Improving postoperative pain care

An Acute Pain Service data analysis

Regina van Boekel

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The studies in this thesis have been performed at the Department of Anesthesiology, Pain and Palliative Medicine of the Radboud University Medical Center.

For reasons of consistency within this thesis, some terms have been standardized throughout the text. As a consequence the text may differ from the articles that have been published.

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If you can’t explain it simply, you don’t understand it well enough.
Albert Einstein (1879-1955)

Dedicated to my family

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Prologue

"Why do I have to suffer so much pain? We fly to the moon, but professionals like you are not able to alleviate this pain? " (patient 1)

"Please, give me this epidural, or I will definitely get a pneumonia!" (patient 2)

"You can't expect me to know all this; if patients are in pain I will call you." (nurse to acute pain service)

"Of course he is not in pain, his pain score is 3." (resident of the surgical department)

Of all the forms of pain, postoperative pain is one of the most ubiquitous. Rarely does someone undergo a surgical procedure without suffering pain, ranging from relatively mild to overwhelmingly severe. So it would be easy to assume that we have a large body of information about postoperative pain management. A lot of research, summarized in guidelines and pain protocols on acute postoperative pain management, has been performed. I read the articles, I worked on a chapter in the new Dutch guideline on postoperative pain management, and I developed the pain protocol for my hospital according to the guidelines. However, in daily practice, I noticed that the protocols did not answer all questions about individual patients.

I have written down some quotes I have heard a lot of times, when attending my shift of the acute pain service (APS) at the Radboud university medical center. Those quotes inspired me to reflect on my knowledge and my work. Some questions were raised. For example, can patients, being treated perfectly according to the guidelines, still be in pain? How do I treat patients who claim that pain is acceptable to them, when having high pain scores. Is it true that patients who are in too much pain develop complications?
Because I work as a clinical pain nursing consultant, nurses and physicians expect me to have specialized knowledge on pain management. I like to share my knowledge and I enjoy teaching. But for me it is very difficult to explain pain issues to health professionals when these issues do not make perfect sense. For example when explaining the assessment of pain. In the Netherlands, many people regard pain scores as objective measures, with a cut-off point for treatment. Explaining that a simple pain score is not enough information to decide on pain treatment is necessary and lacking in our training programs for health professionals.

Being the coordinator of the Dutch national education for clinical pain nursing consultant, I hear many stories about acute pain service in hospitals. Students describe many different types of acute pain services in which they are employed. I noticed that we did not know anything about the acute pain services in the

Netherlands. What are tasks and responsibilities of the acute pain service? Do APS members need to advise, to take over, to teach, or to organize?

The more I knew about postoperative pain management, the more questions were raised on this topic. All these questions stimulated me to put on my own research, finally resulting in my thesis.

Rianne van Boekel

General introduction

1

Postoperative pain is a common occurrence following surgery. Severe postoperative pain increases the incidence of postoperative complications, prolongs length of stay, causes readmissions, and significantly reduces patient satisfaction and quality of life [1, 2]. In addition, it is a considerable burden on health care service costs, both directly as a result of consuming medical care, and indirectly as a result of absenteeism, less labor productivity, and increased social welfare payments [3-8].

In 2010, a total of 1,414,558 operations were performed in the Netherlands [9].
A Dutch study of 1490 surgical inpatients showed that 41 % of patients had moderate-to severe pain on the day of surgery, with almost 15 % of patients reporting moderate-to-severe pain on the fourth postoperative day [10]. In ambulatory surgery, 26 % of the patients had moderate to severe pain on the day of the operation, 21 % on day 1 following surgery, 13 % on day 2, 10 % on day 3, and 9 % on day 4 [11]. Results from other studies also suggest that postoperative pain is common, with a prevalence of moderate to severe pain varying between 47 % and 65 % [6, 12-14].

In this thesis, our focus is on postoperative pain experienced by inpatients in an academic hospital setting in the Netherlands.

Definition of pain

Pain is often the major symptom in many medical conditions and is one of the most important reasons for seeking medical assistance [15]. The internationally recognized definition by the International Association for the Study of Pain states that: “Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” [16]. McCaffrey and Beebe offer an alternative definition: “Pain is whatever the experiencing person says it is, existing whenever the experiencing person say it does” [17]. Both definitions highlight the personal experience of pain as being something greater than tissue damage triggering a response from the nervous system.

Pain can be divided in acute and chronic pain. Acute pain is defined as “pain of recent onset and probable limited duration. It usually has an identifiable temporal and causal relationship to injury or disease” [18]. Chronic pain is defined as “pain that extends beyond the expected period of healing” [16]. In both acute and chronic pain, the experience depends on multidimensional factors, with biological, psychological, societal and spiritual dimensions [19-23]. Thus, pain and the behaviors it elicits are influenced by genetics, emotions, past experience, anticipated consequences, and the environment at the time of an incident.

Acute postoperative pain is defined as “pain occurring in surgical patients following a procedure” [24]. If, after a surgical procedure, the resulting pain continues for at least two months, and other causes of the pain have been excluded [25], then this is termed chronic postoperative pain.

Physiological and psychosocial impact of postoperative pain

Studies show that adequately controlled postoperative pain contributes to the prevention of medical complications [3, 26-28]. The physiology and mechanisms of acute postoperative pain may explain this relation with medical complications. Acute postoperative pain results from inflammation due to tissue damage or/ and nerve injury. In the acute phase, postoperative pain induces the increase in the neuro-humoral stress response, which includes an increase in cortisol, catecholamines, glucagon, protein catabolism and in autonomic activity [29]. These increased responses have metabolic, hemodynamic, hemostatic, gastro-intestinal and immune related consequences [28].

At a behavioral level, common early responses are a lack of movement, lack of deep sighing, and ineffective coughing. This may result in reduced lung volume, reduced clearance of the lungs, and decreased production of surfactant of the lungs, and in the long term, in inhibition of the mobility of the patient. These behavioral responses may thus lead to postoperative motor complications and decubitus ulcers.

On a psychological level, inadequately controlled acute postoperative pain was found to increase the risk of long-term depression, 6 months after cardiac surgery [30]. Several studies have shown a strong negative relationship between pain and quality of life [13, 31]. Studies of the risk factors for developing acute postoperative pain show that genetic factors [32] and environmental factors [33] may contribute to the level of postoperative pain. Several risk factors have been identified, for example: age [33-35], gender [35, 36], Body Mass Index [37], level of preoperative pain [35, 36, 38], preoperative anxiety [35, 39], pain catastrophizing [40, 41], and type of surgery [35]. These findings may also explain why, despite adequate guidelines and execution of pain protocols, some patients do not fully respond to medical pain treatment. Another approach for patients who do not respond to usual care and keep having pain needs further study.

Quality of care in postoperative pain management

Recent initiatives by pain professionals have resulted in improvements in the quality of postoperative pain management. In order to evaluate the progress made in the field of postoperative pain management, we introduce some components of pain management theory. The Donabedian quality of care framework provides a conceptual model for evaluating quality of health care issues. In the framework, information from which inferences can be drawn about the quality of care is classified under three categories: “structure,” “process,” and “outcome” [42]. Structure describes the context in which care is delivered, including acute pain services. Process denotes the transactions between patients and providers throughout the delivery of healthcare, including pain assessments and the adherence to guidelines

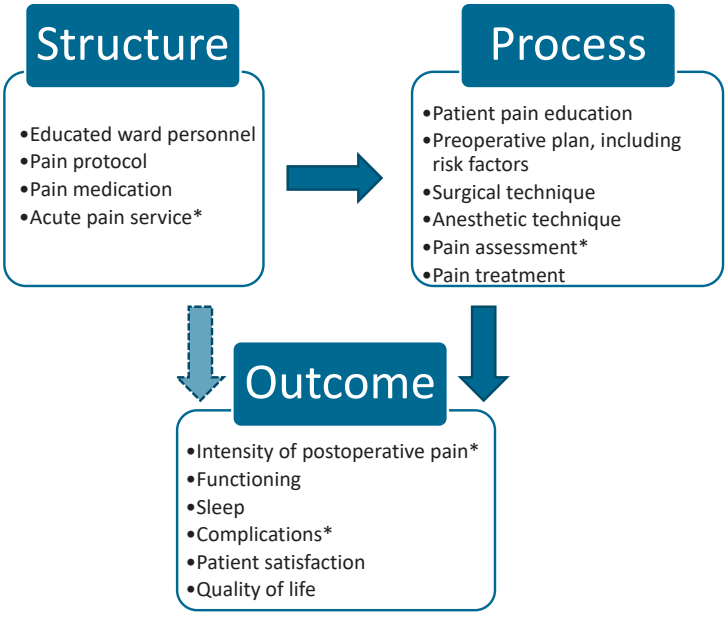

Figure 1 Donabedian's quality of care framework of postoperative pain
Donabedian's quality of care framework of postoperative pain management shows the multifactorial factors responsible for the quality of pain management after surgery, classified under three categories "structure", "process", and "outcome". The factors indicated with * are addressed in this thesis.

or protocols, as well as the use of digital registration tools. Finally, outcome refers to the effects of healthcare on the health status of patients, such as complications after surgery. Preexisting knowledge about the linkage between these categories for postoperative pain management is well known [3, 14, 43]. (see Figure 1)

In Figure 1, the quality cycle of postoperative pain management is explained. The context (structure) in which postoperative pain care is delivered affects the processes and outcomes. For example, if a comprehensive pain protocol is not available or the ward personnel do not know what should be done for a patient in pain, the pain will not be assessed and consequently may be inadequately treated. Outcomes indicate the combined effects of structure and process, which in this example may result in a patient with unacceptably high pain levels, decreased quality of life, or a pain-related complication.
This model serves as a framework for preventing problems related to quality and, should problems still arise, to help improve the quality of care. As only those factors related to structure and process can be manipulated, to improve the outcome, deficiencies can only be corrected by system redesigns and other process inputs. In this thesis, a number of the factors described in each of the three categories will be addressed; Acute Pain Service (APS), pain assessment, intensity of pain and complications. In this way, the Donabedian model is used to evaluate several

quality improving innovations in postoperative pain management [42].

Acute pain service

In the Donabedian model, structural factors such as acute pain services are discussed first. To improve the management of postoperative pain, several hospitals in the Netherlands have initiated an APS. The APS is a dedicated and specialized team of pain specialists and nurses who support and advise on the safety and the effectiveness of acute pain management in a hospital; especially regarding postoperative pain [44-46]. In general its goal is to improve postoperative pain management, to mentor complex pain patients, facilitate a possible reduction in postoperative nausea and vomiting, prevent the development of side effects, increase patient wellbeing, and reduce hospital stay [45, 47-53].
The concept of a structural APS was first noted by Ready in 1988 as an anesthesiology-based postoperative pain management service [54], although in 1976, an anonymous editorial on the creation of analgesia-providing teams had been published in Anaesthesia and Intensive Care.
In the Netherlands, the need for an APS team to improve quality of postoperative pain management was first described in 1994 [55]. In 1991, the Radboud university medical center had already introduced an acute pain protocol and started up a pain service run by anesthesiologists and nurses. Seventeen years later in 2008, the pain service was formally adapted to a nurse-based anesthesiologist-supervised APS [56]. The nurse-based anesthesiologist-supervised APS model was chosen for several reasons. APS nurses are familiar with the wards, are recognizable and easy accessible for ward nurses, and have an affinity with nurses and their routines. This in contrast to residents, who often change positions because of their training. APS nurses thus show continuity, competency and knowledge of practical resources [56]. In addition, compared to involving anesthesiologists or residents, a nurse-based APS is cost-effective [49].
In this type of APS, several healthcare professionals work closely together to deliver the best postoperative pain care. APS nurses standardly visit postoperative patients in (high risk of) pain, do consultations, anticipate patient needs and are always available. On average, patients are seen by the APS nurses for three days after surgery and are available to ward nurses or physicians for consultation in complex postoperative situations. If the APS nurses need advice on complex patients, they can contact the supervising anesthesiologist. In addition to patient-related activities, the APS nurses perform several important non-patient-related activities like education, research and quality improvement, as well as evaluating pain scores and making protocol adjustments [44, 46, 50, 51, 57-59].

Studies show that there is considerable variation in the organization and procedures of APS teams in hospitals [44, 60-62]. Some APS teams restrict their activities to the management of patients after major surgery, others visit all postoperative patients or consult chronic pain patients as well. Not all APS teams perform

non-patient-related activities.
Currently there is no consensus about what constitutes a good APS with respect to standards for staffing, facilities needed, and procedures [58]. In the Netherlands we do not know how many Dutch hospitals have an APS, and where they exist, how the APS is staffed, educated and organized.

Adherence to pain guidelines

Process analysis is the next step in the Donabedian quality improvement model. The complex nature of acute postoperative pain and its management resulted in the development of clinical practice guidelines to promote evidence-based, effective, and safe postoperative pain assessment and management programs/strategies [63]. In 2010, the Dutch Hospital Patient Safety Program was implemented in almost all Dutch Hospitals. The program provides practice guidelines on pain assessment and pain treatment [64]. It states that pain should be assessed at least every eight hours, based on the usual working hours of a nursing shift, and that it should be rated using a standardized numerical rating scale [65] and documented in the patient's medical record; if the pain score is greater than three, then pain should be treated [64]. In 2012, the Dutch Society of Anesthesiology updated the Dutch guidelines for postoperative pain management [66, 67], thus providing evidence-based standards for postoperative pain assessment, pain treatment and acute pain service.

An important measure to improve the process of postoperative pain management is the systematic and standardized assessment of postoperative pain [68]. Patient self-report is the primary source of all pain assessments, as pain is inherently subjective [63]. Differences have been identified between nurses' assessments of patients' pain and patients' self-assessments, with nurses giving consistently lower ratings than patients [69, 70]. Studies report that compliance among doctors and nurses with respect to the systematic assessment of pain is still suboptimal [71] and show that it slowly deteriorates after an education program [72].

Limited information is available about the factors influencing compliance with the guidelines for pain assessments [71, 73-75]. No studies were performed in the Netherlands following the implementation of the Dutch Hospital Patient Safety Program in 2010. It remains unclear whether pain is regularly assessed in Dutch hospitals and if the presence of an APS in the hospital influences adherence to these guidelines.

Standardized digital administration tools for pain data

Quality measurement is fundamental to the systematic improvement of health care [42, 76]. In clinical practice, documenting pain assessments and treatments is essential in order to communicate patient status between different and successive health professionals, such as nurses on daily shifts [77]. At an individual patient level,

documenting pain scores several times each day can clarify the success or failure of pain treatment and the need for adjustment of pain therapy. At group level, documented data of pain assessments is needed for analysis, to identify barriers in optimal pain management, and to promote quality improvement [78-80]. In addition, patient data is needed to identify risk factors and to develop procedures for the optimal prevention of postoperative pain [35].
To reduce workload and minimize the need for special research teams, data collection should be organized efficiently, accurately and reliably. Ideally, data collection should be automatically connected with clinical practice. Improved digital administration will lead to the creation of the 'big data' sets required to create an adequate prediction rule for whether or not a patient will be in pain after surgery [34].

Postoperative pain and the prevention of complications after surgery

The final phase of the Donabedian model describes outcome such as complications after surgery. In the past twenty-five years, many reports of inadequate management of acute postoperative pain have highlighted the humanitarian need to keep patients comfortable and to prevent complications and adverse effects [1, 2].

Inadequate management of postoperative pain, whether undertreatment or overtreatment, is considered to have negative consequences for patients resulting, for example, in cardiac alterations, myocardial ischemia or infarction, thrombo-embolic and pulmonary complications, immune alterations, impaired rehabilitation, increased length of stay and/or hospital readmission, decreased quality of life, and adverse events related to excessive analgesic use [13, 43]. Additionally, acute postoperative pain plays an important, yet not fully understood, role in the development of chronic postoperative pain [81, 82]. Overall, postoperative complications lead to an increase in resource utilization which in turn leads to higher healthcare costs [7, 8].

Currently, there is a lack of scientific evidence for and consensus on the effects of adequate acute postoperative pain management on postoperative outcome [83]. We postulate that the provision of high-quality postoperative analgesia may reduce the development of major postoperative complications. To study this, due to the relatively low incidence of major postoperative morbidity, large patient numbers in any individual clinical trial are needed.

Pain scores and complications

In 2000, the Joint Commission, an independent organization for accrediting and certifying health care organizations and programs in the United States, declared pain as the "fifth vital sign", emphasizing that a pain score of less than 4/10 should

be achieved for all patients. Since then, routine pain assessment and treatment has led to an increased incidence of opioid-related adverse drug events, such as over-sedation and respiratory depression [14, 83, 84].
Similarly in the Netherlands, the Dutch Hospital Patient Safety Program Practice Guideline for (postoperative) pain management suggested a score of >3 on the numerical rating scale (NRS) as a cut-off for pain treatment. Recent Dutch studies have shown, however, that patients and caregivers interpret pain intensity scores differently [85]. Patients may choose not to take more analgesics because they interpret their pain as "bearable" [86, 87]. Another study stressed the difference between pain at rest and movement-evoked pain [88]. Thus, using a firm cut-off score alone as a measure for pain treatment may be dangerous; other outcome measures such as the patient's opinion on the acceptability of the pain should be included [89]. The relationships between patients' postoperative pain scores and their willingness to accept pain, as well as their performance of physical activities has not yet been investigated. In addition, whether or not there is a relationship between the acceptability of the pain and the development of postoperative complications also remains unclear.

Societal impact of acute postoperative pain

Because of the importance and high prevalence of postoperative pain, the Dutch Health Care Inspectorate, the organization that monitors health care quality and safety in the Netherlands, has taken actions to support adequate pain management [90]. In 2003, quality indicators for postoperative pain management were added to the basic set of hospital quality indicators. The Inspectorate considers pain assessment a prerequisite for adequate pain management: only a few patients should have high postoperative pain scores, and all hospitals should have an acute pain service. Therefore, the indicators included a structure indicator, i.e. does the hospital have an APS, a process indicator, i.e. the percentage of postoperative patients with a standardized pain measurement, as well as outcome indicators, i.e. the percentage of postoperative patients with a pain score > 4 and subsequently the percentage of postoperative patients with a pain score > 7.

