 3. Descriptive statistics of the continuous variables selected for Poisson regression

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Range</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervousness weeks before surgery</td>
<td>34</td>
<td>9</td>
<td>0</td>
<td>9</td>
<td>3.47</td>
<td>2.80</td>
</tr>
<tr>
<td>Nervousness right before surgery</td>
<td>33</td>
<td>10</td>
<td>0</td>
<td>10</td>
<td>3.61</td>
<td>2.85</td>
</tr>
<tr>
<td>Pain interference weeks before</td>
<td>34</td>
<td>9</td>
<td>0</td>
<td>9</td>
<td>2.79</td>
<td>2.87</td>
</tr>
<tr>
<td>Pain right before surgery</td>
<td>29</td>
<td>5</td>
<td>0</td>
<td>5</td>
<td>0.55</td>
<td>1.15</td>
</tr>
<tr>
<td>Mood change* during acute opioids</td>
<td>34</td>
<td>7</td>
<td>-4</td>
<td>3</td>
<td>-0.32</td>
<td>1.43</td>
</tr>
</tbody>
</table>

Note: N = number of participants, M = mean, SD = standard deviation. * As measured by the ”feeling good” item.

### 3.3 Opioid drug responses

Contrary to our expectations, mood was not improved by remifentanil administration. Numerical ratings of “feeling good” whilst on the operating table 3 minutes before remifentanil were on average 6.78 ± 2.78 (mean ± SD). One minute after drug administration, mean ratings decreased slightly to 6.53 ± 2.64. A paired t-test showed that this decrease was not significant (p = 0.269). Despite the lack of euphoria reported by patients, the average ratings of feeling high indicated robust drug effects at this time (6.78 ± 2.94). Anxiety ratings decreased after remifentanil, from 3.33 ± 3.14 to 2.68 ± 3.18 (p = 0.013). This anxiolytic effect is consistent with the anesthetists’ rationale for administering remifentanil prior to anesthesia, to reduce discomfort. Nevertheless, mean ratings of discomfort were 4.49 ± 2.92 at this time (before anesthesia).

### 3.4 Post-surgery measures

An overview of key self-reported measures from the T4 interview is presented in Table 4. The most common instruction for pain management was to take paracetamol (1g) every fourth hour, Vimovo
PREDICTING ANALGESIC CONSUMPTION

(500mg) evening and morning, and Oxynorm (5 mg) only if needed to address pain flares. They were also instructed to take Vimovo regardless of pain intensity, as Vimovo has anti-inflammatory effects. Among the patients who took Oxynorm, several of them specifically reported taking them for better sleep, and not for pain flares. The NSAID Vimovo was provided by the hospital for home use to 28 patients (2-3 pills of 500 mg naproxen). The opioid drug Oxynorm was provided to 30 patients (1-5 pills of 5 mg oxycodone hydrochloride). The patients were expected to provide their own paracetamol. At the time of the post-surgery phone interview (T4), 23 patients (85.2%) had taken at least one Vimovo, \((mean = 1.5, SD = 1.3)\). In contrast, only 30% (nine patients) reported having taken Oxynorm at T4, \((mean = 0.4, SD = 0.7)\). Thirty patients (88.2%) also ingested at least one paracetamol pill (500mg pill), \((mean = 5.5, SD = 2.9)\). The mean of all analgesic pills taken (paracetamol and oxynorm) was 6.1 \((SD = 3.1)\).

3.5 Comparison of patients who did and did not choose to ingest opioids postoperatively

We used t-tests to compare how the patients who took opioids with the subgroup who received but did not take opioids, fared post-operatively (Table 4). The variables assessed at T4 for this purpose were pain intensity, pain interference, pain coping, nervousness, feeling good and their reported analgesic effect. Self-reported analgesic effect is a measure of how helpful they perceived the analgesics to be. The group who took opioids felt significantly less well, reported significantly higher pain intensity and interference, significantly lower coping, and they estimated a significantly lower analgesic effect than patients who refrained from taking their Oxynorm pills (Table 4). There was no obvious gender imbalance in the group who took opioids (4 men and 5 women). Among the patients who took opioids post-operatively, 55.6% had taken opioids previously \((N = 5)\). The most common opioids to have previous experience with were morphine and Paralgin Forte (a codeine and paracetamol composition). Five of the nine patients who took opioids had undergone minor abdominal surgeries, two minor gynecological surgeries and one an otorhinolaryngology surgery. Seven out of nine (77.8 %) reported having pain for longer than three months prior to surgery, i.e. qualifying as a chronic pain patient (Treede et al., 2015).
Table 4. Descriptive statistics at T4

<table>
<thead>
<tr>
<th></th>
<th>All participants</th>
<th>Opioids taken</th>
<th>Opioids received, but not taken</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean</td>
<td>SD</td>
<td>N</td>
</tr>
<tr>
<td>Pain intensity</td>
<td>34</td>
<td>2.65</td>
<td>2.46</td>
<td>9</td>
</tr>
<tr>
<td>Pain interference</td>
<td>34</td>
<td>2.68</td>
<td>2.4</td>
<td>9</td>
</tr>
<tr>
<td>Pain coping</td>
<td>34</td>
<td>8.58</td>
<td>1.58</td>
<td>8</td>
</tr>
<tr>
<td>Nervousnessa</td>
<td>34</td>
<td>1.12</td>
<td>1.55</td>
<td>9</td>
</tr>
<tr>
<td>Feeling good</td>
<td>34</td>
<td>7.53</td>
<td>1.86</td>
<td>9</td>
</tr>
<tr>
<td>Analgesic effect</td>
<td>34</td>
<td>7.2</td>
<td>2.16</td>
<td>9</td>
</tr>
</tbody>
</table>

Note: N = number of participants, M = mean, SD = standard deviation. * indicates p < 0.05, ** indicates p < 0.001. aNervousness specifically related to recovery from surgery.