In the Netherlands, the national Hospital Patient Safety Program was launched in 2010 and the "early recognition and treatment of pain" was one of the themes implemented [64]. The program is a part of the safety management system (SMS, or VMS in Dutch) which embeds patient safety in healthcare practice. Hospitals use the SMS to continuously identify risks, implement improvements, and establish, evaluate and modify policy.

Research methodology

Literature on improving postoperative pain management is mostly based on

a commonly used approach for measuring the impact of implementing an APS, the 'uncontrolled before-after study' [50]. However, this type of study tends to overestimate the effects of the treatment or the services under study and datasets are often small. The selection bias of before-after comparisons on this topic may therefore be great and most studies are not run long enough to determine whether the intervention and its apparent effect are sustainable. Due to these concerns, the Cochrane Effective Practice and Organization of Care (EPOC) Group strongly discourages the inclusion of uncontrolled before-after studies in EPO reviews because it is difficult, if not impossible, to attribute their causation [91].

Alternative methods, such as cluster randomization, have been successful in other studies on health system interventions [92]. Randomization minimizes selection bias and a randomized controlled trial (RCT) is therefore often considered to be the gold standard. However, trial participants typically do not represent the complete population as they are preselected. Additionally, study protocols do not always reflect clinical practice. Therefore, results from RCTs may not apply in a more general population as in a randomized population it is not always possible to discriminate which subgroup of participants actually benefited from the intervention being studied and mean scores are not always predictive of individual results [93, 94]. By creating subgroups, researchers can determine which patients with a certain profile possessing certain characteristics will respond to a specific treatment or not. In order to be able to draw conclusions, subgroups have to be of a sufficient magnitude to generate large datasets [34, 35, 95]. These large datasets should be created in the clinical process to avoid high costs and workload. Large prospective observational studies resulting in clinically collected data are therefore needed in order to answer research questions on the quality of postoperative pain management.

Implementation studies often end when the first phases of implementation are completed. This often reduces the attention paid to the process and newly established practices [77]. In clinical practice, new initiatives need to settle in so that users are able to familiarize themselves with the new interventions. Regular incentives help users to remember the newly learned actions, and periodic evaluation is valuable to identify both barriers and facilitators following the implementation of the new intervention.

Aim of the thesis

Inadequate postoperative pain management is associated with several negative consequences, patient discomfort, and is linked to increased healthcare costs. The overall aim of this thesis is to explore the quality of postoperative pain management in hospitals. We used the Donabedian model to assess the quality of postoperative pain management, selecting a set of factors from each of the three categories: structure, process and outcome [42]. The following research questions

were formulated for each category:

The organizational **structure** of pain management in hospitals:

1. How many APS services are available in Dutch hospitals, what is their structure and what responsibilities are delineated?

The **process** of pain assessment in hospitals:

2. Compliance with pain assessment in postoperative patients after implementation of the Dutch Hospital Patient Safety Program:
    a. What is the compliance with pain assessment in postoperative patients after implementation of the Dutch Hospital Patient Safety Program, from the viewpoint of the hospitals?
    b. What is the compliance with pain assessment in postoperative patients after implementation of the Dutch Hospital Patient Safety Program, based on patient records.
    c. Which factors influence the actual compliance with pain assessment in postoperative patients after implementation of the Dutch Hospital Patient Safety Program?

The **outcome** of postoperative pain management in hospitals:

3. The outcome of postoperative pain management in the Dutch Radboud university medical center:
    a. What is the prevalence of moderate to severe acute postoperative pain in hospital patients?
    b. Do neuraxial or regional analgesia provide superior pain relief compared with patient-controlled intravenous analgesia in three different procedures, based on data from the Acute Pain Service?
    c. What are the differences in values for pain measures, such as a numerical pain score, an acceptability score, and a physical functioning score?
    d. Is there an association between unacceptable postoperative pain and complications after surgery?

Outline of the thesis

The thesis is organized in three main parts based on the three factors of Donabedian's framework for modelling the quality of care: structure, process and outcome.
In Chapter 2, the first part of the thesis, we answer research question 1. We present a detailed report on the current state, structure and responsibilities of the APS teams in Dutch hospitals. We also answer question 2a by providing an overview of the "pain theme" of the Dutch Hospital Patient Safety Program and reports from Dutch hospitals on this theme.
In Chapter 3, the second part of the thesis, we review the process of postoperative pain management. We compare data collected in a national survey on the pain assessment compliance of health professionals in Dutch hospitals with the assessments documented in patient records, thus answering question 2b. We then provide an analysis of the association between this compliance and hospital and

APS characteristics, answering question 2c.
In Chapter 4, starting the third part of the thesis, we answer the questions related to the outcomes of postoperative pain management. We first describe the prevalence of moderate to severe acute postoperative pain in patients who underwent major surgery, using a large dataset of clinically collected APS data, thereby answering question 3a. In addition, we compare epidural regional analgesia versus patient-controlled intravenous analgesia on pain scores, answering question 3b. In Chapter 5, we answer question 3c by describing the relationships between different pain measures, such as a numerical pain score, an acceptability score, and a physical functioning score, as well as a cut-off score for pain treatment.
In Chapter 6, we report on the prevalence of moderate to severe acute postoperative pain of surgical patients undergoing all kinds of surgery, thereby adding to the prevalence data resulting from question 3a. We also investigate the association between unacceptable postoperative pain and complications after surgery, answering question 3d. Finally, in Chapter 7, the discussion and conclusions, we summarize our findings in relation to the current situation regarding postoperative pain care, providing directions for future research.

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Part I

Quality of postoperative pain care: structure

Acute Pain Services and Postsurgical Pain Management in the Netherlands: A Survey

2

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Abstract

Background: Acute postoperative pain is still inadequately managed, despite the presence of acute pain services (APS teams). This study aimed to investigate the existence, structure, and responsibilities of Dutch APS teams and to review the implementation of the Dutch Hospital Patient Safety Program (DHPSP).

Methods: Information was gathered by a digital questionnaire, sent to all 96 Dutch hospitals performing surgical procedures.

Results: Completed questionnaires were received from 80 hospitals (83 %), of which 90 % have an APS. Important duties of the APS are regular patient rounds, checking complex pain techniques (100 %), supporting quality improvement of pain management (87 %), pain education (100 %), and pain research (21 %). Concerning implementation of the DHPSP, we found that regular in-hospital pain training is not provided in 46 % of the hospitals. Thirteen percent of the hospitals offer no patient information about pain management.

Conclusions: Almost all hospitals have an APS. They differ in both the way they are locally organized, along with the activities they employ. Future research needs to compare the effect of patient-related and non-patient-related activities of APS teams on outcomes related to pain management.

Introduction

Acute postoperative pain is still inadequately managed all over the world [1-7]. A prevalence of 39 % of severe pain on the first postoperative day is reported. For some surgical procedures up to 75 % of patients have moderate to severe pain [5, 6, 8, 9]. Adequate postsurgical pain management is essential as it contributes to improved clinical outcomes and patient satisfaction [10-13]. To advance hospital postoperative pain management some specific strategies have been proven useful: the structural assessment and registration of pain in patients [14], treating pain consequently [15], educating patients [16-19] and staff [15, 20] about pain management and starting an Acute Pain Service (APS) [21-23].

An APS is a dedicated and specialized team that supports and advises on the safety and the effectiveness of acute pain management in hospitals; especially postoperative pain [10, 24, 25].

APS teams may improve postoperative pain management, facilitate a possible reduction in postoperative nausea and vomiting, prevent the development of side effects, increase patient satisfaction and decrease hospital stay [10, 15, 26-31]. Studies show that there is considerable variation in the organization and procedures of APS teams [22, 24, 32, 33]. Currently there is no consensus about standards for staffing, specific facilities, procedures and criteria on what constitutes a good APS [2].

In the Netherlands hospitals deliver information about the levels of postoperative pain in their patients on a yearly basis*. The presence of an APS in a hospital is mandatory and queried since 2006.

In 2008 the government launched the Dutch Hospital Patient Safety Program (DHPSP)**. This program aimed to “reduce avoidable suffering and pain by the early recognition and treatment of pain”. Recommended interventions are those proven effective, namely that each hospital demonstrates to 1) measure movement evoked pain three times a day, 2) have an operational acute pain protocol and 3) to have a pain education program for ward staff and patients.

The present study aims to investigate the existence, structure and responsibilities of the Dutch APS teams in hospitals and the degree of implementation of the Dutch Hospital Patient Safety Program.

Methods

Study population

Using data from the Dutch Health Care Inspectorate and the Association of Nurse

* Dutch Health Care Inspectorate. Basic set for quality indicators for hospitals 2011 [cited 2012 19 May]. Available from: www.ziekenhuizentransparant.nl

** Dutch Hospital Patient Safety Program. Practical Guide Pain. The Hague. 2009; [cited 2011 May 18]. Available from: http://www.vmszorg.nl/themas/pijn.

Anesthetists, hospitals were identified with their contact persons. These hospitals were approached with a survey about acute pain management. According to the Health Care Inspectorate in 96 hospitals surgical procedures are performed , which are all included in our study*.

Questionnaire

By using a digital questionnaire type and size of responding hospitals, functional and organizational structure of APS teams were identified. We also evaluated the implementation of the DHPSP for pain. Questions about APS concerned the existence of APS in the hospital, organizational embedding of this APS , the number and type of professionals, supervision of the APS and the hours APS is operational. The questionnaire also contained questions about the patients visited by APS and the non-patient-related activities, like education, participation in a pain quality improvement program and pain research. Questions about the implementation of the DHPSP concerned whether pain is assessed, which pain (rest/movement) is assessed, how often and for how long pain is assessed. The questionnaire also contained questions about the access to a protocol for pain after surgery, access to regular in hospital pain training and about the ways patients are informed about pain after surgery. Questions were multiple choice questions, sometimes necessary to indicate more than one choice. Some questions offered the possibility to add some additional information.
The questionnaire was based on the questionnaires used by Powell et al. and Nasir et al. in their studies on APS teams and postoperative pain management in the UK and USA [22, 32]. The questionnaire was piloted for design and content in a small group of anesthetists and nurses in two hospitals.
In the questionnaire an APS was defined as a dedicated service on a consult basis that evaluates pain and adjusts pain treatment in postoperative patients. In hospital training was defined as training provided to ward personnel by the APS teams of that same hospital. Patient-related activities were those that are concentrated around the patient, such as pain assessment and checking epidurals. Non-patient-related activities reflected the activities concerning quality improvement, education and research. These were indirectly related to better pain management, for example helping ward personnel to interpret their pain results, writing pain protocols and implementing a pain measurement tool for children under the of age of four.

Data collection

After approval by the institutional review board a digital questionnaire and covering letter was sent to the contact persons in November 2011. Reminders were sent to non-respondents after 2 weeks and 2 months with a further targeted mailing to

* Dutch Health Care Inspectorate. Basic set for quality indicators for hospitals 2011 [cited 2012 19 May]. Available from: www.ziekenhuizentransparant.nl

a small group of non-responders. In case more than one response per hospital was received (e.g. because of cross-site working), factual data were systematically aggregated to create one record per hospital. Non-responders were asked by telephone if their hospital had an APS (yes/ no).

Data analysis

Quantitative data were coded and entered into the Statistical Package for the Social Sciences (IBM SPSS version 20.0; IBM Corporation, New York, NY, USA) for analysis. Descriptive data were obtained for the existence, structure and responsibilities of APS teams and on respondents' assessment of services in their own hospital. A non-responders analysis was performed on existence of APS in the hospital. Based on functional time equivalents (FTE 0-5 or >5) and the presence of a nurse or nurse anesthetist with specialized pain education (yes/no), a distinction was made between special dedicated APS teams (APS work main target of total duties) and integrated dedicated APS teams (APS work not main target of total duties). This distinction was made because some hospitals have an APS that consists of all members of the postoperative care unit, leading to high numbers of FTE. The mean FTE was used as a cut-off point for dichotomizing this continuous variable.

Results

Response

The response rate of hospitals answering the digital questionnaire was 80 out of 96 (83 %). All university medical centers responded (Table 1).
There was a large variety in the professional background of those completing the

Table 1 Common characteristics of hospitals in the Netherlands reported by a representative of the individual hospitals

	Number of hospitals	N (%)		APS (N (%))	
Type of hospital	80				
District general hospital		20	(25 %)	15	(75 %)[b]
District general hospital (medical education and training)[a]		52	(65 %)	49	(94 %)[b]
University medical centers		8	(10 %)	8	(100 %)[b]
Size of hospital: number of beds	74				
0-200		10	(13 %)[b]	9	(90 %)[b]
200-500		42	(57 %)[b]	36	(86 %)[b]
501-1000		19	(26 %)[b]	19	(100 %)[b]
>1000		3	(4 %)[b]	3	(100 %)[b]

[a] district general hospital with medical education and training are teaching hospitals: hospitals that have medical education and training as a core business, besides patient care.
[b] percentages calculated on numbers of APSs (N)

Table 2 Common characteristics of Acute Pain Services in the Netherlands reported by a representative of the individual hospitals

	Number of hospitals	N (%)	FTE Median (range)[e]
Responsibility of APS[a] taken by	64		
Anesthesiology (including pain clinic)		62 (97 %)	
Other		2 (3 %)	
Health professionals working in APS[b]	52		3,3 (0,50-36,00)[d]
Nurse pain specialist[c]		27 (52 %)	1,5 (0,20- 3,00)
Anesthesiologist		21 (40 %)	2 (0,66- 10,00)
Recovery room nurse		21 (40 %)	4 (0,10- 22,00)
Nurse anesthetist		15 (28 %)	3 (0,50- 16,00)
Nurse practitioner		10 (19 %)	1 (0,70- 4,00)
Physician assistant		6 (11 %)	1 (0,50- 2,00)
Intensive care nurse		3 (6 %)	1 (1,00- 2,00)
Daily responsible supervisor of APS	64		
Anesthesiologist		51 (80 %)	
Nurse pain specialist		5 (8 %)	
Nurse practitioner		4 (6 %)	
Recovery room nurse		2 (3 %)	
Nurse anesthetist		2 (3 %)	
Availability of APS	64		
Mon-Fri office hours		25 (40 %)	
7 days/week office hours		19 (30 %)	
24/7		14 (22 %)	
Other		6 (9 %)	

[a] defines as: acute pain service team: a service or team that evaluates pain management of postoperative patients and treats them on consult basis.
[b] distribution of the group and not of individual APS
[c] number of nurses plus nurse anesthetists who are specialized in pain care.
[d] no difference between parttime and fulltime APS
[e] size of APS measured in full time equivalents (FTE), meaning 36 hours of working time per week per FTE

questionnaire: 38 % of the replies were completed by nurse pain specialists, 24 % by nurse anesthetists, 13 % by nurse practitioners, 11 % by anesthesiologists, 9 % by recovery room nurses and 5 % by physician assistants.

APS

Ninety percent of the responding hospitals reported having an APS (Table 1). All university medical centers have an APS as do most of the district general hospitals with medical education and training. The non-responders analysis showed that 9 of 16 non-responding hospitals had an APS.

Organization of APS

Almost all hospitals indicate that the responsibility for the APS is within the department of anesthesiology (including pain clinics) (Table 2). Only a small number are within the responsibility of the department of surgery or the department of emergency medicine, as mentioned in some written comments.
The median number FTE of APS members is 3,3 with a range of 0,5-36,0 FTE (Table 2). Most team members are nurses, of which some are specialized in the treatment of pain. In the majority of APS teams an anesthesiologist is the responsible supervisor, other reported supervisors are a nurse practitioner or a nurse pain specialist.
Education of APS members focuses merely on education for nurses and nurse anesthetists, because these professionals are highly represented in Dutch APS teams. Various types of specialized pain education for this group is mentioned; in hospital training for APS (51 %) and specialized institutional pain education for nurse pain specialist (38 %). Few APS teams have a medical consultant especially educated in pain (8 %).
Fifty eight percent of APS teams are special dedicated, while 42 % of APS teams are integrated dedicated, according to criteria described in methods.
Twenty two percent of APS teams are on duty 24/7, 40 % during office hours on week days while some of the other APS teams indicated that they offer services after office hours depending on the anesthesiologist on call (Table 2).

Patient-related activities

All APS teams make regular patient rounds checking complex pain techniques like epidural, loco-regional analgesia or patient controlled analgesia (Table 3). Twelve percent of the APS teams visit all postsurgical patients during their daily pain rounds. Some APS teams mention treatment of patients after being consulted by ward nurses or doctors for patients with complex pain or unusual pain medication. Some APS teams visit patients after an automatically received message when a high pain score is digitally entered into a hospital database.

Non-patient-related activities

All APS teams participate in pain educational programs (Table 3). Education for nurses is more often reported than for medical doctors. Although more than half of APS teams participate in regular hospital refresher courses for nurses, most APS teams provide on demand education. Written comments described bedside teaching or discussing case reports during coffee breaks of ward staff.
APS teams support improving pain management in the hospital, mostly in the area of bedside pain registration and feedback about pain results on the wards. Thirteen percent of APS teams do not participate in quality improvement programs.
The majority of APS teams does not participate in pain research. Slightly more university hospitals than teaching hospitals participate in pain research.

Table 3 Patient and non-patient-related reported activities of Acute Pain Services in the Netherlands

	Total number of hospitals	N APSs (%)
Patient-related activities		
Postoperative patients visited by a member of APS on a daily round[a]	64	
All patients		8 (12 %)
Patients with PCIA		54 (84 %)
Patients with epidural		64 (100 %)
Patients with regional catheter		48 (75 %)
Patients with unusual pain medication		22 (34 %)
Other		15 (23 %)
Non-patient-related activities		
Educational tasks performed by members of APS[a]	63	
Any education		63 (100 %)
Regular		
Undergraduate nursing school[b]		16 (25 %)
Undergraduate medical school		3 (5 %)
Postgraduate nurses		14 (22 %)
Postgraduate medical doctors		2 (3 %)
Regular in hospital training nurses		34 (54 %)
Regular in hospital training medical doctors		8 (13 %)
On demand		
On demand in hospital training nurses		46 (73 %)
On demand in hospital training medical doctors		23 (36 %)
Participation in a pain quality improvement program	62	54 (87 %)
In the following areas[a]:		
Registration of pain scores		41 (66 %)
Pain treatment		30 (48 %)
Discussion with wards about pain results		41 (67 %)
Pain audit at wards		11 (18 %)
Participation in a research programme by members of APS	63	
Yes		13 (21 %)

[a] more than one choice could be indicated per APS
[b] medical specialists in training (graduates) were not included in this survey
APS means acute pain service team

Implementation of DHPSP

Almost all hospitals have specific pain protocols and assess pain in surgical patients (Table 4). The majority of hospitals measure pain with movement as well as pain at rest at least three times a day. However more than half of the responding hospitals do not proceed pain assessment during the entire hospitalisation of the patient. Approximately half of the hospitals offers no access to regular in hospital pain training for their ward staff and if they do, training is mostly addressed to nurses.

Table 4 Reported postoperative pain management in the Netherlands: implementation of the Dutch Hospital Patient Safety Program

	Total number of hospitals	N (%)
Pain assessment in surgical patients	71	
Yes		70 (99 %)
Type of pain assessed	68	
Pain at rest		3 (4 %)
Pain with movement		3 (4 %)
Pain at rest as with movement		57 (84 %)
Unknown		5 (8 %)
Frequency of pain assessment in surgical patients	69	
Two times a day		7 (10 %)
Three times a day		55 (80 %)
>three times a day		7 (10 %)
Duration of pain assessment	68	
One day after surgery		1 (1 %)
Two days after surgery		3 (4 %)
Three days after surgery		19 (28 %)
>three days after surgery		8 (12 %)
All hospitalized days		31 (46 %)
All hospitalized days and after discharge		6 (9 %)
Access to protocol for pain after surgery	70	
Yes		68 (97 %)
Access to regular in hospital pain training	68	
Nurses		25 (37 %)
Medical doctors		1 (1 %)
Both nurses and medical doctors		11 (16 %)
No access		31 (46 %)
Way to inform patients about pain after surgery[a]	80	
None		10 (13 %)
Website		26 (32 %)
Leaflet		65 (81 %)
Film		7 (9 %)
Conversation polyclinic surgery		15 (18 %)
Conversation polyclinic anesthesiology		61 (76 %)
Conversation on surgical ward		40 (50 %)
Conversation APS		29 (36 %)
Other		5 (6 %)

[a] more than one way to inform patients could be indicated per hospital.

Hospitals offer several ways to inform patients about pain after surgery. Information is mostly provided by leaflet and oral explanation on the preoperative anesthesiological polyclinic. Thirteen percent of the hospitals offers no information about pain after surgery to their patients.

Discussion

This study investigated the existence, structure and responsibilities of APS teams and the reported implementation of the Dutch Hospital Patient Safety Program.
Ninety percent of Dutch hospitals reported having an APS, which are predominantly nurse based and mostly supervised by an anesthesiologist. The majority of team members are nurses. APS members make daily rounds to evaluate surgical patients with complex pain treatments like epidural, loco-regional analgesia or patient controlled analgesia. All APS teams have educational tasks and some participate in quality improvement projects of pain management. Research by APS teams is not common. Furthermore, all hospitals have structured pain assessment and pain protocols, however 46 % offer no access to regular in hospital pain training and 13 % do not inform patients about pain after surgery.
In comparison to the UK (83 %) and the USA (74 %) the percentage of hospitals with an APS in the Netherlands is high [22, 32]. Nurse pain specialists dominate the APS teams (52 %), like in the USA (45 %) and UK (nurses: 91 %).
The main components of an APS will be discussed: (1) designated personnel, (2) variety of patients consulted, (3) surgeon participation and (4) non-patient-related activities like ongoing teaching and quality improvement programs [2].
APS teams show large variation in the professional background of their employees, yet the nurse based model in which nurses and/or nurse anesthetists are supervised by the anesthesiologist is predominant. Ideally, all members of an APS form a dedicated team to support the professionals of a surgical ward offering the best possible pain management after surgery throughout the hospital [2, 15, 24, 25, 29, 34]. Fifty eight percent of hospitals is estimated to have a special dedicated APS, i.e. having a nurse or nurse anesthetist with specialized pain education and 0-5 FTE APS. APS teams are integrated dedicated, meaning staffed by an entire team of recovery room nurses or nurse anesthetists who combine their tasks in the APS with their regular duties on the recovery room or in the operating theatre. Whether and how this type of APS teams influences patient outcome on pain is unknown. It might be possible that an integrated dedicated APS invests less time and organizational efforts in non-patient-related activities. Lack of continuity by changing shifts might discourage long term follow up of patients after surgery, leading to an ad hoc treatment of pain problems without broad professional look of pain management as a whole [35].
This study shows that APS teams differ in their visiting procedures. All APS teams make daily pain rounds on the surgical wards and visit patients with complex techniques of pain treatment, like epidurals. Research shows that monitoring these techniques by APS is essential [3, 36]. However while some APS teams tend to visit only the “major” procedures with complex pain techniques of pain treatment, recent studies show that pain scores are often highest in “minor” procedures [9]. Visiting patients based solely on complexity of techniques might not be right. APS teams should evaluate pain scores on all procedures and develop procedure-specific

optimized pain management. Some small hospitals visit all postoperative patients. The benefit of visiting all postoperative patients or those at risk, should be investigated for its outcome and cost-effectiveness.

Surprisingly, no surgeons are involved in the APS teams. In one hospital the department of surgery is responsible of APS. As suggested by the study of Nasir et al, surgeons appear to play a limited role in APS teams. The role of surgeons in post surgical pain management needs further research because surgeons are responsible for patient care on wards where APS teams, supervised by anesthesiologists, visite their patients. Involvement of surgeons in APS teams might lead to better pain management, when optimal collaboration of all professionals is provided [2, 21].

Non-patient-related activities like education, research and quality improvement by evaluating pain scores and making protocol adjustments, generally are considered important components of the APS [2, 15, 24, 25, 29, 34, 37]. For that reason the "Royal College of Anaesthetists" in the United Kingdom has incorporated training, education and research by APS teams in their guidelines. Our results indicate that 13 % of the APS teams do not participate in quality improvement and nearly no APS teams are involved in pain research. International data are not available to compare these results. Acute pain management is spread across different departments which tend to have different levels of competence and priorities . Acute pain management is a shared responsibility across departments and requires effective communication and teamwork throughout the entire organization [38]. We feel that APS teams are a widely needed organization to professionally support and coordinate pain education, quality improvement and pain research.

Reported adherence to the recommended implementation of the DHPSP, i.e. pain assessment, pain protocol, pain education of health professionals and patients, show that not all hospitals perform pain assessment during the entire hospital admission. For early recognition of pain one should keep asking the patient about pain during the entire stay in the hospital. At present, the discussion when to stop asking the patient regarding the pain has been emerging. Clearly, our data are a reflection of this discussion. Since pain is considered as the fifth vital sign, it is recommended to measure pain daily three times and to balance need and nurture individually [39-41].

A considerable number of hospitals do not offer any training program for pain management to their personnel. The importance of pain education has been emphasized for all health professionals that treat patients with pain on the wards and for APS teams [20, 37, 42-46]. If health professionals are educated in pain management, pain is assessed better and more often leading to better decision making in pain treatment [43, 44, 47].

Eighty-seven percent of responding hospitals have a standard procedure to educate on patients about pain after surgery, which is important for patients understanding of necessity and cooperation of postoperative pain treatment [16-19]. The many procedures reflect the lack of evidence in this field and the need for more research into the way how patient education can be tailored to the specific needs of each individual patient.

The response rate of this national survey was very good with 83 % of the hospitals responding, only 16 hospitals did not respond at all. A non-responder analysis of the existence of an APS showed that there was some response bias. Additionally, the results would not have been different when all hospitals would have responded. No clear definitions exist about special dedicated APS teams or integrated dedicated APS teams, which limits the ability to compare APS modalities and responsibilities. Possibly, using a different approach in searching for data e.g. by site visits can result in different data but is much more time consuming. However, with our methodology we had a very high response with a high confidentiality. Since in this survey the aim was to describe the existence, structure and function of Dutch APS teams and what constitutes such a service in a hospital, no outcome parameters were included in the questionnaire or have been specifically measured. Therefore no outcome predictions can be done about the effects of APS teams in Dutch hospitals on the pain levels in postoperative patients. As a result, our statements needs further elaboration, since it is based on data of structure and process, rather than outcome.

Conclusion

Because of a published prevalence of at least 39 % of severe pain on the first postoperative day research for more effective APS is required. We think that APS teams should invest in patient care as well as non-patient-related activities enhancing organizational improvement of postoperative pain management. It would be preferable if all APS teams evaluated the outcome of all postoperative patients in their hospital for procedure-specific optimized pain management and tailored educational programs for ward personnel as well as patients. The way forward might include organizational changes of APS teams [48]. Now that APS teams are widespread in the Netherlands, further studies are needed to specify which patient and non-patient-related activities of APS teams influence the pain levels of postoperative patients and their recovery.

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Part II

Quality of postoperative pain care: process

Postoperative pain assessment in hospitalized patients: national survey and secondary data analysis

3

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Abstract

Background: Measuring pain is important for the adequate pain management of postoperative patients. The actual compliance with pain assessment in postoperative patients after implementation of a national safety program is unknown.

Objectives: The aim of this study is to examine the compliance with pain assessment in postoperative patients after implementation of a national safety program, according to the national quality indicators for pain assessment in postoperative patients. Furthermore, organizational factors associated with this compliance were determined.

Study design: In this study, two data sources were used: 1) data from an evaluation study of the Dutch Hospital Patient Safety Program; and 2) data from a questionnaire survey.

Methods: The compliance with two different pain process indicators was determined: 1) 3 pain measurements a day, all three full days after surgery; and 2) ≥1 pain measurement a day, all three full days after surgery. Multilevel logistic regression analysis was used to investigate the association between organizational factors in hospitals and compliance with pain process indicators.

Results: Data of 3,895 patient records from 16 hospitals was included in this study. In 12 % of the postoperative patients, pain was measured 3 times a day, all three full days after surgery. In 53 % of the postoperative patients, pain was measured ≥1 time a day, all three full days after surgery. Compliance was highest in general hospitals compared to tertiary teaching and academic hospitals, and was statistically significantly higher at the surgery and surgical oncology department compared to the other departments.

Conclusions: Low compliance was shown with pain assessment in postoperative patients, according to the process indicator pain after surgery in Dutch hospitals. This suggests that the implementation of measuring pain in hospitals is still insufficient.

Introduction

Postoperative pain management is an important element of adequate postoperative care [1]. During the past two decades, there has been increased attention for improving postoperative pain management as a result of several new guidelines and improvements of techniques in managing perioperative pain. Despite these improvements, postoperative pain management is often unsatisfactory and may increase the risk for patients to develop chronic pain conditions [2, 3]. Approximately 20 to 80 % of postoperative patients experience moderate to severe postoperative pain, and the prevalence has remained consistently high over the past two decades [4-8].

Numerous factors might be responsible for inadequate pain management, including inadequate staff training, insufficient knowledge on the part of nurses and physicians, unhelpful staff- and patient attitudes, fear of analgesic side effects, lack of accountability, and poor pain assessment [9]. If pain is not assessed systematically, it is difficult for practitioners to determine the effect of pain treatment and to adjust the treatment if necessary. Systematic pain assessment and documentation of pain scores help in characterising pain patterns precisely in individual patients [10, 11]. Previous research showed that systematic pain assessments can be integrated into the daily routine of nurses [12], and that an education program led to an improvement in the pain knowledge of nurses and even to a decrease in a patient's pain intensity [13].

Despite the known positive effects of systematic pain measurements in postoperative patients, the compliance with assessing pain is still suboptimal [12]. It has also been shown to slowly deteriorate after an education program [13]. No information is available about the actual compliance with the quality indicators for pain measurements. Limited information is available about the factors influencing the compliance with the guidelines for pain measurements [11, 12, 14, 15]. A study among inpatient palliative care centers showed that variations in pain management outcomes were affected by organizational factors such as organizational size and ownership [16]. A recent systematic review studied the effect of implementation strategies on pain assessment and showed that, besides organizational factors, also lack of knowledge and low priority given to pain management still influence adherence to pain assessment or clinical guidelines [12]. Another organizational factor that might influence positively the execution of postoperative pain measurements is the presence of an Acute Pain Service (APS) team, which has been introduced in most hospitals [17] to facilitate improvements in postoperative pain management and patient outcomes [18-21]. Insight into the factors related to the organization structure associated with the execution of pain measurements is necessary, as this information may be used to influence these factors, if possible, and improve the assessment of pain.

The aim of the present study is to examine the compliance with pain assessment in postoperative patients after implementation of a national safety program.

Furthermore, organizational factors including hospital characteristics and APS characteristics associated with this compliance will be determined.

Methods

Study design

For the present study, we used data from two sources. Data source 1 was a nationwide evaluation study of the Dutch Patient Safety Program (hereafter referred to as Safety Program), performed during the final period of the Safety Program [22]. Data was collected between November 2011 and December 2012, in a sample of 19 hospitals (2 academic, 6 tertiary teaching and 11 general hospitals), representing 20 % of all Dutch hospitals. Hospitals were randomly selected using a stratified sample based on geographical regions and type of hospital. In each participating hospital a measurement was performed every four to six weeks by a trained research assistant during one year. This resulted in a total of 10 measurements for each hospital. During every measurement period in each hospital, a random sample of 20-25 patient records was drawn from all patient records of postoperative adult (≥18 year) patients admitted in the week before the measurement period.
Data source 2 was a nationwide survey in Dutch hospitals concerning the management of postoperative pain, performed between November 2011 and February 2012 [17]. Data was collected in 80 of the 96 Dutch hospitals performing surgical procedures. Information about the functional and organizational structure of APS teams was collected on the hospital level by means of a digital questionnaire. Flow diagram 1 displays the steps taken for inclusion of patient records in data source 1, for extraction of organizational factors on hospital characteristics in data source 1, for extraction of organizational factors on Acute Pain Service (APS) characteristics in data source 2, and the final combination of data source 1 and 2 for analysis.

Pain measurement (data source 1)
The patient records were evaluated using a checklist focusing on: (1) the frequency of assessing standardized pain scores; (2) the severity of the pain by pain scores; and (3) interventions taken in the case of moderate to severe pain (pain score ≥ 4). For the present study, only patients hospitalized for at least three full days after surgery were included in the analyses. A documented patient self-reported pain score, which was obtained with a Numeric Rating Scale (NRS) or a Visual Analogue Score (VAS), was defined as a standardized pain assessment [23].

Process indicator pain (data source 1)
To support hospitals in the implementation of structured pain assessments, early recognition and treatment of pain was one of the ten themes within the national Safety Program [22]. Another measure that supports the implementation of

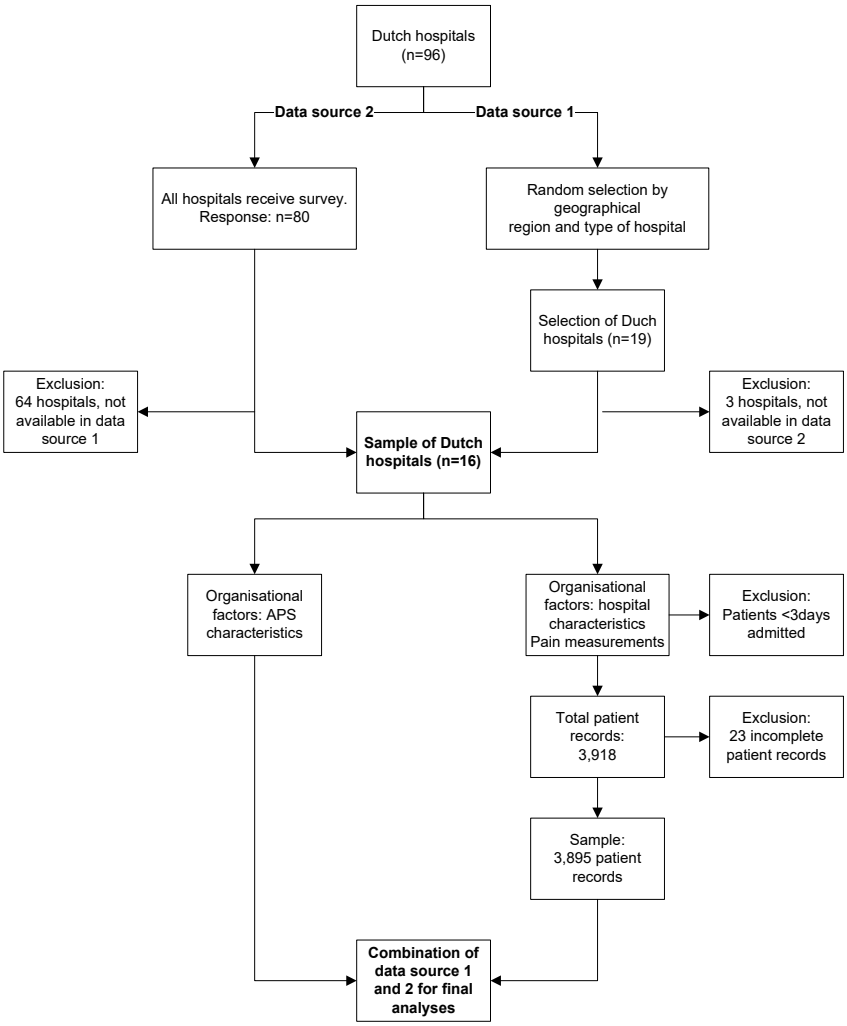

Figure 1 Flow diagram that displays the steps taken to obtain the final combination of data source 1 and 2 for analyses

structured pain assessments is the addition of a process indicator for pain to the quality indicators of the Dutch Health Care Inspectorate (IGZ in Dutch, hereafter abbreviated as HCI), the organization that monitors health care quality and safety in the Netherlands. Following the national quality indicators for pain, the process indicator for pain is defined differently by the Safety Program and the HCI. In the present study, these process indicators were described as Pain Safety Program (Pain assessment-SP) and Pain Health Care Inspectorate (Pain assessment-HCI). Pain assessment-SP was defined as: the percentage of postoperative patients with ≥***3 pain measurements*** a day, all three full days after surgery. We defined

Pain assessment-HCI as: the percentage of postoperative patients with ***≥1 pain measurement*** a day, all three full days after surgery. Both process indicators were calculated on the patient level (data source 1). Additionally, the mean reported Pain assessment-HCI of the included hospitals was calculated on the hospital level by using data from the open access webpage of the Health Care Inspectorate [24].