Figure 3A displays the mean reports of pain intensity at T1, T2 and T4 for the patients who took opioids, and the ones who did not. Figure 3B displays the mean level of pain interference for the two groups at T1, T2 and T4. The “opioid group”, who did decide to ingest opioids, showed higher levels of both pain and pain interference at all time points compared to the group who did not; however, this difference was only significant at T4 (t-test of values at T1, p = 0.192 for pain intensity, p= 0.395 for pain interference).

Figure 3. Ratings of pain intensity and pain interference displayed by group (Mean and standard error mean for patients who had ingested opioids at the time of the T4-interview in blue). * indicates p < 0.05, ** indicates p < 0.001.
3.6 Exploring predictors of post-surgery analgesic consumption

As a first step in model selection, I performed bivariate regressions to assess the predictive value of each of the chosen predictor variables on the amount of analgesia consumed one day post-surgery (Table 5). These analyses showed that operation category, pain interference weeks before surgery, pain right before surgery and nervousness weeks before surgery were significantly associated with amount of analgesics taken the following day after surgery.

Neither of the variables categorized as substance abuse variables reached significance when considered as individual predictors of post-surgery analgesics intake (tobacco, prior opioid exposure and mood changes during acute opioids). This was also the case for participant sex and nervousness right before surgery. Pain levels right before surgery showed the lowest BIC value, but this model did not include all 34 participants. Pain interference weeks before surgery, was the only variable to show a p-value lower than .001. The slope estimate (β-coefficient) showed an increased intake of 1.096 pills per 1-point increase in pre-surgical pain interference scores. Operation category, pain right before surgery and nervousness weeks before surgery were also significant (at an α-level of < 0.05). Accordingly, pain interference weeks before surgery was chosen as the starting point for further model selection.
Surprisingly, there was no evidence of positive mood changes after remifentanil treatment (as measured by ratings of “feeling good” at T3 pre- and post-drug, mood changes during acute opioids). Furthermore, the patients who did show mood improvements from remifentanil did not ingest more analgesics at T4; instead we found a negative (non-significant) correlation between mood changes and the main outcome, r = -2.73. Change in mood (difference score) was not a significant predictor in the bivariate regression (Table 5).

Table 5. Results from bivariate regression models

<table>
<thead>
<tr>
<th>Model nr.</th>
<th>Regressor</th>
<th>F</th>
<th>df</th>
<th>N</th>
<th>p</th>
<th>BIC</th>
<th>Exp (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Operation category</td>
<td>11.86</td>
<td>4</td>
<td>34</td>
<td>.018*</td>
<td>189.9</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Pain interference weeks before surgery</td>
<td>11.30</td>
<td>1</td>
<td>34</td>
<td>.001**</td>
<td>179.4</td>
<td>1.10</td>
</tr>
<tr>
<td>3</td>
<td>Tobacco</td>
<td>.644</td>
<td>1</td>
<td>34</td>
<td>.422</td>
<td>192.9</td>
<td>1.20</td>
</tr>
<tr>
<td>4</td>
<td>Sex</td>
<td>.070</td>
<td>1</td>
<td>34</td>
<td>.791</td>
<td>194.1</td>
<td>1.05</td>
</tr>
<tr>
<td>5</td>
<td>Prior opioid exposure</td>
<td>1.01</td>
<td>1</td>
<td>31</td>
<td>.315</td>
<td>180.1</td>
<td>1.22</td>
</tr>
<tr>
<td>6</td>
<td>Pain right before surgery</td>
<td>4.36</td>
<td>1</td>
<td>29</td>
<td>.037*</td>
<td>168.9</td>
<td>1.14</td>
</tr>
<tr>
<td>7</td>
<td>Nervousness weeks before surgery</td>
<td>3.83</td>
<td>1</td>
<td>34</td>
<td>.050*</td>
<td>189.2</td>
<td>1.06</td>
</tr>
<tr>
<td>8</td>
<td>Nervousness right before surgery</td>
<td>3.35</td>
<td>1</td>
<td>33</td>
<td>.067</td>
<td>185.8</td>
<td>1.05</td>
</tr>
<tr>
<td>9</td>
<td>Mood changes during acute opioids</td>
<td>2.26</td>
<td>1</td>
<td>34</td>
<td>.133</td>
<td>190.2</td>
<td>.907</td>
</tr>
</tbody>
</table>

*significant at 0.05. **significant at 0.01

In the next step, regression models were made by adding two variables into the regression, namely pain interference weeks before surgery in combination with the other significant variables. Since there was an uneven distribution of men and women in the operation category groups, participant sex was added to the simple regression model to adjust for potential effects of sex. The inclusion of the sex variable did not improve the BIC value compared to the simple model, and sex did not significantly explain variance in the analgesic consumption. In the model consisting of pain right before surgery and pain interference, the BIC-value continued to be very low, at 160.1. In comparison, this was lower than when pain right before surgery was the only regressor. However, all models including pain levels right before surgery had fewer data points, N=29 compared to N=34. To be able to compare different model fits using BIC values (which requires equal sample size), we ran an additional bivariate regression for pain interference in the 29 participants for whom we had T2 pain scores. This enabled us to assess formally whether including T2 pain scores...
improved the model, which was not the case (the bivariate n=29 BIC for pain interference was 156.8).

The only variables that significantly predicted analgesic consumption were *pain interference weeks before surgery* and *operation category*. None of the other models combining other predictor variables with pain interference showed significant predictive value. Table 6 displays all values for regression models with two independent (predictor) variables.

**Table 6. Results of Poisson regressions with two predictors.**

<table>
<thead>
<tr>
<th>Model nr</th>
<th>Regressors</th>
<th>F</th>
<th>df</th>
<th>N</th>
<th>p</th>
<th>BIC</th>
<th>Exp(B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Pain interference weeks before surgery</td>
<td>9.80</td>
<td>1</td>
<td>34</td>
<td>.002*</td>
<td>182.3</td>
<td>1.086</td>
</tr>
<tr>
<td></td>
<td>Nervousness weeks before surgery</td>
<td>0.62</td>
<td>1</td>
<td>.431</td>
<td>1.021</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Pain interference weeks before surgery</td>
<td>9.58</td>
<td>1</td>
<td>29</td>
<td>.002**</td>
<td>160.1</td>
<td>1.110</td>
</tr>
<tr>
<td></td>
<td>Pain right before surgery</td>
<td>.29</td>
<td>1</td>
<td>.592</td>
<td>1.020</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td><strong>Pain interference weeks before surgery</strong></td>
<td>11.60</td>
<td>1</td>
<td>34</td>
<td>.001**</td>
<td>182.9</td>
<td>1.081</td>
</tr>
<tr>
<td></td>
<td><strong>Operation category</strong></td>
<td>10.28</td>
<td>4</td>
<td></td>
<td>.036*</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>13</td>
<td>Operation category</td>
<td>19.33</td>
<td>4</td>
<td>34</td>
<td>.001**</td>
<td>191.7</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Participant sex</td>
<td>2.09</td>
<td>1</td>
<td>.149</td>
<td>.816</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Pain interference weeks before surgery</td>
<td>9.88</td>
<td>1</td>
<td>34</td>
<td>.002*</td>
<td>182.7</td>
<td>1.090</td>
</tr>
<tr>
<td></td>
<td>Mood improvement after during opioid</td>
<td>.192</td>
<td>1</td>
<td>.661</td>
<td>.975</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*significant at 0.05. **significant at 0.01

Figure 5 displays the two main predictors of analgesic consumption day one post-surgery, namely *operation category* and *pain interference weeks before surgery*. The figure has dual Y-axes, mean pain interference weeks before surgery to the left, illustrated by the bars, and the mean analgesic consumption to right, illustrated by the dots. Operation category is presented on the X-axis.
Figure 5. Red dots indicating mean analgesic consumption per operation category, height of bar indicating mean level of pain interference per operation category. Min. Gyn. = Minor Gynecological, Otorhin = Otorhinological, Min. Abdo. = Minor Abdominal.
4 Discussion

One of the main objectives of this pilot study was to assess how pre-operative measures of distress, pain, pain interference, and history of opioid use relate to immediate post-operative use of analgesics, and in particular opiate drugs. Our analyses indicated that pain interference weeks before surgery and operation category were the most important predictors of postoperative analgesic consumption. Unlike previous studies (Bedard et al., 2018; Brummett et al., 2017; Inacio et al., 2016; Johnson et al., 2016), gender was not a significant predictor in our sample.

Another primary objective of the pilot study was to explore key features of patients who chose to use opioid drugs following surgery and those who did not. The results showed that patients who took opioids had significantly higher levels of pain interference postoperatively. Since the measures of pain interference and analgesic consumption were recorded at the same time, one day after surgery, it is also possible to view this association the other way around, namely that patients with higher levels of pain interference were the ones who chose to take opioid analgesics. Further, the opioid group also reported experiencing lower analgesic effect from the medications they had ingested. All of these findings are relevant to our main objective, which was to provide sufficient information about the patient group in order to plan for a larger prospective study.

The results of the pilot study revealed pain interference weeks before surgery was an important predictor for analgesic consumption. In addition, high levels of pain interference day one post-surgery were one of the main characteristics of the group who took opioids. This is in line with previous prospective studies on opioid use following surgery (Rosenbloom et al., 2017). Pain interference is as mentioned a measure that includes cognitive, affective, physical and behavioral elements (Holen et al., 2008). During the T4 interview, the participants were encouraged to explain how they experienced the pain as interfering. These responses were not quantified, but were collected to better understand the post-operative experience. Common examples of how they experienced pain interference were functional mobility problems, not being able to drive and anxiety related to the prospect of bodily movements (only for colorectal surgical patients). In the main study, quality of life will be assessed by the “Life Satisfaction Questionnaire” (LISAT-9). This is a validated questionnaire that cover several life domains, namely work, finance and leisure, social and sexual life, self-care, family life and relationships (Fugl-Meyer, Bränholm, & Fugl-Meyer, 1991). A possible way to better understand how pain interference affects the patients’ quality of life in the post-surgery period, would be to compare the data from the LISAT-9 with other validated forms of pain interference measurements, such as items from the BPI used here (Holen et al., 2008).
The patients who ingested opioids post-surgery had mean pain interference scores post-surgery that were more than 3 points higher on the NRS scale than patients who did not take the Oxynorm pill(s) they had received at discharge from hospital. This is above what is considered a clinically important change (Farrar, Portenoy, Berlin, Kinman, & Strom, 2000). When asked, the patients complained about the pain getting in the way of them going about with their daily routines. Patients not taking opioids described the opposite, that they had a normal day and were feeling good about that. Some of them also explained that they had prepared for the post-surgery period by planning activities that could be done despite pain and lower functioning (example; having bought new yarn for knitting). The opioid group also reported experiencing lower analgesic effect. This was a subjective measure where the patients reported their perceived effect of the analgesics, and was not based on pain levels before and after ingesting analgesic medication. As the mean reported analgesic effect in the group who took opioids was lower, and the mean difference in pain interference was more than 3 points on the NRS scale, it is possible that this group would benefit more by getting help to reduce the experience of pain interference as opposed to taking opioids for pain relief. This is in line with previous research showing higher correlation between pain interference and opioid consumption, than pain levels and opioid consumption (Adams et al., 2018). There is also a growing trend in the pain management field prioritizing psychological interventions for pain, and these are often targeted towards reducing pain interference and improving pain cognitions, i.e. reducing pain catastrophizing (Darnall, Sturgeon, Kao, Hah, & Mackey, 2014). Psychological interventions to treat opioid misuse and taper opioids are also increasing (Abid Azam et al., 2017; Darnall et al., 2014; Garland et al., 2014).