Organizational factors: hospital characteristics (data source 1)
Hospital characteristics were collected during the measurement in the hospitals. ***Admission department*** was determined in the patient record on the patient level and subsequently categorized to the departments cardiology, urology, surgery, orthopaedics, surgical oncology, and others. Other characteristics were collected at the hospital level, and could be identified on public websites about Dutch hospitals (e.g. Wikipedia). ***Type of hospital*** was categorized in academic (university medical center), tertiary teaching, and general hospitals. In the Netherlands, teaching hospitals provide specialized medical care and are committed to training and education. The ***size of the hospital*** was defined as the number of beds, ranging from 197 to 1,320 in the participating hospitals.

Organizational factors: APS characteristics (data source 2)
The standardized ***visit of the APS*** for all postoperative patients was dichotomized to yes (all postoperative patients) and no (no visit, or only patients with intravenous patient-controlled analgesia/ epidural catheter/loco regional catheter/uncommon pain medication/others). The ***feedback of the results to the department*** was dichotomized to yes (feedback was delivered to the department) and no (no feedback was delivered). The ***presence of a periodic training program by the APS*** was also dichotomized to yes (training for nurses, physicians or both) and no (no training).
The final factor included as organizational factor was the ***method of delivering data on the process indicator pain to the HCI***. All hospitals deliver information annually about the process indicator for pain defined as the percentage of standardized pain measurements performed in postoperative patients. The information about the method used for delivering the process indicator is published on the website of the HCI [24]. The data was collected from this website and dichotomized into: (1) deliver continuously; and (2) deliver a sample of measurements.

Statistical analysis

For the present study, only matched data from hospitals included in both data sources (N=16) were included. The mean percentages Pain assessment-SP and Pain assessment-HCI were calculated on the patient level. A multilevel logistic regression analysis was conducted to investigate the association between organizational factors and compliance with the process indicators. A two-level multilevel structure was used, whereby the measurements on the patient level were clustered within hospitals. Separate multilevel logistic regression analyses were performed

using compliance with the process indicators as dependent variables, and the organizational factors as independent variables. Categorical independent variables were analysed by adding separate indicator variables for the categories to the model. The proportion of variance (R^2) was calculated for the investigated factors, and can be interpreted as the percentage of the variance between hospitals in the compliance with the process indicator that can be explained by the organizational factors investigated. The intraclass correlation coefficient (ICC) was calculated to investigate the proportion of the total variance that remains after correction of the organizational factor. This indicates if any relevant, unexplained influence of the difference between individual hospitals on the pain outcome remains.
Descriptive analyses were performed using Stata version 12.1 and the multivariate analyses were executed using MlwiN version 2.24.

Results

The number of included records from data source 1 ranged from 210 to 283 in each hospital. Records with missing data for the process indicator pain were excluded (N=23), resulting in a sample of 3,895 patient records. Table 1 shows the admission characteristics and the mean pain process indicators of the included patients and hospitals. The results are shown on patient level, even though characteristics were determined on hospital level, as in the multilevel analyses data was also analysed on patient level. The mean age of the patients in the sample was 63.9 (SD 15.6) years and the majority was female (55.6 %; N=2,201 (missing sex N=263). In 75.5 % of the patients (N=2,450), not all postoperative patients were automatically visited by APS teams, but only specific patient groups. In almost two-thirds of the patients hospital APS teams delivered feedback regarding the department results on pain measurements to the department (N=2,045; 63.0 %). In 65.5 % of the patients (N=1,931), the APS teams provided a periodic training to nurses, physicians or both. In the majority of the patients hospitals delivered data on the process indicator continuously to the Health Care Inspectorate (N=2,659; 72.2 %). Some hospitals delivered random samples, which meant that they only sent data on pain measurements of a selected group of patients (see Table 1).

Process indicator pain

In 11.7 % (SD 32.1) of the patients, at least 3 pain measurements were performed on all three full days after surgery (Pain assessment-SP). The percentage increased if the process indicator of the HCI was used (Pain assessment-HCI). The mean percentage for observed Pain assessment-HCI was 53.3 % (SD 49.9). The mean reported Pain assessment-HCI was 78.2 % (SD 19.2).
In Table 2 is shown how many pain measurements were performed on each day of the three full days after surgery.

Table 1 Admission characteristics and pain process indicators in 3,895 postoperative patients from 16 hospitals[a]

Characteristics	N patients (%)	
Type of hospital		
Academic	475	(12.2)
Tertiary teaching	930	(23.9)
General	2,490	(63.9)
Admission department		
Surgery	2,005	(51.5)
Urology	154	(4.0)
Cardiology	97	(2.5)
Orthopaedics	1,091	(28.0)
Surgical oncology	186	(4.8)
Others	362	(9.3)
Number of beds, mean (SD)	488.2	(293.3)
APS visit		
No	2,450	(75.5)
Yes	797	(24.6)
APS Feedback to department		
No	1,202	(37.0)
Yes	2,045	(63.0)
APS Training		
No	1,018	(34.5)
Yes	1,931	(65.5)
Delivering method process indicator to HCI		
Continuous	2,659	(72.2)
Sample of measurements	1,023	(27.8)
Pain assessment-SP[a], % (SD)	11.7	(32.1)
Pain assessment-HCI[b], % (SD)	53.3	(49.9)
Reported Pain assessment-HCI[c], % (SD)	78.2	(19.2)

APS, Acute Pain Service; Pain assessment-SP, Pain Safety Program; Pain assessment-HCI, Pain Health Care Inspectorate

[a] Process indicator Pain Safety Program: percentage postoperative patients with ≥3 pain measurements a day, all 3 full days after surgery

[b] Process indicator Health Care Inspectorate: percentage postoperative patients with ≥1 pain measurement a day, all 3 full days after surgery

[c] Process indicator Health Care Inspectorate, reported by the included hospitals (N=16).

Factors influencing pain documentation

Table 3 presents the results of the multilevel analyses of the association between organizational factors and compliance with process indicators. The ICC was high for all organizational factors, at least 24.92, showing high variation between hospitals in the compliance with the process indicator pain. The R^2 was highest for type of hospital (23 %), indicating that this factor explained to the largest extent the differences between hospitals in compliance with Pain assessment-SP. In tertiary

Table 2 Compliance with pain assessments in three days after surgery (N=3,895)

Day after surgery	Number of pain assessments	N patients (%)	
Day 1	0	493	(12.7)
	1	637	(16.4)
	2	856	(22.0)
	≥3	1,909	(49.0)
Day 2	0	909	(23.3)
	1	624	(16.0)
	2	931	(23.9)
	≥3	1,431	(36.7)
Day 3	0	1,640	(42.1)
	1	680	(17.5)
	2	751	(19.3)
	≥3	824	(21.2)

teaching hospitals, pain was statistically significantly less often measured for both process indicators (2 % and 27 %) compared to academic hospitals (7 % and 56 %) and general hospitals (11 % and 59 %). 25 % (ICC 24.92) of the total variance in compliance with the process indicator Pain assessment-SP cannot be explained by type of hospital. The compliance with the process indicator was highest on the surgical oncology department, but was not statistically significant due to the relatively low number of records. The surgery and orthopaedics department had a statistically significantly higher compliance with the pain process indicators compared to the other departments. The negative R^2 for the factor Admissions Department (-15.56), showed that the differences between hospitals were covered by this factor, resulting in an underestimation of 16 % of the differences in compliance with Pain assessment-SP between hospitals.
The absence of a periodic training program by the APS was associated with a higher compliance with the process indicator Pain assessment-HCI. For the other APS characteristics, no statistically significant association was found.

Discussion

This study provides insight into the compliance with pain assessment in postoperative patients after implementation of a national safety program, and examined organizational factors on the hospital level and the department level associated with this compliance. The results of this study showed a low compliance with pain assessment in postoperative patients, according to the process indicator pain after surgery in Dutch postoperative patients. In 53 % of the postoperative patients, pain was measured at least once a day on all three full days after surgery. In only 12 % of the postoperative patients was pain measured at least three times a day, all three full days after surgery.
Following our results of the compliance with pain assessment in postoperative

Table 3 Multilevel logistic analysis of the association between organizational factors and compliance with process indicators Pain assessment-SP and Pain assessment-HCI

	Pain assessment-SP [a] **% compliance (95 % CI)**	**R^2** [b]	**ICC hospital** [c]
Type of hospital		23.44	24.92
Academic	6.61 (1.41 – 25.91)*		
Tertiary teaching	2.08 (0.64 – 6.49)*		
General	10.57 (5.67 – 18.86)		
Admission department		2.12	31.87
Surgery	8.96 (4.80 – 16.13)**		
Urology	6.26 (2.51 – 14.74)		
Cardiology	3.37 (1.07 – 10.08)		
Orthopaedics	5.61 (2.84 – 10.77)*		
Surgical oncology	9.85 (1.07 – 52.40)		
Others	1.91 (0.64 – 5.31)		
Number of beds, estimate (SE)	-0.001 (0.001) [e]	5.08	30.90
APS visit		5.42	27.02
No	6.21 (3.10 – 12.03)		
Yes	11.91 (3.54 – 33.28)		
APS feedback to department		3.49	27.57
No	5.09 (1.81 – 13.49)		
Yes	8.97 (4.22 – 18.07)		
APS Training		11.38	27.03
No	11.78 (4.13 – 29.30)		
Yes	5.35 (2.44 – 11.34)		
Delivering method process indicator to HCI, N (%)		-0.40	33.39
Continuous	6.66 (3.10 – 13.71)		
Sample of measurements	8.32 (2.36 – 25.41)		

APS, Acute Pain Service; Pain assessment-SP, Pain assessment Safety Program; Pain assessment-HCI, Pain assessment Health Care Inspectorate

*P <0.05, **P<0.01, ***P<0.001

[a] Process indicator Pain Safety Program: percentage postoperative patients with ≥3 pain measurements a day, all 3 full days after surgery

patients, according to pain process indicators, general hospitals had a better compliance with pain measurements compared to tertiary teaching and academic hospitals. This difference could not be explained by the size of the hospital, as the number of beds was not associated with compliance. Other factors that were not measured might possibly play a role in the varying compliance, for example hospital or department culture, priorities of the organization, education possibilities or research. The compliance with the process indicator was relatively high for patients admitted to the surgical oncology department and statistically significantly higher for the surgery and orthopaedics departments compared to the other departments. This might be explained by the relatively high percentage of patients with pain on these departments [25], whereby the importance of measuring pain is stressed and is more part of the daily routine. In future qualitative studies,

Table 3 Continued

Pain assessment-HCI [d] % compliance (95 % CI)	R^2	ICC hospital	
	15.33	26.71	Type of hospital
56.03 (21.42 – 85.62)			Academic
27.22 (10.97 – 53.17)*			Tertiary teaching
59.22 (42.18 – 74.30)			General
	-15.56	36.46	Admission department
49.05 (32.38 – 65.93)***			Surgery
25.36 (13.17 – 43.21)***			Urology
38.73 (21.14 – 59.84)***			Cardiology
53.93 (36.50 – 70.45)***			Orthopaedics
89.18 (62.93 – 97.56)***			Surgical oncology
30.55 (17.17 – 48.27)			Others
-0.0006 (0.001) [e]	0.27	31.46	Number of beds, estimate (SE)
	1.75	33.90	APS visit
47.42 (28.45 – 67.16)			No
66.52 (30.57 – 89.97)			Yes
	5.34	32.66	APS feedback to department
39.05 (17.02 – 66.68)			No
59.80 (38.01 – 78.29)			Yes
	18.27	28.60	APS Training
71.95 (44.95 – 88.96)*			No
38.23 (21.56 – 58.24)			Yes
	2.22	32.19	Delivering method process indicator to HCI, N (%)
44.89 (27.77 – 63.32)			Continuous
62.20 (32.13 – 85.12)			Sample of measurements

[b] Proportion of variance between hospitals that can be explained by the investigated factor
[c] Proportion of total variance after correction of the investigated factor
[d] Process indicator Health Care Inspectorate: percentage postoperative patients with ≥1 pain measurement a day, all 3 full days after surgery
[e] Because this analysis concerns a continuous outcome variable, the estimate and SE were shown.

more information should be collected about facilitators and barriers of performing pain measurements. This information might assist in distinguishing strategies for good compliance with pain measurements, which may help other hospitals to improve compliance.

Frequent assessment of pain in patients provides information to decide on interventions enhancing optimal pain relief [26]. The optimal frequency of pain measurements is unknown and depends on the needs of an individual patient. Important is that pain intensity is assessed regularly, using a standardized measuring instrument [27]. In our study, we used the national quality indicators for pain assessment, the process indicator of the Safety Program and the HCI, with ≥3 and ≥1 pain measurements a day respectively. The process indicator of the Safety Program is rather strict, demanding a pain measurement every eight hours (based

on the usual working hours of a nursing shift). In only 12 % of the postoperative patients pain was measured at least three times a day, all three full days after surgery. This percentage is quite low, however, ≥3 pain measurements a day in all postoperative patients may be rather ambitious and not relevant in all cases. Otherwise, the compliance with the process indicator of the HCI, asking for ≥1 pain measurements a day, was not higher than one out of two (53 %), which does not apply to the definition of "regularly". Therefore, there is room for improving the nurses' adherence to pain assessment recommendations.

Remarkably, we found that hospitals with a training program by the APS for nurses and/or physicians had a lower compliance with the pain process indicators. Education of nurses in pain management has been shown to improve nurses' knowledge of pain [28]. Successful use of guideline recommendations in clinical practice does however not only depend on education alone but also on the availability of staff and time, cooperation with other professionals, and attitudes of nursing personnel [29-31]. A negative attitude toward pain assessment and management is a barrier in implementing practice change [32]. In our study we did not have information about participation, experiences with, and duration of the training. The compliance may decrease if the interval between periodic training is too long [13]. Presumably, hospitals with no training by the APS do have a hospital-wide program whereby the hospital takes responsibility for the training and possibly more personnel is trained in pain management.

The other investigated organizational factors were not associated with compliance with the process indicator pain. We expected a better compliance with pain measurements if the APS was implemented in hospitals [17], but having a standardized visit of the APS for all postoperative patients did not influence the compliance. The delivering of feedback of results to the department did not influence this either. The content, timing and method of delivering feedback was not investigated and might differ between the hospitals. These results emphasise the need to investigate the use of the APS in hospitals and to implement the APS on an evidence-based and unambiguous manner.

Our results of observed Pain assessment-HCI showed a much lower compliance percentage (53 %) compared to the data reported by hospitals to the HCI (78 %). This discrepancy might be explained partly by a different interpretation of the definition of the process indicator. No time period is included in the definition of the HCI and, whereas we defined the Pain assessment-HCI as performing at least one pain measurement a day after surgery, it can also be interpreted as at least one pain measurement on any day after surgery. This will then increase the calculated process indicator, but at the same time make it less useful for the improvement of patient care as the pattern of pain experienced by a patient cannot be measured with just one measurement. Furthermore, if pain was asked about but not measured or documented in a standardised manner (NRS or VAS) it was not counted as measurement, but could be reported as measurement to the HCI. Another explanation might be the external pressure to publish the process indicator, which determines the ranking of the hospital on various ranking lists [33].

The national safety management system (SMS, or VMS in Dutch) embeds patient safety in healthcare practice. It is the system through which hospitals continuously identify risks, implement improvements, and establish, evaluate and modify policy. The national Safety Program was part of the safety management system and "early recognition and treatment of pain" was one of the implemented themes. Also in other countries, Safety Programs were installed, such as in Canada [34] and Scotland [35]. All countries claim that the awareness of patient safety has increased. However, limited or no data is available on specific themes, such as pain. Additionally, differences in measurements and the data collection method made it impossible to compare our results with other national programs. Another regional program: the "Health care services project 'Action Alliance Pain-Free City Münster", which was conducted from January 2010 to December 2013 in Germany did not report on compliance with pain measurements in hospitals [36, 37]. Based on a single quasi-experimental study in an academic hospital, a percentage pain assessment during 24 hours of 55 % was measured [38]. This percentage may be comparable to our findings of the process indicator of the HCI (53 %).
Despite recommendations of the national Safety Program and the mandatory character of reporting the process indicator to an external Inspectorate, the results of this study suggested that the implementation of pain measurements in hospitals is still insufficient. An explanation of this might be the lack of knowledge or awareness of the importance of measuring pain in postoperative patients on a structured daily basis [9, 14, 15], low priority given to pain management, time constraints, insufficient medication orders [15], or lack of local opinion leaders or champions involved [39, 40]. However, measuring and documentation of pain every day in a structured manner will improve the individual care of patients and the overall quality of care by enabling the analysis of aggregated data [18, 41]. Therefore, better implementation strategies to improve the nurses' adherence to pain assessment recommendations should be considered. As studied in a recent systematic review, implementation strategies vary and there is no preferred strategy available [12]. The best suggestion of implementing postoperative pain assessment in hospitals may be a strategy based on an analysis of barriers, experienced by nurses in the hospital. A multifaceted strategy would be best, addressing at least good education on the importance of pain assessment itself, the disappearance of organizational barriers, and feedback on personal performance of nurses [12]. Involving the patient by a patient- centric strategy may also be worthwhile, but this should be explored in future research [42, 43].

Strengths and limitations

The strength of this study is the representativeness of the included hospitals, whereby the results can be generalized to the national hospital population. Combining data of two studies enables analysing the association between several organizational factors and the compliance with process indicators for pain. However, we were limited to the variables measured in the two studies. Possibly other

factors, for example other organizational factors, team characteristics, personnel characteristics or patient characteristics such as diagnosis, comorbidity or disease complexity influence the execution of pain measurements, but we were limited to the measured variables.
A limitation of combining the datasets is, however, that some hospitals were not included in both studies and had to be excluded for the analysis. Because of the low number of included hospitals, department level could not be used in the multilevel analyses and we could only analyze the influence of the presented organizational factors separately. Additionally, the composite explained variance of the investigated factors could not be determined. Our study showed that the departments certainly have some influence, due to the large differences in compliance, but it is also the fact that the hospitals had systematic influence. Adding Admissions Department to the multilevel model for Pain assessment-HCI resulted in a negative R^2, suggesting that the differences between hospitals is masked by this factor. In future studies, a sufficient number of hospitals, and measurements of each department should be included to determine the differences on both hospital and department level.