Regulating or removing negative affect is an important function of substance abuse (Khantzian, 1997). When asked to describe their first “opiate experience”, patients who misuse their opiates describe their first encounter with opiates as more pleasant compared to those in chronic opioid treatment who adhere to treatment (Bieber et al., 2008; Skala et al., 2013). However, this increase in reports of drug high and euphoria may be due to memory bias. Overall, our patients showed a reduction in anxiousness levels after remifentanil administration at the operating table. This indicates that they experienced a reduction of negative affect from the opioid drug. We did not observe an increase in “feeling good” following the remifentanil administration. It is possible that the fairly rapid administration of remifentanil is associated by unfamiliar somatic sensations that could be experienced as “strange” rather than “good”. Rapid opioid administration is, however, associated with higher levels of drug liking and drug high (Marsch et al., 2001). Longitudinal follow-up data obtained in the main study in a substantially larger sample will enable us to test of whether early drug experiences are indeed predictive of subsequent risk of misuse.
Compared to the group who did not take opioids, the group who took opioids in the postoperative period reported higher levels of pain, as well as experiencing lower pain relief from the analgesics they had ingested. There was a mean difference on both measures at around 2 points on the 11-point NRS scales. A 2-point reduction in pain intensity scores is considered a cutoff for clinically relevant effects (Farrar et al., 2000; Farrar, Young, LaMoreaux, Werth, & Poole, 2001). When specifically asked during the phone interview if they experienced pain relief from the opioids, several participants replied that it did not help particularly with the pain, but that the opioids helped them sleep. Taking opioid analgesics to improve sleep rather than as prescribed, namely for pain relief, may be considered opioid misuse. However, we have no reason to suspect prolonged opioid misuse, since patients did not receive more than a maximum of five Oxynorm tablets at discharge, and the pilot study did not include data beyond day 1 post-surgery. The phenomenon of high consumption of analgesics without appropriate pain relief is established among chronic pain patients (Goesling et al., 2016).

The main objective of this pilot study was to gather instructive information about the patient group, and their typical range of state effects and drug consumption, to design a larger study. The descriptive statistics from this pilot has shown that there is a considerable variability in the patients’ responses to the different mood and state items. Further, we also observed that the variability in pre-drug subjective experience (such as pain interference) can explain variance in analgesic use the day following surgery. Further, mean difference in pain interference between the groups who took opioids and not during the phone call interview is in line with previous opioid studies, showing that patients who receive opioids for pain also report higher pain interference compared to pain patients who do not receive opioids (Moryl et al., 2018). However, our opioid group included only nine patients, so generalizations must be made cautiously.

4.1 Suggestions for the main study

The general set-up of the study was successful, and many aspects worked well. Most of the patients at the surgical clinic fulfilled the inclusion criteria, and none of patients declined the invitation to join the study. Further, many patients reported in the T4 phone call that they liked filling in the T2 form, as they had nothing else to do while they waited. The T3 interview was feasible for both participants and staff. After having altered the wording of the questions, most of the patients understood well what they were asked. The T4 interview also worked out nicely. Several patients expressed gratitude for being called and checked in on. These experiences are valuable as they confirm that the set-up and items works well and can be used in the main study. Nevertheless,
converting the pilot study has revealed several design aspects that can be improved in the main study.

Through the interviews at T4 it became clear that many of the patients had had the same, or similar operation before, and this had an impact on their psychological status: the ones who had a previous successful surgery reported lower levels of nervousness both pre- and post-operatively. This association was discovered after 17 of the 34 interviews done, and from then on patients were asked specifically if they had had the same surgery before, and if they had any previous experience with anesthesia. This measure could not be included in the analysis of the pilot data, but may contain important covariates or predictors in the main study. Whether or not the previous operation was successful should probably also be included as a measure. In addition, any negative experiences associated with similar surgery should be reported, as patients could have had bad or even traumatic experiences from the surgery irrespective of whether or not the surgery was successful.

Some patients reported that they had had surgery as a consequence of previous trauma (assault and rape). This information also emerged during the follow-up phone call, and the patients themselves brought it up. Patients also reported that these experiences impacted their levels of nervousness and distress experienced before surgery. However, if this type of information were to be systematically collected in the main study, it would have to be carefully planned and conducted in a sensitive manner that safeguards the patients. Care must also be taken to ensure that collecting information on trauma does not impact upon key outcome measures or any part of the treatment. This is a difficult task and would need careful consideration and additional ethical approval.

If trauma were to be included, items from a validated instrument, like Trauma History Screen (THS) should be used (Carlson et al., 2011). The THS is divided into several parts. The first part presents the respondent with different types of events. The participant simply responds “yes” or “no” to each item indicating having experienced the event in question or not. The advantages with this type of instrument is that patients are not required to go into the specifics of what they experienced. The items are also easy to quantify for later analyses. However, any form of trauma measure can potentially be a strain on some patients, and the design of the main study will have to take this into account. A possible solution would be to make sure that trained staff is available to safeguard the ones who need it. As this is a clinical study, and the patients are undergoing surgery, this information should not be collected right before the procedure, to avoid any potential negative priming affects. The design should also ensure that patients are in direct contact with qualified research or clinical staff who can help them manage the potential distress this may cause them.
Other useful measures to consider for the main study would be assessment of personality traits and tendency for pain catastrophizing. During the pilot, we discussed that the responses to the measure of nervousness obtained weeks before surgery (“How nervous are you about having surgery/anesthesia) could mainly reflect *trait* anxiety, whereas levels of nervousness right before surgery may to a greater extent reflect *state* anxiety. Neurotic personality traits are associated with higher levels of pain intensity: it lowers the threshold at which the pain is perceived as threatening, resulting in emergence of pain catastrophizing (Goubert, Crombez, & Van Damme, 2004). Optimally there should be validated personality trait measures at T1, and more precise measures of nervousness related to the coming surgery at T2. In addition to this, including a measure of impulsivity may also yield interesting results. Impulsivity is a known vulnerability marker for SUD (Verdejo-Garcia, Lawrence, & Clark, 2008), and there have been studies showing that impulsivity correlates with prescription opioid abuse in chronic pain patients (Vest, Reynolds, & Tragesser, 2016).

The T4 phone call revealed that patients have different attitudes towards analgesics, and also different experiences with them. More than half the sample reported having pain for more than three months, i.e. qualifying as a chronic pain patient (Treede et al., 2015). Some patients did not have a high threshold for taking the opioids, whereas others showed more ‘respect’ or hesitancy towards them and reported that they would only use opioids if they pain became unbearable, i.e. only taking opioid analgesics to tackle pain flares. Many of the patients who reported high analgesic effect by the medications provided elaborated this by explaining that it was because they usually *never* took analgesics, due to their *unusually high* pain threshold. This reasoning for experiencing good analgesic effect was brought forth conspicuously often. Information about the patients’ previous habits of using non-prescription analgesics, as well as their own beliefs about their ability to cope with pain and pain threshold, are interesting psychological measures. More elaborate, and qualitative, information concerning the psychology of the at-risk group for prescription opioid misuse, could also be used for better tailoring psychological interventions and pain treatments.

After having interviewed approximately ten patients, I started postponing the call to late in the afternoon, preferably after 6pm. It became apparent that patients who were called in the early evening had had the chance to take more of the analgesics provided than the ones who were called earlier in the day. Subsequent interviews were conducted after 6 pm. Not determining a specific and later timing of the phone interview was perhaps the most problematic aspect of the study that became evident in the pilot study. At discharge, the patients received analgesic medications to last approximately three days. Based on the experiences from the pilot, it seems prudent to postpone the
PREDICTING ANALGESIC CONSUMPTION

timing of the follow-up call until day 3. Thus, patients will have had time to ingest all of the
analgesics provided, and a more comprehensive profile of medicament consumption can be
recorded. In addition, the post-operative patterns of pain will have had time to unfold. Some
patients will at this time be pain free, whereas other may be experiencing more post-operative pain.
Some of the patients who experienced high levels of pain also reported low levels of nervousness
because it was still “early days”, and it felt natural and as expected for them to feel pain. This might
not be the case if they are interviewed at day three post-surgery and after they have ingested all
their take-home analgesia. This would also be a good opportunity to assess pain catastrophizing.

Another improvement of the study design inspired by the pilot study is that we have now
listed more types of opiates in the list of previously taken drugs. Neither Tramadol nor Dolcontin
were included in the original form, but there have been cases where the patients have either written
them down on the T2 form, or they have mentioned them in the T4 phone call. It is important that
we list all relevant prescription opioid analgesics in the questionnaire, to avoid false negatives
(categorizing these patients as opioid naïve). According to the annual report from Norwegian
Prescription Database (NorPD) from 2018, the most common prescription opioids are the
combination of codeine and paracetamol, tramadol and oxycodone compounds (Berg C (red),
2018). The majority of our listed opioids should be from these compositions, but rarer forms of
opioids should also be included.

We did not include any measures for misuse of opioids in the pilot. During the T4 phone
call, patients were asked about which types and how much analgesic medication they had
consumed, but not specifically about their reasons for using these. Several of the patients who did
ingest opioids said explicitly that they used medication to improve quality of sleep, and not to
tackle pain flares. However, there was no way to quantify this in the pilot data. We did include a
variable to measure whether or not they had adhered to their pain management plan. The most
common way to deviate from the pain management plan was to take less than what was
recommended, and in some cases, not take anything at all. In a study investigating risk factors for
opioid abuse liability, precise measures of potential misuse should be included.

In both T1 and T2 there was a problem of missing data entries. All patients had received the
questionnaires, but some did not respond to all the items on the form. The same problem was
encountered during the T4 interviews. Some patients indicated that they did not deem it necessary
to answer questions that appeared irrelevant to their situation. For instance, patients who did not
feel particularly nervous initially answered “pass” when I asked them about their nervousness
levels. After explaining again that this is a quality assurance study, and that their answers would not
in any way inflict upon their medical treatment, or be documented in their medical journal (which
PREDICTING ANALGESIC CONSUMPTION

was already clarified in the consent form), they were happy to answer questions. It is probable that it may have been the same reasoning behind the missing answers at T1 and T2, where the patients were not in direct contact with researchers who could clarify and repeat the study objectives, and perhaps encourage them to answer all questions. A possible solution to this might be to introduce the study more thoroughly in the beginning of each written questionnaire, and perhaps make it clearer that their answer to all items are of use to the research project even if some items might appear irrelevant to their current experience. We could also include a section explaining that their answers are important for the hospital to maintain high quality treatment.