Conclusions

This study showed a low compliance with pain assessment in Dutch postoperative patients after implementation of a national safety program, according to the process indicators for pain after surgery, suggesting that the implementation of pain assessment in hospitals is still insufficient.

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Part III

Quality of postoperative pain care: outcome

Comparison of epidural or regional analgesia and patient controlled analgesia: a critical analysis of patient data by the acute pain service in a university hospital

4

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Abstract

Objectives: A large number of patients still suffer from pain after surgery. This study investigates if epidural or regional analgesia (CPNB) provide superior pain relief compared to patient controlled analgesia (PCIA) and identifies the incidence of minor and major adverse effects or complications of these techniques.

Methods: Prospectively collected data of postoperative patients from an online data registration system of a special dedicated nurse based acute pain service (APS) were analyzed. The APS consultations were documented from January 2008 to August 2013 in a university hospital in the Netherlands.

Results: An analysis was applied on data of 12,399 consecutive patients. Results showed that patients who received epidural analgesia and CPNB reported lower pain scores than those who received PCIA, after undergoing the same procedures. Additionally, pain scores at rest were significantly lower than movement evoked pain scores, in abdominal surgery. Severe nausea was mostly observed in patients with PCIA and itching was most common in patients with epidural analgesia. Opioid induced respiratory depression was found in five patients with PCIA.

Discussion: Epidural analgesia and CPNB provide better pain relief to patients than PCIA, especially in dynamic pain scores of patients. Evaluating real patient data on every patient visit is important for further improvement of the quality of postoperative pain management. Pain scores may vary widely between patients with similar surgical procedures. Therefore, we recommend that future research focuses on personalized pain measurement and pain management, to improve clinical practice more intensely.

Introduction

Adequate postoperative pain management is important to prevent complications, delayed recovery, prolonged hospitalization and the development of chronic pain [1]. Many patients still suffer from moderate to severe pain after surgery [2]. Specialized postoperative pain management methods (SPPM), such as intravenous patient controlled analgesia (PCIA) [3], patient-controlled epidural analgesia (PCEA) [4], and continuous infusion peripheral nerve blocks (CPNB) [5], are considered to provide superior analgesia when compared to bolus-admitted systemic opioids. Especially epidural analgesia is considered the optimal technique for pain relief after major surgery. However, recently a critical assessment was published, evaluating several studies on this topic, and they concluded that neither neuraxial nor regional techniques improve perioperative outcomes in general surgical patients [6, 7]. Additionally, reported adverse effects related to epidural and opioid analgesia give reason for questioning the risks and benefits of SPPM [8, 9].
In this study we aim to investigate if neuraxial or regional analgesia provide superior pain relief compared to PCIA in three different procedures, based on the total population of five years APS data in a third referral university medical center. Furthermore, the incidence of minor and major adverse effects or complications of these techniques is identified.

Materials and Methods

Study population

Since an APS needs to supervise patients with SPPM to minimize the risk of severe complications [10-12], a copy of the APS database in the period from 1 January 2008 to 1 August 2013 was obtained. After institutional approval by the ethics committee of the Radboud university medical center, prospectively collected data of consecutive postoperative patients, monitored by the APS, were identified from the database.
Inclusion criteria for the study sample were as follows: patients who underwent a surgical procedure, received postoperative epidural analgesia, CPNB or PCIA and were visited by the APS. Surgical procedures were categorized into ten groups: laparotomy, upper laparotomy, lower laparotomy, laparoscopy, sternotomy, thoracotomy, thoracoscopy, flank, extremities and other. Table S1 is provided with more detail on the categorization.
The APS database contained information about minor and major adverse effects and complications of patients, treated with specialized postoperative pain management techniques. However, some complications might occur outside APS consultations. For this reason, the intensive care and neurologists' records were analyzed. They recorded complications due to (regional) analgesia in postoperative patients. Data were used from the database from the Department of Neurology

from 2008 to 2013, and the data from the database of the Department of Intensive Care from 2012 and 2013, to search for opioid induced respiratory depression (OIRD), epidural hematoma, epidural abscess or nerve damage due to CPNB.
In the selected study period, standing operating procedures, including the APS procedures, did not change. Since 2011, PCEA was no longer available because, for unclear reasons, all the PCEA pumps were disappeared. Hence, only CEA was prescribed.

Standing operating procedures perioperative analgesia

The anesthesiologist's choice of postoperative pain treatment technique is determined by a multidisciplinary hospital-based protocol, and considers the type of surgery, the expected pain after surgery, and the patients consent. The medication used in the hospital-based protocol is provided in Supplemental Digital Content 2. Acetaminophen and NSAIDS were given to each postsurgical patient, unless contraindicated. Morphine was used for PCIA as a first choice (See Table S2). When a patient responded inadequately to morphine, opioid rotation was performed to piritramide or fentanyl. Continuous infusion epidural analgesia (CEA) and PCEA was performed using bupivacaine mixed with morphine, ropivacaine, or ropivacaine mixed with sufentanil (for patients younger than 70 years) (See Table S2). For CPNB, ropivacaine was prescribed, dosage depending on the type of nerve block. All patients received esketamine, when pain relief was not sufficient.
Patients receiving regional analgesia with a catheter were visited by the APS at least once every day. Patients receiving PCIA were visited only the first day after surgery, unless problems, such as nausea, occured. For collecting pain scores, the numerical rating scale was used (NRS). The NRS pain score is an 11-point scale where 0 indicates no pain and 10 indicates the worst imaginable pain [13]. Previous studies highlighted the importance of the distinction in pain at rest (PAR) and movement evoked pain (MEP). Moderate pain was defined as an NRS (MEP or PAR) 4-7. Severe pain was defined as a NRS (MEP or PAR) above 7. Concerning nausea and itching, the severity of either nausea or itching was determined by the patient, who could choose "none", "moderate", or "severe" [14].
The treatment of pain in surgical patients in this context is the responsibility of the primary treating physician as directed by the hospital wide protocol of postoperative pain management. This protocol was developed and is supervised by the APS. The nurse-based, anesthesiologist supervised APS forms part of the Department of Anesthesiology, Pain and Palliative Medicine. The APS is available seven days a week, and supports the treatment of postoperative pain in patients with complex pain treatment techniques. During daily patient rounds, the APS collects all patient data through a digital record by a web-based program, linked with the hospital system. Data are entered online by a mobile handheld computer, wirelessly connected with the hospital system for real time registration.

Statistical analysis

Data was analyzed using the Statistical Package for the Social Sciences (IBM SPSS version 20.0; IBM Corporation, New York, NY, USA). Descriptive analyses were done on the gender, age, Body Mass Index (BMI), type of pain treatment technique, type of procedure, level of insertion of the epidural catheter, use of esketamine, and mean duration of APS consult.
Additionally, the prevalence of moderate and severe pain during the first four postoperative days, based on the NRS (PAR and MEP), was calculated. Descriptive data were presented in tables.
Since pain scores may depend on the type of operation, procedure-specific dynamic NRS (MEP) in patients undergoing thoracotomy, abdominal surgery, and extremity surgery were analyzed in subgroups, comparing epidural, CPNB, or PCIA during the first four postoperative days, and presented in boxplots. The group of patients undergoing abdominal surgery was further analyzed, comparing PAR and MEP. Since the data were not normally distributed, the Kruskal-Wallis test with post hoc tests by Kruskal-Wallis was used, to compare groups. The Bonferroni method was used for correcting for multiple comparisons, meaning that the traditional P=0.05 definition of significance was reduced to a new threshold of P=0.001.
Other descriptive analyses concerned the minor and major adverse effects and complications of SPPM. The Chi-squared test was used to determine whether there was a significant difference between groups. Finally, one major complication, OIRD, was closely examined and reported for case reports from the years 2012 and 2013.

Results

Patient characteristics

From the APS database, 29,081 records of consultations were retrieved. These records contained data of 12,399 patients. The patients were visited by the APS, between 1 January 2008 and 31 August 2013, in the Radboud Medical Center in the Netherlands. In 2008 the APS did 2,781 consultations, in 2009; 2,886, in 2010; 5,801, in 2011; 6,442, in 2012; 6,931, and in 2013; 4,240. For this study, we excluded the patients that received both epidural analgesia and PCIA, and the patients that received both locoregional analgesia and PCIA, leaving 22,513 records of consultations of 10,666 patients.
Table 1 shows descriptive information of the study sample of 10,666 patients from the APS database.

Medication prescribed to patients with epidural was ropivacaine 0.2 % mixed with sufentanil (61 %), ropivacaine (24 %), bupivacaine 0.75 % mixed with morphine (6 %), and other medication (9 %). Other medication consisted of epidural medication, specifically prepared for patients, who did not respond to protocol medication.

Table 1 Characteristics of patients visited by the Acute Pain Service on the first day after surgery

Total:		**Continuous infusion Epidural Analgesia**			**Patient Controlled Epidural Analgesia***			**Patient Controlled Intravenous Analgesia**[a]			**Locoregional Analgesia**		
N= 10,666		2,462	N	%	573	N	%	7,035	N	%	596	N	%
Gender		2,462			573			7,035			596		
	Male		1,347	54.7		314	54.7		2,776	39.5		269	45.1
	Female		1,115	45.3		259	45.3		4,259	60.5		327	54.9
Age		2,452			571			7,014			595		
	< 18 years		200	8.2		4	0.7		239	3.4		142	23.9
	18 – 65 years		1,412	57.6		404	70.8		5,334	76.0		291	48.9
	> 65 years		840	34.2		163	28.5		1,441	20.5		162	27.2
BMI[c]		2,176			523			5,643			424		
	Underweight (< 18.5)		155	7.1		15	6.3		173	3.1		62	14.6
	Normal weight (18.5 – 24.99)		1,018	46.8		240	46.6		2,288	40.5		174	41.0
	Overweight (25.0 – 29.99)		722	33.2		197	34.0		2,042	36.2		125	29.5
	Obese (> 30.0)		281	12.9		71	13.1		1,140	20.1		63	14.8
Type of surgery		2,425			568			6,814			575		
	Laparotomy		775	32.8		206	36.3		951	14.0		23	4.0
	Laparotomy upper		471	19.6		117	20.5		292	4.3		0	0.0
	Laparotomie lower		444	18.9		122	21.5		1,541	22.6		3	0.5
	laparoscopy		28	1.3		12	2.1		540	7.9		3	0.5
	Sternotomy		7	0.3		2	0.4		23	0.3		0	0.0
	Thoracotomy		272	10.2		32	5.6		62	0.9		9	1.6
	Thoracoscopy		165	5.7		6	1.1		65	1.0		0	0.0
	Flank		34	1.6		14	2.5		202	3.0		4	0.7
	Limbs		90	3.6		18	3.1		2,056	30.2		477	83.0
	Rest		139	5.9		39	6.9		1,082	15.9		56	9.7

Table 1 Continued

Total:		Continuous infusion Epidural Analgesia		Patient Controlled Epidural Analgesia*		Patient Controlled Intravenous Analgesiaa		Locoregional Analgesia	
N= 10,666	2,462	N	%	573	N	%	7,035	N	%	596	N	%
Level of epidural catheter insertion	2,244			538			N/A[b]			N/A		
Thoracic (Th1 – Th12)		1,914	85.3		449	83.5		N/A	N/A		N/A	N/A
Lumbar (Th12 – L5)		330	14.7		89	16.5		N/A	N/A		N/A	N/A
Esketamine	2,462	78	3.2	573	45	7.9	7,035	1,374	19.5	596	40	6.7
Mean (SD) duration of therapy (days)		2.1	2.0		2.1	1.5		N/A	N/A		2.2	2.3

[a] Patients receiving PCIA were visited only the first day after surgery to advise on continuation.
[b] N/A indicates "Not Applicable".
[c] BMI means Body Mass Index. * PCEA was not prescribed since 2011.

Patients with CPNB received ropivacaine 0.2 % (99 %), and bupivacaine 0,25 % (1 %). Of the patients with PCIA, 70 % received morphine, 29 % received piritramide, and 1 % fentanyl. Over the years, morphine was prescribed less in favour of piritramide; in 2008, the morphine-piritramide percentage ratio was 82.2-17.5, and in 2013, this ratio was 51.6-48.2. Esketamine was prescribed in 1,497 patients (14 %).

Effectiveness of pain treatment

The overall prevalence of moderate and severe pain was 50.3 %, and 9.2 % respectively for MEP. For PAR, the overall prevalence of moderate and severe pain was 28.0 %, and 2.5 % respectively. Table 2 shows the prevalence of moderate and severe pain on the first four days after surgery.

Subgroup analyses on three types of surgical procedures, i.e. abdominal surgery, thoracotomy, and extremity surgery, are provided in Figure 1. In boxplot A of Figure 1, NRS scores of movement evoked pain of patients undergoing abdominal surgery is shown. In this group of patients, CEA and PCEA provided superior pain relief, defined as lower NRS scores, compared with PCIA on all four days after surgery (P<0.001). The effectiveness of pain treatment in patients undergoing thoracotomy is shown in boxplot B of Figure 1. The median NRS scores of movement evoked pain in patients receiving CEA and PCEA is around 3, during all four postoperative days. Epidural analgesia provided more effective pain relief, defined as lower NRS scores, compared with PCIA , especially on day 4 in this group of patients (P<0.001).

Table 2 Prevalence (%) of moderate and severe pain during the first four postoperative days based on the numerical rating scale (NRS)

	N	Moderate pain (NRS 4-7)		Severe pain (NRS 8-10)	
		PAR[1]	MEP[2]	PAR[1]	MEP[2]
Day 1	8,673	29.2	51.6	2.7	10.4
Day 2	4,134	25.0	50.4	1.7	7.4
Day 3	2,194	22.2	43.8	1.7	6.6
Day 4	827	28.0	48.9	2.0	8.0

[1] PAR: pain at rest; [2] MEP: movement evoked pain.

NRS scores of patients undergoing extremity surgery and receiving PCIA, shown in boxplot C of Figure 1, are significantly higher on the first two days after surgery than those of patients with epidural analgesia or CPNB. In all three boxplots the range of NRS scores on all four days is very high, showing a considerable number of patients with pain scores above 7.

Further analyses of the group of patients, undergoing abdominal surgery from 2008 to 2013, showed that NRS scores at rest are significantly lower than NRS scores of MEP (P<0.001) (see Figure 2). In Figure 2, median NRS scores at rest appear constant from 2008 to 2012. Median NRS scores at rest in 2013 are lower, compared to the previous years. NRS scores of MEP are more fluctuating; however, the median NRS scores of epidural analgesia are 4 or lower, in contrast to the median NRS scores of PCIA.

Adverse effects and complications of postoperative pain treatment techniques

In Table 3 is shown that epidural analgesia, as well as PCIA, have a significantly higher incidence of nausea and vomiting, compared to CPNB (P<0.001). Severe nausea was mostly observed in patients with PCIA (see Table 3). Patients with epidural analgesia suffer from itching significantly more often, than patients with PCIA and CPNB do (P<0.001).

All records of the APS, the database of the Department of Neurology, and the database of the Department of Intensive Care were analyzed for OIRD, epidural hematoma, epidural abscess or nerve damage due to CPNB (see Table 3). It was found that only five cases of OIRD took place in 2012 and 2013. In 2012, there were 2,274 patients with PCIA, and in 2013 there were 1,403 cases. In these two years, the incidence of OIRD was 0,14 %. In Table 4, characteristics of the cases are reported. In four cases, patients used PCIA with morphine.

Table 3 Incidence of minor and major adverse effects and catheter related complications on the first postoperative day

	Epidural (CEA and PCEA) N=3,035		PCIA N=7,035		CPNB N =596	
Adverse effects	**N**	**%**	**N**	**%**	**N**	**%**
Nausea						
Moderate	334	11.7	756	11.4	30	5.3[ab]
Severe	84	2.9	276	4.2	5	0.9[b]
Vomiting	144	4.7	289	4.1	12	2.0
Itching						
Moderate	265	0.5	183[a]	3.1[a]	3	0.6[a]
Severe	34	1.4	48	0.8	0	0.0
Opioid induced respiratory depression	0	0.0	5[d]	0.1[d]	0	0.0
Epidural hematoma	0	0.0	N/A[c]		N/A	
Epidural abscess	0	0.0	N/A		N/A	
Nerve damage due to CPNB	N/A		N/A		0	0.0
Disconnection (>2 h) with subsequent removal of the catheter	14	0.5	N/A		0	0.0
Dislocation of the catheter	15	0.5	N/A		0	0.0
Postspinal headache	3	0.1	N/A		N/A	

Chi-square test is used and having adverse effects are compared with having no adverse effects. [a] significant difference compared with epidural analgesia (P<0.001); [b] significant difference compared with PCIA (P<0.001); [c] N/A means "Not applicable"; [d] calculated in 3,677 patients with PCIA in 2012 and 2013. CEA indicates continuous infusion epidural analgesia; CPNB, continuous infusion peripheral nerve block; NA, not applicable; PCEA, patient-controlled epidural analgesia; PCIA, patient-controlled
analgesia.

Discussion

In this study we investigated if neuraxial or regional analgesia provided superior pain relief compared to PCIA in different procedures. Furthermore, the incidence of minor and major adverse effects or complications of these techniques was identified.

Although a large variability on pain scores was seen, results showed that patients who received epidural analgesia and CPNB reported lower pain scores than those who received PCIA, after undergoing the same procedures. Additionally, PAR scores were significantly lower than MEP scores, as illustrated in abdominal surgery from 2008 to 2013. The incidence of severe nausea was mostly observed in patients with PCIA and itching was most common in patients with epidural analgesia. A major adverse effect, i.e. OIRD, was found in five patients with PCIA.