A major limitation of this pilot study was the sample size. Our collaboration is only with Kongsberg Hospital, a small, local hospital. To explore the variables of interest a larger sample size would be optimal. With data from 34 participants, we can generate new hypotheses, but should exercise care in generalizing results to the larger population of (Norwegian) day surgery patients. As the motivation for this study centers on opioid analgesics, it would also be preferable to use a measure of opioid consumption as the main outcome. Here, our exploratory regressions assessed a combination of paracetamol- and opioid consumption. The decision was based on the fairly low ratio of patients choosing to ingest opioids, as well as to avoid data loss by excluding patients who did not receive opioids from the hospital from the regressions. The patients were told to take the NSAID Vimovo regardless of pain, due to its anti-inflammatory effects. Accordingly, we did not include Vimovo consumption in the measure of analgesic medications ingested. Since this drug is also an analgesic, however, our outcome measure was less precise than anticipated. With a larger sample size in the main study, we will have enough data on opioid use to draw more accurate conclusions about the patient groups’ patterns of use and misuse of opioids post-surgery.

The dataset from the pilot is quite extensive, with 80 variables. In addition to predict analgesic consumption post-operatively, it would be equally interesting to predict post-operative pain. With the current data set, this is possible, as we have measured many variables linked to predicting chronic pain (Ip, Abrishami, Peng, Wong, & Chung, 2009). However, this would have been outside the scope of this thesis.

We were unable to thoroughly assess levels of anxiety and depression in the pilot study. Due to the previous literature highlighting the increased risk of prolonged opioid misuse in people with anxiety and depression, the main study will measure symptoms of affective disorders using SCL-25, a validated symptom check-list (Derogatis, Lipman, Rickels, Uhlenhuth, & Covi, 1974). In addition, other measures relevant for abuse liability, such as social support, anhedonia and quality of life will also be measured with validated instruments. Importantly, the main study will collect long-term data on subsequent prescription opioid use, not just at three days after surgery, but
PREDICTING ANALGESIC CONSUMPTION

also at 6 and 12 months follow-up (using prescription registry data). This design will allow us to prospectively assess the real-life consequences of exposure to opioid drugs during a stressful event such as day surgery. It will also enable us to assess predictors of prolonged prescription opioid use in a Norwegian sample.
5 Conclusion

This pilot study has shown us that our study design works, in the sense that relevant information can be gathered and is shown to contain sufficient variance to warrant further investigation using an observational study design. We have acquired valuable information about how the patients experience minor day surgery at Kongsberg Hospital. Our results show that there is sufficient variety in their responses, particularly regarding anxiety and pain, that we can attempt to explain in a statistically sound way with the larger sample of the main study. Furthermore, we have experienced that the design of our study is manageable for both staff and patients. Interviewing the patients while they are on the operating table has proved to be a source of useful information about their opioid experiences. Most of the patients showed interest in the follow-up phone call the day after surgery and did not display any reluctance to share aspects of their physical and emotional challenges. Our preliminary results highlight prior levels of pain interference, and operation category, as important predictors for acute post-operative analgesic consumption. Higher levels of pain interference were also reported by patients who took opioids at home after surgery. These preliminary results can be used to further improve the main study, so that the study is better tailored to the patient group in question.
References


PREDICTING ANALGESIC CONSUMPTION


NorPD. (2018). Norwegian Prescription Database.


PREDICTING ANALGESIC CONSUMPTION

Patients With Musculoskeletal Complaints. *Spine (Phila Pa 1976).*
doi:10.1097/brs.000000000002847


Appendix 1 Study Protocol for T1
EGNE OPPLYSNINGER

Mobiltlf ___________________ Annen tlf eller epost du kan nås på: ______________________________

Har du vært innlagt eller fått behandling på sykehus utenfor Norden de siste 12 månedene? ja ☐ nei ☐
Gjelder også polinklinisk kontakt i utlandet der sprøyter er gitt i huden, tannbehandling eller sårbehandling
Hvis ja, - hvor og når? ______________________________

Har du blitt operert tidligere? ja ☐ nei ☐
Hvis ja, - hvilket inngrep, når og ved hvilket sykehus?

<table>
<thead>
<tr>
<th>Hvilken operasjon</th>
<th>År</th>
<th>Sykehus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Har du hatt komplikasjoner i forbindelse med narkose eller bedøvelse? ja ☐ nei ☐
Hvis ja, hvordan? ______________________________

Hadde du kvalme og/eller oppkast etter operasjonen? ja ☐ nei ☐
Hvis ja, - hvor lenge? flere dager ☐ hele dagen ☐ noen timer ☐ bare litt kvalm ☐
Er du plaget av "reisesyke" / sjøsyke? ja ☐ nei ☐

Bruker du medisiner regelmessig? (inkl. smertestillende, p-piller, etc.) ja ☐ nei ☐
Hvis ja, - hvilke medisiner? Send med kopi av medisinkort, hvis du bruker mer enn 3 medisiner

<table>
<thead>
<tr>
<th>Medisinens navn</th>
<th>Medisinens styrke</th>
<th>Hvor ofte tar du medisinen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Har du, eller har du hatt hjertesykdom: ja ☐ nei ☐
Hvis ja; - brystsmarter (angina) høyt blodtrykk hjerteinfarkt, evt. når ______________________________
annet ______________________________

Har du diabetes (sukkersyke): ja ☐ nei ☐. Hvis ja, bruker du: insulin ☐ tablett ☐ diett ☐ insulinpumpe ☐

Lungesykdom: ja ☐ nei ☐. Hvis ja: astma ☐ bronkitt ☐ tuberkulose ☐ KOLS ☐ annet ______

Nyresykdom: ja ☐ nei ☐. Hvis ja: nyresvikt ☐ operasjon ☐ annet __________

Leversykdom: ja ☐ nei ☐. Hvis ja: hepatitt ☐ annet ______

Har du noen sykdom eller funksjonshemming som du synes vi bør vite om? ja ☐ nei ☐

Allergi mot legemiddel: ja ☐ nei ☐
Hvis ja, - hvilke legemiddel og hvilke reaksjoner? ______________________________

Andre allergier: (pollen, nikkel, latex, annet)? ja ☐ nei ☐
Hvis ja – hvilken reaksjon?