Our results show that since the nurse based APS started in 2008, each year the number of consultations increased. Before the year 2008, the APS was

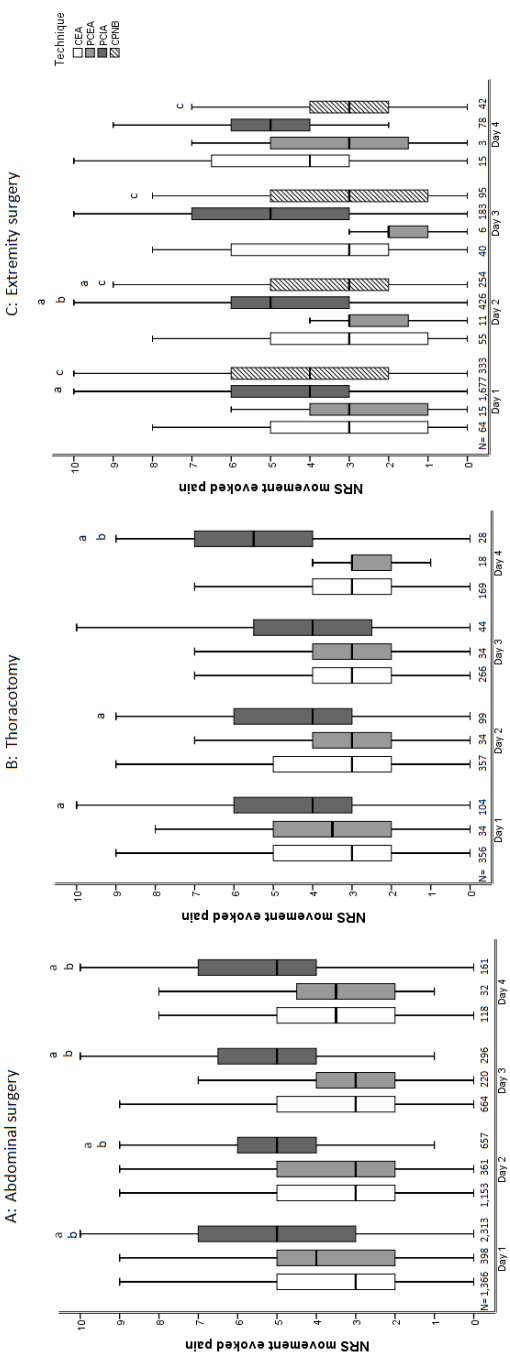

Figure 1

Procedure-specific NRS (movement evoked pain) in patients undergoing abdominal surgery(A), thoracotomy(B), and extremity surgery (C). Comparison of epidural, patient controlled intravenuous and locoregional analgesia during the first four postoperative days. (a: significant difference compared with continuous epidural analgesia (CEA) P<0.001; b: significant difference compared with patient controlled epidural analgesia (PCEA) P<0.001 c: significant difference compared with PCIA P<0.001 according to the Kruskal Wallis test with post hoc tests by Kruskal-Wallis).

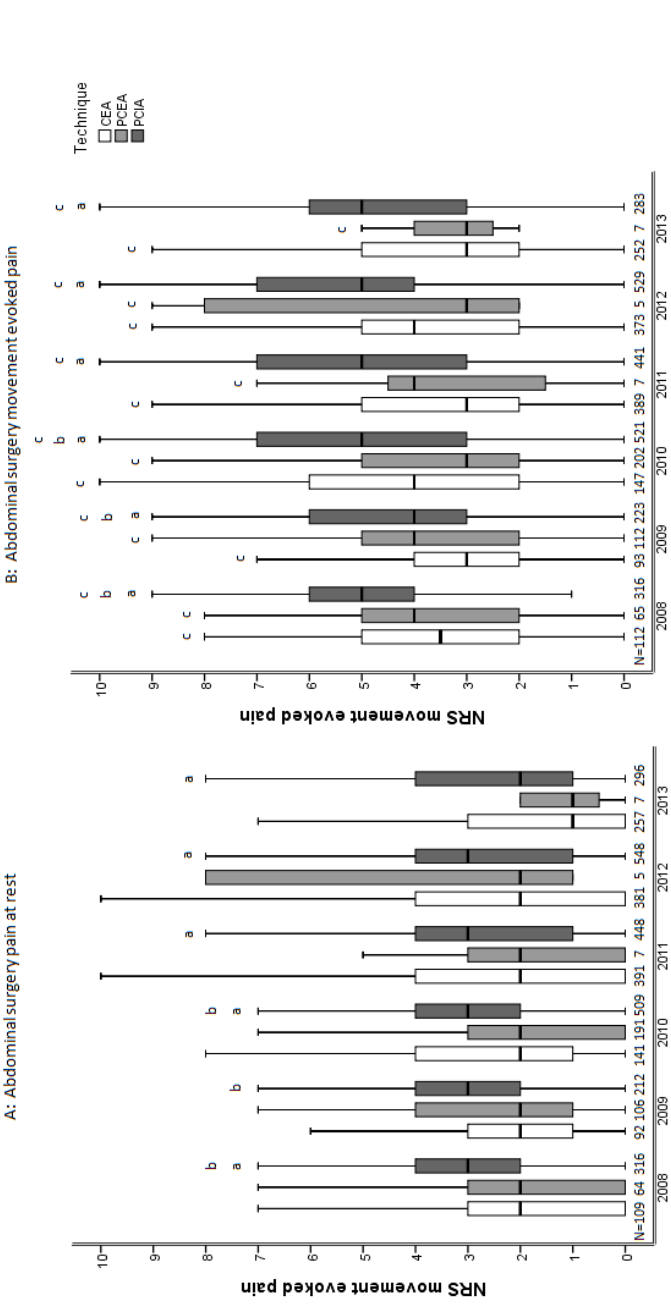

Figure 2

Procedure- specific NRS scores; A: Pain at rest and B: Movement evoked pain in patients undergoing abdominal surgery. Comparison of continuous epidural (CEA), patient controlled epidural analgesia (PCEA) or patient controlled intravenous analgesia (PCIA) on the first postoperative day over the years 2008-2013. (a: significant difference compared with CEA: P<0.001; b:significant difference compared with PCEA: P<0.001; c: significant difference compared with NRS rest of the same year P<0.001), according to the Kruskal-Wallis test with post hoc tests by Kruskal-Wallis.

Table 4 Overview of patients developing respiratory depression after opioid intoxification in the year 2012 and 2013

Case file	Gender	Age	Past medical history	Surgery	Analgesia	Intervention/outcome
1	Female	65	Hypertension, depression	Abdominal surgery	Epidural: ropivacaine/sufentanil (6-8 ml h-1) with 20µg sufentanil Removed and replaced with intravenously PCIA pump: 18mg morphine in 2,5 hours.	Intubation and transfer to ICU and treated with naloxone. Outcome: complete recovery and back to surgery ward after 1 day.
2	Male	52	CVA, pancreatitis	Abdominal surgery	PCIA pump: 75mg morphine in 24hours. Additional oxycodone 2x 10mg	Transfer to PACU infusion with naloxone. Outcome: back to surgery ward after 1 day.
3	Male	74	Pacemaker, DM II, multiple knee surgery	Orthopaedic surgery	Peroperative spinal analgesia. Back to PACU because of persisting pain: esketamine (5mg h-1) and 10 mg morphine. At orthopaedic ward: PCIA 30mg morphine in 12 hours.	Medium care with saturation of 80 %; naloxone infusion bolus and 1 day continous. Outcome: complete recovery
4	Female	54	Marfan syndrome, COPD, depression	Abdominal surgery	PCIA with piritramide 49mg in 24 hours.	To PACU and naloxone infusion. Within 30 seconds Glasgow Coma Scale 15. Outcome: complete recovery
5	Female	23	Borderline, PDD-NOS, 5 suicide attempts, multiple pelvic surgery	Orthopaedic surgery	PCIA 143mg morphine in 24 hours. Pain is not acceptable, switch to fentanyl.	Mask ventilation and transfer to MCU and naloxone infusion. Outcome: not reported.

PCIA indicates Patient Controlled Intravenous Analgesia
PDD-NOS indicates Pervasive Developmental Disorder Not Otherwise Specified
ICU indicates Intensive Care Unit
PACU indicates Post Anesthesia Care Unit
CVA indicates Cerebro Vasculair Accident
COPD indicates Chronic Obstructive Pulmonary Disease
MCU indicates Medium Care Unit

anesthesiologist based, which meant that patients with SPPM were monitored by resident anesthesiologists. As the number of annual surgeries remained equal, the pain nurses seemed to attract more consultations each year. We think that the pain nurses are invaluably bridging the gap between doctors and bedside nurses, diminishing the psychological barrier for bedside nurses to ask for help, when encountering problems managing pain in patients with SPPM [15].

Our results showed that patients with (P)CEA had lower MEP scores after thoracotomy, abdominal surgery, and extremity surgery, than patients treated with PCIA . These findings are similar to those of Pöpping et al., and Gerbershagen et al. [2, 10]. Pöpping and co-workers reviewed the APS data of 18,925 patients on the quality of pain relief, major complications, and adverse effects. The median pain scores, described by them, were one to three points lower than the median pain scores reported in this research on those procedures, possibly because they used the Visual Analoge Scale (VAS), while in this research pain was measured with the Numeric Rating Scale (NRS). The VAS and NRS are both instruments that measure pain intensity, but they are not directly comparable [13].

Gerbershagen and co-workers made a comparison between surgical groups and found that the median pain intensity (with NRS) during movement on the first postoperative day in orthopedic surgery, abdominal surgery, and cardiothoracic surgery, was 4 (IQR, 2-6), which is similar to the data in this research.

Additionally, similar to previous studies, the PAR scores in this research are lower than the MEP scores, however, both delivering information about the effectiveness of pain management [16]. It is stated that high MEP scores have a negative effect on recovery after surgery, and that treating MEP with opioids is difficult [16, 17]. Epidural analgesia in abdominal surgery from 2008 to 2013 show median MEP scores of four and lower, which seems to provide better dynamic pain relief than PCIA does. This finding might support the statement that treating patients with high dynamic pain scores is difficult, while only using intravenous medication, such as opioids and esketamine [16].

Furthermore, previous studies described a high overall prevalence of moderate to severe postoperative pain, which is constant over the years [2, 11, 18, 19]. The data in this research also shows that the percentage of patients with moderate to severe pain is still high, which might suggest that there is room for improvement. It could be argued that decreasing the prevalence of moderate to severe postoperative pain is possible, if personalized pain treatment is implemented. The focus in daily practice, and in this study, is mainly on surgery related factors. However, the figures in this research show a large variability on pain scores, indicating that other variables, most likely individual patient factors, must be responsible for the ultimate pain score. Therefore, inter-individual variability in postoperative pain experience needs to be explored, in order to improve postoperative pain management.

In literature, the incidences of postoperative nausea are reported from 18 % to 45 % and of vomiting from 16 %-25.5 % [14]. The incidences in this research are quite low, compared to those in literature, suggesting that the chosen antiemetic strategy is adequate. With regards to major adverse effects and complications, no

epidural hematomas, abscesses or peripheral nerve damage was found resulting from CPNB. However, five cases of OIRD were found in the years 2012 and 2013. The reported incidence in international literature varies from 0.2 % to 0.9 % [20]. From 2008 to 2012, the intensive care records were not reliable, due to lack of systematic documentation. The restrictive data of only the years 2012 and 2013 does not allow the five cases to be benchmarked against findings from previous research. However, OIRD is a serious complication that needs further attention. In a recent publication of Overdyk et al., 105 case reports with OIRD were analyzed on case and patient-related factors [21]. One of the conclusions was that OIRD in the acute setting refers to complex and interrelated factors and can be a cause of preventable morbidity and mortality [21]. Another recent publication made use of non-invasive respiratory volume monitoring to show that unsafe respiratory patterns occur frequently after surgery [22]. This might suggest that real-time monitoring of respiratory function of every postoperative patient is needed for safety reasons. Furthermore, pharmacological strategies that prevent respiratory depression without affecting analgesia are needed [23]. An example is the use of esketamine, which is a strong analgesic that does not influence respiratory volume and pattern and therefore less opioids are needed to provide good analgesia [24].

This study gives an overview of the outcome of APS data of consecutive patients, provided by a special dedicated nurse based APS team, using an unique registration tool. However, some limitations have to be addressed. Firstly, data collection took place on hospital rounds, while performing an APS consult by the APS nurse, and not by a dedicated study nurse. Nevertheless, the APS team consists of dedicated and well trained nurses, who work according to the multidisciplinary protocols.

Secondly, data concerning CPNB were not so extensive as for the epidurals and the PCIA. Yet, the median pain scores were comparable to international literature and this could be attributed to the good standard of practice maintained by the CPNB team that performed these procedures using ultrasound techniques.

Thirdly, a pitfall, experienced in our department, was the disappearance of the PCEA-pumps. We assumed that they were stolen. Unfortunately, financial reserve was not sufficient to become new pumps, which left our anesthesiologists with only the CEA for epidural analgesia. However, as stated by Duncan et al., collecting real patient data on every patient visit systematically is the foundation for future outcome research [11]. Therefore, we deliberately used the data of all patients, reflecting daily activities in clinical practice.

Finally, due to organizational issues, the major complications could only be shown for the years 2012 and 2013, which may be incomplete. For this reason these data were not benchmarked.

Conclusions and recommendations

The digitally collected data of APS patients highlighted three important facts. Firstly, epidural analgesia and CPNB provide better pain relief to patients than PCIA, especially in MEP scores of patients. Secondly, evaluating real patient data on every

patient visit is important for further improvement of the quality of postoperative pain management [11]. Thirdly, pain scores may vary widely between patients with similar surgical procedures. Pain is a multifactorial problem that requires caution with regard to its diagnosis and its management. Protocol-based management is less appropriate than personalized pain measurement and pain management. Therefore, we recommend that future research focuses on personalized pain measurement and pain management, to improve clinical practice more intensely.

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Table S1 Surgical procedures, categorized in ten groups

Group	Procedure	Preferenced specialized postoperative pain management method (SPPM), if not contra-indicated (for example negative patient consent)
Laparotomy	Hyperthermic Intraperitoneal Chemotherapy (HIPEC), colectomy, hepatectomy, Whipple procedure, pelvic or retroperitoneal lymph node dissection, Oscar Ramirez procedure, adhesiolysis.	Epidural analgesia
Upper laparotomy	Gastrectomy, pancreatectomy, splenectomy, esophageal resection, cholecystectomy.	Epidural analgesia
Lower laparotomy	Abdominal hysterectomy, appendectomy, cystectomy, prostatectomy, sectio caesarea, debulking, rectum or sigmoid resection.	Epidural analgesia
Laparoscopy	Laparoscopic cholecystectomy, nefrectomy, colectomy, adrenalectomy, prostatectomy, hysterectomy.	Intravenous patient controlled analgesia
Sternotomy	Coronary bypasse, thymectomy, metastasectomy, and pericard resection.	Epidural analgesia
Thoracotomy	Lobectomy, pneumectomy, tracheal resection.	Epidural analgesia
Thoracoscopy	Video assisted surgery or thorascopic surgery, such as pleurectomy, bullectomy, Nussbar surgery, video-assisted thorascopic surgery.	Epidural analgesia
Flank	Nefrectomy, adrenalectomy.	Intravenous patient controlled analgesia
Extremities	Total knee arthroplasty, total hip arthroplasty, acetabulum arthroplasty, arthodesis of limbs, arthrotomy, osteotomy.	Intravenous patient controlled analgesia
	Amputations of limbs, pelvectomy.	Epidural analgesia
	Neer surgery, hand surgery, foot surgery.	Continuous infusion peripheral nerve block
Rest	Mastectomy, lumpectomy, laminectomy, spondolydesis, head or face surgery, hernia inguinalis.	Intravenous patient controlled analgesia

Table S2 Protocol for postoperative pain treatment technique and medication used

Pain treatment technique	**Medication**
Acetaminophen	4 dd 1000 mg daily
Diclofenac	3 dd 50 mg daily
PCIA	Morphine 2 mg ml^{-1}, bolus 1 mg, lock-out time 6 minutes
	Piritramide 2 mg ml^{-1}, bolus 1 mg, lock-out time 6 minutes
	Fentanyl 50 µg ml^{-1}, bolus 25 µg, lock-out time 6 minutes
CEA	bupivacaine 0.75 % mixed with morphine 0.2 mg ml^{-1} 1-2 ml $hour^{-1}$
	ropivacaine 0.2 % 4-12 ml $hour^{-1}$
	ropivacaine 0.2 % mixed with sufentanil 1 µg ml^{-1} 4-12 ml $hour^{-1}$
PCEA	ropivacaine 0.2 % mixed with sufentanil 1 µg ml^{-1} 4-10 ml hour, bolus 2 mg, lock-out time 20 minutes
CPNB	ropivacaine 0.2 % 5-10 ml $hour^{-1}$
Esketamine	5-10 mg $hour^{-1}$

Moving beyond pain scores: multidimensional pain assessment is essential for adequate pain management after surgery

5

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Abstract

Background: Clinical experience teaches us that patients are willing to accept postoperative pain, despite high pain intensity scores. Nevertheless, relationships between pain scores and other methods of pain assessment, e.g. acceptability of pain or its interference with physical functioning, are not fully established. Our aims were to examine these relationships.

Methods: A cross-sectional study was conducted on patients who underwent major surgery between January 2008 and August 2013. Using logistic regression, we quantified the relationships between movement-evoked pain scores on the numerical rating scale (NRS-MEP) and three dichotomous dependent variables: patient's opinion on acceptability of pain (PO: acceptable or unacceptable pain); nurses' observation of patient's performance of necessary activities to expedite recovery (NO: good or bad performance); a compound measure judging the presence of the clinically desirable situation of acceptable pain associated with good patients' performance (PONO: present or not). Using Receiver Operating Characteristics (ROC) analysis, NRS cut-off points were determined such that they best discriminate between patients having one versus the other outcome for PO, NO and PONO.

Results: 15,394 assessments were obtained in 9,082 patients in the first three postoperative days. Nine percent of the patients had unacceptable pain while having an NRS-MEP of 0-4. An estimated 47 % (95 % CI=45 %-49 %) of patients with an NRS-MEP of 7 described their pain as acceptable on day one. Moreover, 33 % (31 %-35 %) performed all required physical activities, and 22 % (21 %-24 %) combined acceptable pain with appropriate movement. NRS cut-off points for PO, NO and PONO were five, four and four, respectively, but had insufficient discriminatory power.

Conclusions: Our results suggest pain management should be guided by the many dimensions of the patient's pain experience, not solely by NRS cut-off points. Future research should evaluate the impact of such multidimensional pain assessment on patients' functional outcome.