Har du hatt /har plager i mage-tarm regionen? ja ☐ nei ☐
Hvis ja: magesår ☐ blødninger ☐ magesmerter/kronisk betennelse ☐ Annet: __________

Røyker/snuser du? ja ☐ nei ☐ Hvis ja, hvor mye sigaretter/tobakk daglig? ______________________________

Spiser du vanlig mat? ja ☐ nei ☐
Er det mat du ikke kan spise? ______________________________

SNU ARKET
**Forstår du / snakker du norsk?** ja ☐ nei ☐

Hvis ikke, hvilket språk snakker du? ___________________________ Trenger du tolk? ja ☐ nei ☐

---

Hvor nervøs er du for operasjonen/bedøvelsen? (sett ring rundt ett tall)

Ikke nervøs 0 1 2 3 4 5 6 7 8 9 10 Svært nervøs

Er det noe vi kan gjøre for at du skal grue deg mindre? ____________________________________________

Har du hatt smerter den siste uka? ja ☐ nei ☐

Hvis ja: Anslå din gjennomsnittlige smerte (sett ring rundt ett tall)

Ingen smerte 0 1 2 3 4 5 6 7 8 9 10 Verst tenkelige smerte

- Hvor mange måneder eller år har du hatt disse smertene? Måneder (0-12): _____ År (0-99) _____
- Er smerten kontinuerlig? Ja, jeg kjener den hele tiden ☐ Nei, den er av og på ☐

Hvor plagsomme har smertene vanligvis vært? (sett ring rundt ett tall)

Ikke plagsomt 0 1 2 3 4 5 6 7 8 9 10 Verst tenkelige plage

---

**Høyde**

**Vekt**

Hvilket tidsrom passer best for en operasjon?

Kan komme på kort varsel: 1-3 dager ☐ 1 uke ☐

Din fastlege:

Navn på din nærmeste pårørende som kan kontaktes: Ditt yrke: __________________________

Navn: __________________________ Din arbeidsgivers navn og adresse: __________________________

Født: __________________________

Slektskap: __________________________

Mobiltlf: __________________________ Din stillingsprosent: __________________________

**Hvordan kommer du deg hjem fra sykehuset?**

Helseekspress/Taxi ☐ Privat bil (blir hentet) ☐ Offentlig kommunikasjon ☐


Hvis du skal til en operasjon der det brukes kamera til å se, vil det bli lagret en kopi av filmen i din journal. Hvis du har innvending mot dette, eller at videoen blir brukt anonymt til undervisning/forskning; vennligst si i fra til din operatør operasjonsdagen.

**Vær vennlig å kontakte oss hvis opplysningene du gir nå, endrer seg frem til operasjonsdagen.**

Dato:………………….. Din signatur:……………………………………………………………

---

**Fylles ut av sykehuset:**

Preoperative prøver / undersøkelser:

- EKG ☐
- Fastende blodsukker ☐
- INR ☐
- Antikoagulasjon prosedyrer ☐
- Diabetes prosedyre ☐

Annet __________________________

BMI __________________________

Foreslått anestesiform:

- TIVA ☐
- Regionalanestesi ☐
- Lokalanestesi ☐
- Sevofluran ☐
- Marevan HR ☐ LR ☐

Annet __________________________

Tilsend resept på følgende medisiner:

Anestesilege
Appendix 2 Study Protocol for T2
Spørreundersøkelse før operasjon

Under følger en rekke spørsmål som kan beskrive hvordan du har det AKKURAT NÅ. Vennligst sett ring rundt et tall som best beskriver hvor mye av ordet du opplever:

**Hvor bra føler du deg akkurat nå på en skala fra 1 til 10?**

<table>
<thead>
<tr>
<th>Ikke bra</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Veldig bra</th>
</tr>
</thead>
</table>

**Hvor irritabel føler du deg akkurat nå på en skala fra 1 til 10?**

<table>
<thead>
<tr>
<th>Ikke irritabel</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Veldig irritabel</th>
</tr>
</thead>
</table>

**Hvor trygg føler du deg akkurat nå på en skala fra 1 til 10?**

<table>
<thead>
<tr>
<th>Ikke trygg</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Veldig trygg</th>
</tr>
</thead>
</table>

**Hvor engstelig føler du deg akkurat nå på en skala fra 1 til 10?**

<table>
<thead>
<tr>
<th>Ikke engstelig</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Veldig engstelig</th>
</tr>
</thead>
</table>

**Hvor selvsikker føler du deg akkurat nå på en skala fra 1 til 10?**

<table>
<thead>
<tr>
<th>Ikke selvsikker</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Veldig selvsikker</th>
</tr>
</thead>
</table>

**Hvor opprørt (oppskaket) føler du deg akkurat nå på en skala fra 1 til 10?**

<table>
<thead>
<tr>
<th>Ikke opprørt</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Veldig opprørt</th>
</tr>
</thead>
</table>

**Hvor trist føler du deg akkurat nå på en skala fra 1 til 10?**

<table>
<thead>
<tr>
<th>Ikke trist</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Veldig trist</th>
</tr>
</thead>
</table>

**Hvor glad føler du deg akkurat nå på en skala fra 1 til 10?**

<table>
<thead>
<tr>
<th>Ikke glad</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Veldig glad</th>
</tr>
</thead>
</table>

**Hvor nervøs føler du deg akkurat nå på en skala fra 1 til 10?**

<table>
<thead>
<tr>
<th>Ikke nervøs</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Veldig nervøs</th>
</tr>
</thead>
</table>
Spørsmål om smerter og bruk av smertestillende

Har du hatt smerter den siste uka? ja □  nei □

Hvis ja: Anslå din gjennomsnittlige smerte (sett ring rundt ett tall)

Ingen smerte 0 1 2 3 4 5 6 7 8 9 10 Verst tenkelige smerte

Har du smerter akkurat nå?
Ingen smerte 0 1 2 3 4 5 6 7 8 9 10 Verst tenkelige smerte

Hvor plagsomme er smertene akkurat nå?
Ikke plagsomt 0 1 2 3 4 5 6 7 8 9 10 Verst tenkelige plage

Har du noen gang brukt opiater? ja □  nei □

Sett strek under de preparatene du husker å ha brukt/fått:
morfin kodein paralgin forte pinex forte oxynorm oxycontin remifentanil

Har du noen gang brukt opiater i mer enn 2-3 uker? ja □  nei □

   a. Hvis ja, hvilke medikamenter: ___________________________________________

   SLUTT

Dette var alle spørsmålene. Tusen takk for at du tok deg tid til å svare oss! Vennligst lever skjemaet tilbake til personen du fikk det fra.

Lykke til med operasjonen!
Appendix 3 Study Protocol for T3
T3 – på operasjonsbordet

**Før remifentanil administreres**

_Hvor bra føler du deg akkurat nå på en skala fra 1 til 10?_

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ikke bra</td>
<td>Veldig bra</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

_Hvor engstelig føler du deg akkurat nå på en skala fra 1 til 10?_

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ikke engstelig</td>
<td>Veldig engstelig</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Nå får du medisinen, si ifra når du kjenner noe.

**Remifentanil administreres**

Etter 60 sekunder: _Føler du effekt av legemiddelet du fikk, akkurat nå?_ ja □  nei □

_Hvor bra føler du deg akkurat nå på en skala fra 1 til 10?_

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ikke bra</td>
<td>Veldig bra</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

_Hvor rusa føler du deg akkurat nå på en skala fra 1 til 10?_

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ikke rusa</td>
<td>Veldig rusa</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

_Hvor mye liker du noen av effektene av medikamentet på en skala fra 1 til 10?_

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liker ikke</td>
<td>Liker veldig godt</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

_Hvor ubehagelige er effektene av medikamentet?_

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Misliker ikke</td>
<td>Misliker veldig</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

_Hvor engstelig føler du deg akkurat nå på en skala fra 1 til 10?_

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ikke engstelig</td>
<td>Veldig engstelig</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**30 sekunder etter propofol:**

_Hvor bra føler du deg akkurat nå på en skala fra 1 til 10?_

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ikke bra</td>
<td>Veldig bra</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 4 Study Protocol for T4
T4 – dagen etter operasjon på telefon

1. Hvordan går det med deg? (conversation starter..)

2. Hvor **bra** føler du deg akkurat nå på en skala fra 0 til 10?
   - Ikke bra 0 1 2 3 4 5 6 7 8 9 10 Veldig bra
   - a) Har vært igjennom denne operasjonen før? Ja ☐ Nei ☐ Narkose Ja ☐ Nei ☐

3. Har du **smerten akkurat nå**?
   - Ingen smerte 0 1 2 3 4 5 6 7 8 9 10 Verst tenkelige smerte

4. Hvor **plagsomme** er smertene akkurat nå
   - Ikke plagsomt 0 1 2 3 4 5 6 7 8 9 10 Verst tenkelige plage

5. Hvor mye oxy fikk du med deg fra sykehuset?

6. Har du brukt **smertestillende siden du dro fra sykehuset?** Ja ☐ Nei ☐
   - i. Paracet____ Dose _______ Hyppighet __________
   - ii. Vimovo____ Dose _______ Hyppighet __________
   - iii. Oxynorm____ Dose _______ Hyppighet __________
   - iv. Annet _______ Dose _______ Hyppighet __________
   - b. I hvor stor grad har behandlingen eller medisiner lindret smertene dine de siste 24 timene? Oppgi svaret på en skala fra 0 til 10, der 0 er ingen lindring og 10 er fullstendig lindring____
   - c. Har du tatt medisinene annerledes enn hvordan de ble forskrevet? Ja ☐ Nei ☐
   - i. Hva ja, hvordan __________

7. Har du **hatt lyst på** noen spesielle smertestillende? (feks. opiater?) __________

8. Har du fått i deg mat? Ja ☐ Nei ☐
   - a. Hvis ja, hva slags og hvor mye __________

9. Har du fått sove? Ja ☐ Nei ☐
   - a. Hvis ja, hvor mye og hva slags kvalitet __________

10. Har du vært kvalm? Ja ☐ Nei ☐
    - a. Antall brekninger? __________

11. Hvor godt føler du selv at du takler smertene dine på en skala fra 0-10, der 0 er at du takler dem svært dårlig og 10 at du takler dem svært godt? __________

12. Er du nervøs for tilfriskningen din nå etter operasjonen? Ja ☐ Nei ☐
    - a. Hvis ja, hvor nervøs er du på en skala fra 0-10, der 0 er ikke nervøs og 10 er svært nervøs __________
    - b. Er det noe som hjelper deg å reducere smertene, eller eventuell nervøsitet __________


IDnr: _________________________
Operert: _______________________
Ringt: ___________ Kl: ___________
Registrert: ______________________