Introduction

Many patients experience acute postoperative pain after major as well as minor surgery [1, 2]. Clinical experience teaches us that really adequate treatment of postoperative pain is not easy to achieve. To balance treatment options, treatment starts with assessing the pain. As pain is a complex and subjective experience, also in the postoperative period, various methods exist to evaluate key aspects of acute pain after surgery.

Most of these assessment methods rely on the perception of pain and pain- related phenomena by either the patient or a professional caregiver [3, 4]. Self-assessment of pain by the patient may use a pain intensity scale and yes/no answers to questions such as "Is the pain acceptable?" [5, 6]. Self-reporting values the subjective nature of pain. Evaluation of pain by a professional may include objective assessment of the functional impact of pain. The professional therefore judges if the pain prevents the patient from moving appropriately or from performing the necessary activities to expedite recovery [7]. One clinically important goal could be a level of pain that is not only acceptable for the patient, but also allows the patient to move appropriately as judged by a professional.

The numerical rating scale (NRS), a validated instrument to assess pain intensity by self-reporting, is widely used for assessing pain on a scale from zero (no pain at all) to 10 (worst possible pain). Certain NRS scores have even been used as cut-off points to guide initiation or cessation of treatment in an individual or even as indicator of the quality of pain management in a population [8-10].

Relationships between NRS and other methods of pain assessment, e.g. acceptability of the pain or its interference with physical functioning, are not fully established. In the clinical setting, some patients report a high movement-evoked pain score, yet claim that their pain is acceptable to them [11]. Patients may even refuse to take pain medication when an NRS cut-off point demanding treatment according to a pain protocol is reached or crossed [12]. A further complicating factor is that some patients and pain professionals interpret pain scores differently [3]. As a result of these discrepancies or unclear relationships between different pain assessments, difficulties in treatment decisions may arise.

Our aims therefore were *first*, to quantify relationships between NRS and other methods of pain assessment and *second*, to examine the ability of an NRS cut-off point to predict either patients' willingness to accept pain or functional capacity. Potential benefit of the study is that its results may aid to develop and corroborate clinical guidelines to tailor postoperative pain management in a way that will meet the unique needs of each patient.

Materials and Methods

Approval

The Institutional Review Board of the Radboud university medical center (Nijmegen, The Netherlands) approved the study (2013/428). No informed consent was obtained from the participants because data were anonymized.

Study design and patients

This cross-sectional study was conducted on patients older than 18 years who had been admitted in a large regional academic medical center in the period from 1 January 2008 to 1 August 2013. The study used the prospectively collected pain assessments of postoperative patients who had been treated by the acute pain service (APS).
We quantified the relationships between movement-evoked NRS and acceptability of pain, functional impact of pain, and a measure combining the two. The latter measure serves to judge whether or not a clinically desirable situation occurs where acceptable pain coexists with good physical functioning. A potential influence of gender, age or body mass index (BMI) was investigated.

Data handling

Assessments
The APS nurses use a standardized multidimensional assessment to evaluate postoperative pain. This assessment includes: (1) the NRS for movement-evoked pain (NRS-MEP) [7], (2) the patient's opinion (PO) whether the pain is acceptable because the patient's appreciation of the pain is clinically important for making the patient comfortable [13], and (3) the nurses' observation (NO) on the patient's ability to make appropriate movements. NRS-MEP and NO are important because adequate treatment of pain experienced during pain-provoking maneuvers may reduce complications after surgery [14, 15].
The NRS-MEP is an 11-point numerical rating scale with end points representing the extremes of the pain experience: 0 = "no pain at all" and 10 = "worst possible pain". All nurses and patients received education on how to use the NRS-MEP appropriately [15].
The PO is determined by asking the patient whether the pain is acceptable or not, making it a binary yes-or-no variable [11].
The NO scoring mirrors the Functional Activity Score (FAS) described by Scott and McDonald [16] and adopted by the Australian and New Zealand College of Anaesthetists. The FAS, recommended in several textbooks [17, 18], was recently integrated in the updated Australian and New Zealand guideline on acute pain management [19]. The FAS (designed to be applied at the bedside) is a simple

three-level ranked categorical score to assess whether the patient can undertake appropriate activity at his or her current level of pain control.
The APS nurses rely on an operation-specific protocol offering clearly defined criteria to judge patient's ability to perform physical activities on the first three days after surgery—like coughing, deep breathing, early movement and walking [20]. Some examples of operation-specific protocols are the ability to sit on a chair for thirty minutes on the first morning after a patient has had a laparotomy and the ability to walk to the bathroom for a patient on the first day after a total hip replacement. Patient's performance is qualified as: "good", "moderate" or "bad". A "good" means patient is able to make all appropriate movements and is not hindered by pain. "Bad" means patient is totally unable to make appropriate movements because of the pain. "Moderate" is chosen when observing neither "good" nor "bad". The results for NO are dichotomized into two outcome categories, "good" or "moderate and bad". Accordingly, NO is also a binary yes-or-no variable.
In addition, combining PO and NO yields a third binary yes-or-no variable, i.e. PONO. This variable is not part of the multidimensional assessment at the bedside, but was created for study purposes only. One result for PONO is when "acceptable pain" accompanies "good movements", thus reflecting a clinically desirable situation. The ultimate goal of postoperative pain treatment is that a patient qualifies the pain as acceptable and is able to perform appropriate movements. The other result for PONO is chosen for each of the three remaining combinations of PO and NO.

Database of Acute Pain Service
The nurse-based, anesthesiologist supervised APS is part of the Department of Anesthesiology, Pain and Palliative Medicine. The organization of this type of APS has been described elsewhere [21, 22]. The APS has a team of five dedicated well-trained nurses who strictly use hospital protocols to assess postoperative pain in patients. The APS is available seven days a week and supports the treatment of postoperative pain with specialized or complex pain management techniques. The APS treats patients from the first day after major surgery, but not on the day of surgery. Typical surgical procedures are listed in the supplementary information (see Supplement S1, Table S1 in Supplemental Digital Content S1).
After each visit to a patient, the dedicated nurse enters the obtained data (inter alia values for NRS-MEP, PO and NO) into a new digital record of the APS database. As each visit yields one record in the database, multiple records per patient are possible per day. Data are entered on a mobile handheld computer wirelessly connected with the hospital system for real time registration.
Standard information about postoperative pain and its management is given preoperatively to patients. The information is recorded in a pain protocol. Anesthesiologists give oral information supported by a leaflet during the preoperative consultations. Patients are also invited to watch a movie online. Prior to the actual pain assessment, APS nurses check patient's knowledge and, if necessary, still inform the patient using the appropriate information.

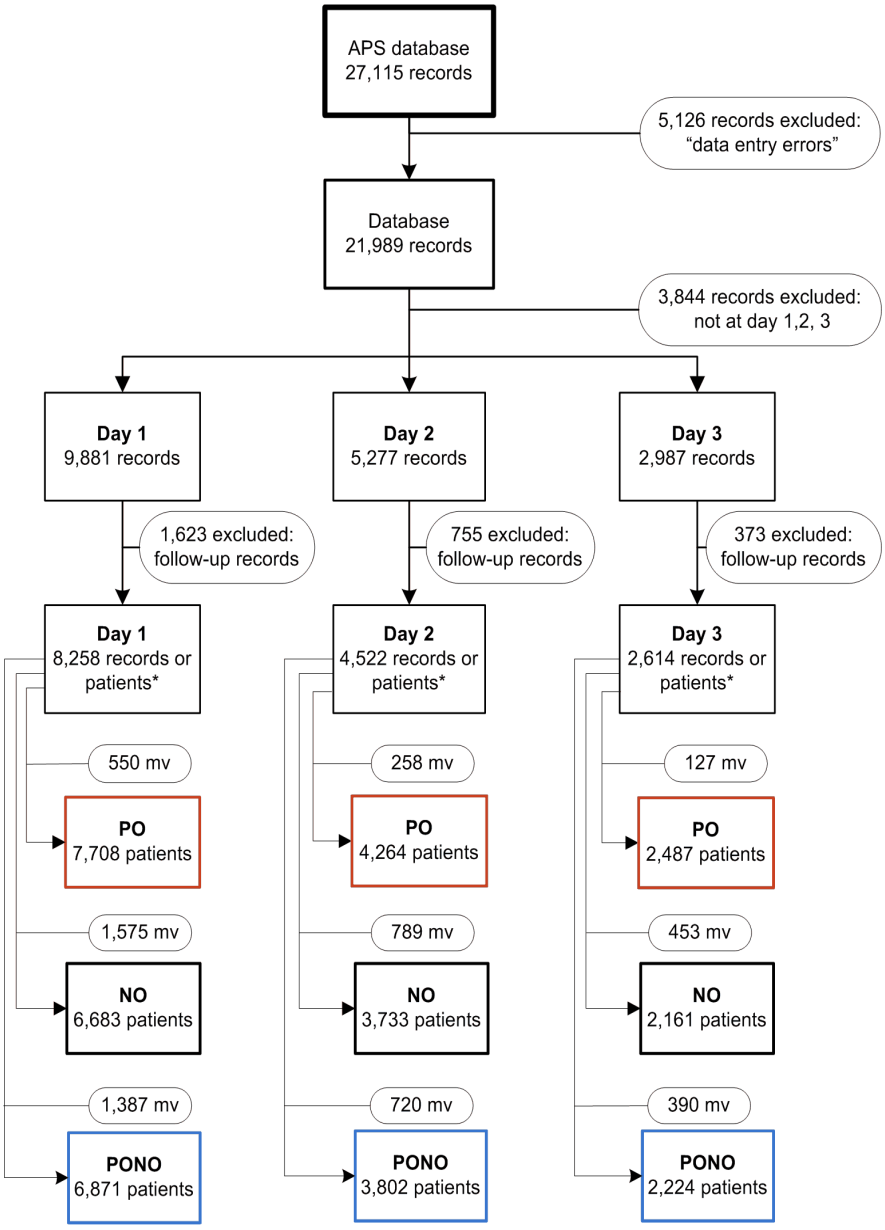

Figure 1 Flow chart: Transforming the database of the Acute Pain Service (APS) into nine data sets

For each of the three postoperative days, three data sets are created: one for patient's opinion (PO), one for nurses' observation (NO) and one for the combined variable (PONO). Results for these nine data sets are shown in Fig 3 and Table 3. *Before this point multiple records are possible per patient but after this point the number of records equals the number of patients. mv=missing values.

Creating data sets

Fig 1 illustrates the various steps to create datasets ready for valid analyses from the APS database. Editing the raw APS database was necessary because of data entry errors. Data entry errors were found in records with pain scores above ten and records where pain scores were not entered or patients were unable to give an NRS score. As multiple records per patient were possible per day for many days in a row, we made a selection first, by taking the records of the visits of the first three days after surgery and second, by selecting the record of the first visit to a patient per day to stay in the database. As a result, the number of records equaled the number of patients on day 1, day 2, and day 3 after surgery.

As the APS database consists of the real time online registration during the work of the APS nursing staff, some missing values were also inevitable. These missing values were counted per day for the PO-, NO- and PONO-variables (Fig 1). To avoid the bias that would be induced by restricting the analyses to patients without missing observations, we did not exclude patients because of incompleteness of the pain assessments.

Statistical analysis

To explore the relationships between PO, NO, PONO and NRS-MEP, the relative frequencies of the two possible outcomes for PO, NO, and PONO during the first three postoperative days were pooled and were plotted against the NRS for MEP. To quantify these relationships, a logistic regression model was estimated using the 11-point NRS for MEP as primary independent explanatory variable for each of the three dependent variables PO, NO, and PONO. Thus PO, NO, and PONO

Table 1 Name, abbreviation, values and coding of variables used in the logistic regression models to estimate the relationships between four explanatory variables and each of three response variables

	Variable name	Abbreviation	Values	Coding
Explanatory variables	Numerical Rating Scale	NRS	0–10	0 = no pain 10 = worst pain imaginable
	Age	A	0 or 1	0 = younger than 65 years 1 = 65 years or older
	Gender	G	0 or 1	0 = female 1 = male
	Body mass index	BMI	0 or 1	0 = BMI < 30 kg m-2 1 = BMI ≥ 30 kg m-2
Response variables (One per model)	Patient's opinion	PO	0 or 1	0 = pain is not acceptable 1 = pain is acceptable
	Nurses' observation	NO	0 or 1	0 = no appropriate movement 1 = appropriate movement
	Combined PO+NO	PONO	0 or 1	1 = PO=1 and NO=1 0 = otherwise

served as gold standards. As gender, age and BMI may influence the results, these patient characteristics were introduced as extra dichotomous explanatory variables (covariates) into the logistic model [9, 23-25]. Details on the model variables are given in Table 1. A model was calculated for each of the three postoperative days.

Receiver Operating Characteristics (ROC) curves were made to estimate the ability of the computed models to correctly discriminate between those who found their pain acceptable or not, made appropriate movements or not, and those who combined acceptable pain with appropriate movements or not. First the sensitivity and specificity of NRS-MEP were calculated for each of the 11 points of the NRS-MEP score. Then the sensitivities (true positive fractions of subjects) were plotted versus 1-specificities (false positive fractions of subjects) to obtain the ROC curves. The area under the curve (AUC) quantifies how well the NRS-MEP predicts PO, NO or PONO: the larger the area, the better. If AUC=1.0, sensitivity and specificity equal both 100 %. If AUC=0.5, use of NRS-MEP is no better than flipping a coin.
The statistically optimal cut-off point was determined where the sum of the sensitivity and the specificity minus one (Youden's J-statistic) was maximal. Thus sensitivity and specificity were regarded as being equally important. This is the best cut-off point for the prediction of a positive response under the condition of equal "costs" of misclassifications.
The Statistical Package for the Social Sciences (IBM SPSS version 22.0; IBM Corporation, New York, NY, USA), Statistical Analysis System (SAS version 9.2; SAS Institute Inc., Cary, NC, USA), and R (R version 3.1.2 (2014-10-31); The R Foundation for Statistical Computing, Vienna, Austria) were used. Threshold of statistical significance was 0.05.

Results

Patient characteristics

15,394 assessments were obtained in 9,082 unique individual patients. For each of these patients data were obtained on: one of the three postoperative days, or any combination of two days, or all three days. Consequently, we had data from these 9,082 individual patients for 8,258, 4,522 and 2,614 of them on day 1, day 2 or

Table 2 Numbers and characteristics of patients

Day after surgery	N	Male (%)	Age (years) (mean (SD))	BMI (kg m-2) (mean (SD))*
1	8,258	44.0	53.5 (16.3)	26.2 (4.9)
2	4,522	51.5	56.5 (15.4)	25.8 (4.7)
3	2,614	55.5	56.8 (15.3)	25.7 (4.6)

* Because of missing values for length and/or weight the means (SD) for BMI are based on 8,042, 4,406, and 2,546 patients for day 1, day 2 and day 3, respectively.

day 3, respectively (Fig 1). The number of patients diminished across the three days as a part of the patients left the hospital after one or two days. A detailed account of the numbers of patients and assessments is given in Supplement S2 (see Table S2 in Supplemental Digital Content S2, which is a comprehensive table listing the number of patients, the number of unique, individual patients and the number of assessments of patients categorized per day or per combination of days).
Table 2 shows patients' characteristics categorized per day. They were similar when further categorized per data set.

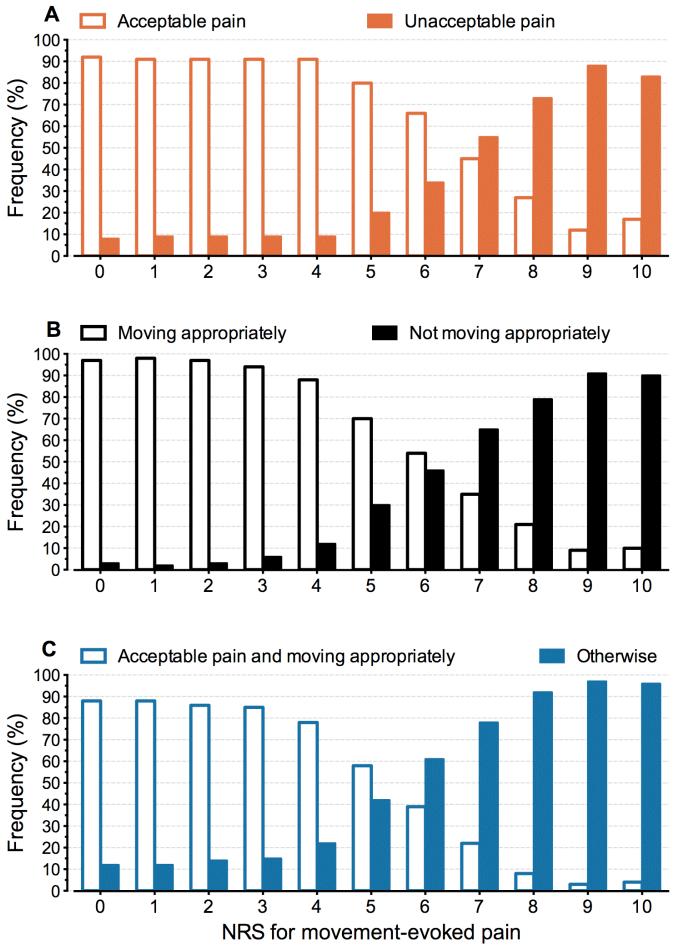

Figure 2 Relative frequencies for observations of patients' opinion (A), nurses' observation (B), and the measure combining patient's opinion and nurses' observation (C) against NRS-MEP scores
The observations in all patients gathered during the first three postoperative days were pooled.

Relationships between components of pain assessment

Observations

Fig 2 depicts the nature of the relationships between components of pain assessment. Pooled observed relative frequencies for PO, NO and PONO are plotted against NRS-MEP scores. The sigmoid shape of the relationships suggests using a logistic model for further analysis.

Fig 2A shows the observed relationship between the NRS-MEP scores and the acceptability of the pain. Patients associated low NRS-MEP scores 0-4 with unacceptable pain in approximately 9 % of the observations. On average, in 23 % of the observations patients with an NRS-MEP of 8-10 considered their pain acceptable.
Fig 2B shows that, on average, in 17 % of the observations patients with an NRS-MEP of 8-10 showed appropriate movements.
Fig 2C shows the observed relationship between the NRS-MEP scores and the presence of a clinically desirable situation where acceptable pain coexists with pain-free physical functioning. This situation is present in 22 % of the observations with an NRS-MEP=7, and, on average, in 7 % of the observations with an NRS-MEP of 8-10.

Model-based relationships

Binary logistic regression analysis revealed strong mathematical relationships between components of pain assessments, but age, gender and BMI were of no influence. All fitted models were adequate (likelihood ratio statistic: all P- values < 0.001).
NRS-MEP was related to PO, NO or PONO on each of the three postoperative days (all P-values < 0.001). The procedure to assess the influence of age, gender and BMI on the prediction models yielded 27 P-values (three days times three covariates times three response variables). Of these 27 P-values, only one was below the threshold of statistical significance (P=0.0423 for gender on the prediction of NO on day 1). As even in the absence of any relation between these covariates and the three outcomes, by pure chance one out of 20 P-values can be expected to be <0.05, these P-values were interpreted as indication that extension of the models with these covariates was not indicated. Therefore, we only present analyses using NRS-MEP as sole covariate. Details on the estimated models, including estimated regression coefficients, odds ratios and ROC curves, are given in Supplement S3 (see Table S3).
Fig 3 shows the estimated logistic curves with their 95 % confidence bands for the nine data sets created as shown in Fig 1. Wider 95 % confidence bands reflect smaller numbers of patients. Each of the curves shows the estimated proportion of patients that possess the outcome measure of interest as a function of NRS-MEP

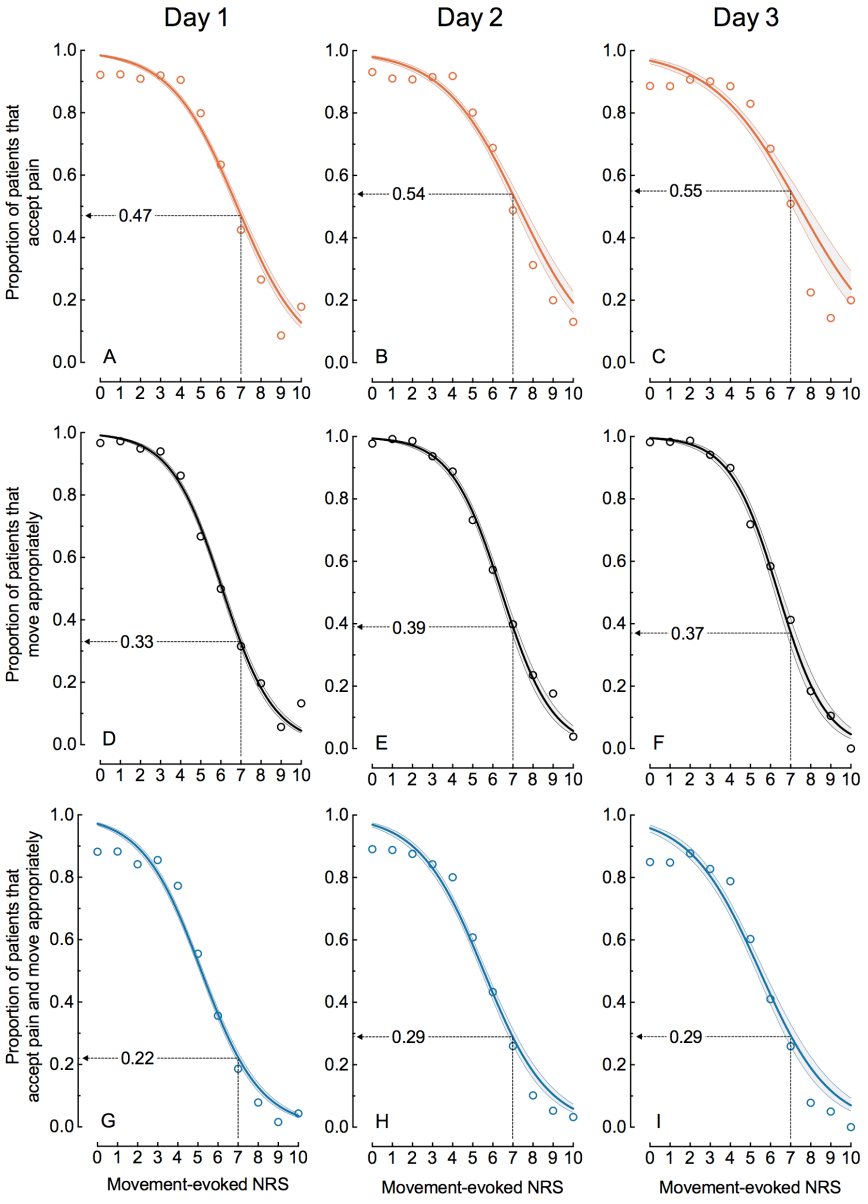

Figure 3 Estimated proportion (solid curve with its 95 % confidence band) of patients that accept the pain (A-C), move appropriately (D-F) or accept the pain and move appropriately (G-I) as a function of NRS-MEP for day 1, 2 and 3 after surgery

The open circles represent the observed proportions of patients at each of the eleven points of the NRS. For each of the nine data sets, one estimated proportion is computed and shown at NRS-MEP = 7.

Table 3 Cut-off points obtained from the logistic regression model using the 11-point Numerical Rating Scale for movement-evoked pain as explanatory variable for each of the three dependent variables PO, NO, and PONO. Shown are the statistically optimal cut-off points with their associated sensitivities and specificities, as well as the areas under the ROC curves (AUC)

Day after surgery	Dependent variable	N	Cut-off point	Sensitivity (%)	Specificity (%)	AUC	(95 % CI)
1	PO	7,708	5	83	68	0.81	(0.79-0.82)
	NO	6,683	4	71	87	0.86	(0.85-0.87)
	PONO	6,871	4	75	80	0.84	(0.83-0.84)
2	PO	4,264	5	83	61	0.77	(0.75-0.79)
	NO	3,733	4	69	87	0.86	(0.84-0.87)
	PONO	3,802	4	73	77	0.81	(0.79-0.82)
3	PO	2,487	5	87	53	0.73	(0.71-0.76)
	NO	2,161	4	76	85	0.87	(0.85-0.89)
	PONO	2,224	4	79	69	0.79	(0.76-0.81)

PO, patient's opinion on whether the pain is acceptable; NO, nurses' observation on the patient's ability to make appropriate movements; PONO, combined measure of PO and NO: is "acceptable pain" associated with "good appropriate movements" or not. Details on PO, NO, and PONO are given in Table 1.

[26]. The estimated curves for NO strongly match the data for nurses' observations indicated by open circles. For PO and PONO the curves closely follow observed proportions for 3≤NRS≤8 but mostly overpredict the observations for NRS≤2 and NRS≥9.

Fig 3 shows that, despite an NRS-MEP = 7, roughly half of the patients accept the pain (Fig 3A-C) and at least one third of the patients move appropriately (Fig 3D-F). Fig 3 suggests that these proportions increase with time. In spite of an NRS-MEP=7, at least one patient in five finds the pain acceptable and moves appropriately (Fig 3G-I): estimated proportions are 0.22 (95 % CI=0.21-0.24), 0.29 (95 % CI=0.26-0.31) and 0.29 (95 % CI=0.26-0.33) for day 1, 2 and 3, respectively.
Table 3 presents the statistically optimal cut-off points with their associated sensitivities and specificities. The number of patients decreases across the days. The cut-off points, however, remain stable: five, four, and four for PO, NO and PONO, respectively. Fig 4 shows graphs of the ROC curves. The closer a ROC curve is to the upper left corner, the better NRS-MEP discriminates between those patients who experience the outcome of interest, e.g. the pain is acceptable, versus those who do not.
The AUC for PO decreases across the days from 0.81 to 0.73. The latter figures indicate that NRS-MEP is not a perfect predictor for patients' willingness to accept their pain. The areas under the curve for NO are larger than those for PO and PONO on each of the three days. The AUC for NO implies that the NRS-MEP is fairly accurate in predicting the NO for all three days [27].
Four is the statistically optimal cut-off point for NRS-MEP based on the combination of patients' opinion and the nurses' observation. Nevertheless, 17 %, 15 % and 17

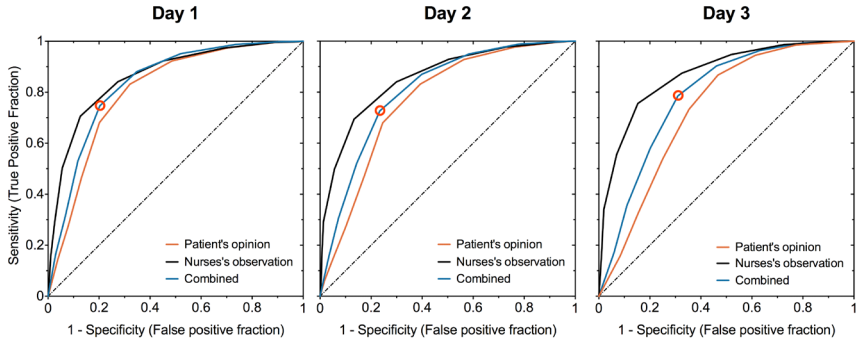

Figure 4 ROC curves for the dependent variables PO, NO and PONO for the three first postoperative days

The dashed line is the line of identity where the AUC = 0.5. Open circles are the points where Youden's J-statistic is maximal for PONO. These points are, by definition, the 'optimal' cut-off points.

% of those patients, who scored an NRS-MEP≤4, found their pain unacceptable or did not show good physical functioning or both, on day 1, 2, and 3, respectively. Fig 3G shows that the steepest part of the sigmoid curve starts at the cut-off point (odds ratio=0.51 with its 95 % CI=0.49-0.52 for day 1; other odds ratios are given in Supplement S3 (see Supplemental Digital Content S3)).

Discussion

To our knowledge, this is the first study in a broad surgical population to quantify the relationships between movement-evoked NRS and acceptability of pain, functional impact of pain, and a measure combining the two as a clinically desirable situation. Since the outcome of pain assessments has clinical consequences for all surgical patients, we consider our findings important to all health professionals involved in peri-operative care.

This study shows that the unidimensional NRS does not entirely reflect the multidimensional aspects of postoperative pain. Low pain scores do not guarantee that patients find their pain acceptable. Nor do high pain scores invariably mean that patients are not satisfied by their pain levels. Approximately one out of ten patients had unacceptable pain but reported a low NRS-MEP of 0-4. Despite a high pain score of NRS-MEP=7, at least one in five patients were willing to accept their pain and, at the same time, performed the required physical activities (Fig 3G-I).

According to the Youden's index, we found an 'optimal' NRS cut-off point for PONO of four. However, this threshold value is a rather poor predictor at the patient's level. Approximately 16 % of those patients who score an NRS-MEP equal to or lower than four, found their pain unacceptable or did not show good physical functioning or both. Taken together, the body of our findings points out that caregivers should prefer multidimensional assessment of pain, moving beyond the sole use of cut-off

points on the NRS to make clinical decisions.
Generally, low pain scores will not encourage health professionals to adjust pain treatment [28]. When health professionals do not ask patients whether pain is acceptable to them, pain may be undertreated. On the other hand, our study confirms the willingness of many patients to accept high-intensity pain. Maroney and co-workers observed that 31 percent of 1,249 patients, who reported severe pain on a four-item scale, found their pain acceptable [11]. In our larger study 23 % of patients, on average, proved to tolerate their pain despite an NRS-MEP of 8-10 (Fig 2A). At NRS-MEP=7, the estimated proportion of patients tolerating their pain was even 55 % (95 % CI=51 %-59 %) on the third postoperative day (Fig 3C). These discrepancies may be explained by patients' satisfaction with postoperative pain treatment, which may be more associated with impressions of improvement and appropriateness of care than with the actual pain experience [29, 30]. Additionally, patients and caregivers interpret pain intensity scores differently [3]. A recent study showed that some patients are not able to use the NRS reliably [31]. Patients may choose not to take more analgesics because they interpret their pain as "bearable" [12, 32]. Professionals need to be aware of this complex array of factors determining patients' experience of the pain. Therefore, the patient perspective should be assessed and valued in the care process [29].
To fully estimate patients' experience of pain an NRS score is not sufficient and other dimensions of pain should be assessed to balance treatment options [33, 34]. The internationally recognized definition by the International Association for the Study of Pain is: "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [35]. McCaffrey and Beebe offer another definition:"Pain is whatever the experiencing person says it is, existing whenever the experiencing person says it does" [36]. Both of these definitions highlight that a painful experience is more than just tissue damage triggering a response from the nervous system. The management of pain thus involves more than simply treating the tissue injury [37-39]. NRS-scores should be interpreted individually, after communicating with patients about their pain and observing them [12]. Observing the capacity to mobilize, breathe deeply or cough may inform the professional on the functional capacity of the patient in relation with the pain score [7]. Restrictions of these activities may be a consequence of inadequate analgesia, which may not be discovered solely with patient-reported outcomes [4].
As nurses have more patient contacts than other health professionals, regular pain assessment and reassessments usually fall to the nursing domain [40]. Pain assessment is a complex communication process between the patient and health professional with diverse interpersonal and intrapersonal dimensions interacting and affecting each other [13, 41]. In this way a balanced decision on pain treatment can be described as the result of a social transaction between the patient and the health professional [13, 42]. The combination of the patients' opinion and the nurses' observation, as the balancing variable, may therefore be a first step in the direction of the future.

A specified value on the NRS has been frequently used as a single 'cut-off point' to divide patients into two categories: those who are in need of pain treatment and those who are not [8]. However, cut-off points are far from perfect discriminators between the two categories (Table 3). Also, there is no convincing evidence for the choice of a certain cut-off point, and consequently no consensus [8, 12, 15]. Threshold values of six [9], seven [15], or eight have been used to define the lower limit for severe pain. The Dutch Health Care Inspectorate classifies NRS ≥ 8 as severe pain and considers the percentage of patients with an NRS 8-10 to be a quality indicator of postoperative pain management [10]. Furthermore, there is no evidence that the use of cut-off points improves pain control [13].

The "optimal" cut-off point for NRS-MEP we defined here holds under the condition that costs of misclassifications are equal, thus weighing under- and over-treatment equally. However, our choice for this equality cannot be corroborated because it is unknown what is more harmful. In this study no outcome data were included and therefore we cannot discuss our results from this perspective. Nevertheless, we may point out two directions for future research. On one hand, questions should be answered whether treating unacceptable pain and better education of patients and professionals may prevent pain-related complications [14]. On the other hand, a hypothesis to be tested is: "Treating pain during routine hospital ward care, only because a pain score is higher than a predefined cut-off value, is potentially hazardous".

In our study, we did not exclude patients because of incompleteness of the pain assessments. By doing so, we avoid the bias that would be induced by restricting the analyses to only patients without missing observations, the so-called complete case analysis. A complete case analysis is unbiased if data are missing completely randomly, meaning that the chance of data being missing is unrelated to any of the variables involved in the analysis. If data are not missing completely randomly, analyzing only the complete cases will probably lead to biased estimates [43]. Even when complete case analysis would be unbiased, discarding all the information from the incomplete cases is inefficient.

This study has limitations. First, there are no "gold standard" objective measures of the pain-related functional capacity in postsurgical patients [44]. Nevertheless, various measures have been developed to quantify treatment related changes in the physical abilities of individuals with acute pain [4, 16]. The FAS is such a nonvalidated —because of lacking standards— measure. Not only has the FAS been adopted by the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine [19], but also it has been advocated for clinical use [16-18]. The FAS proved to be very useful and generally applicable in daily practice. Second, we could not include all confounding factors. Gender, age and BMI were introduced as covariates in the logistic model because they are risk factors for the development of acute postoperative pain [9, 23-25]. Gender, age and BMI showed no influence, but we do not know if other factors might. Other factors may be: type of operation, anxiety or catastrophizing [9, 45], preoperative information, expectations about pain levels, psychological profile and motivation. The impact of these factors with the

relationships between NRS-MEP, PO, NO and PONO could be a topic of future prospective studies. For example, pain anticipation can be assessed by asking the patient preoperatively to mark a point on the NRS that describes the anticipated pain after surgery [46]. Third, our findings do not apply to all hospitalized patients because we only studied patients after major surgery. One next step is to validate our results for other patient categories, such as patients after minor surgery and patients with cancer pain.

Conclusions

The nature and strength of the relationships we found lead to clinically important findings and implications. Almost one in ten patients has unacceptable pain even if they report a low pain score. One in five patients with a high pain score accepts the postoperative pain and still moves appropriately. We encourage health professionals to use a multi-source pain evaluation by assessing NRS, the acceptability of the pain and physical functioning in order to balance pain treatment options and possible complications. The sole use of NRS cut-off points is not adequate. Adequate pain assessment appears to become a form of social transaction between patient and caregiver. Future research should focus on the improvement in pain-related outcomes in relation to multidimensional pain assessment and treatment decisions.

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Table S1 Surgical procedures, categorized in ten groups

Group	N	Procedure
Laparotomy	3,610	Hyperthermic Intraperitoneal Chemotherapy (HIPEC), colectomy, hepatectomy, Whipple procedure (pancreaticoduodenectomy), pelvic or retroperitoneal lymph node dissection, Oscar Ramirez procedure (abdominoplasty), adhesiolysis.
Upper laparotomy	1,857	Gastrectomy, pancreatectomy, splenectomy, esophageal resection, cholecystectomy.
Lower laparotomy	2,792	Abdominal hysterectomy, appendectomy, cystectomy, prostatectomy, sectio caesarea, debulking, rectum or sigmoid resection.
Laparoscopy	581	Laparoscopic cholecystectomy, nephrectomy, colectomy, adrenalectomy, prostatectomy, hysterectomy.
Sternotomy	62	Coronary bypass, thymectomy, metastasectomy, pericard resection.
Thoracotomy	943	Lobectomy, pneumectomy, tracheal resection.
Thoracoscopy	402	Video assisted surgery or thorascopic surgery, such as pleurectomy, bullectomy, Nussbar surgery, video-assisted thorascopic surgery.
Flank	311	Nephrectomy, adrenalectomy.
Orthopaedic surgery	2,966	Total knee arthroplasty, total hip arthroplasty, acetabulum arthroplasty, arthrodesis of limbs, arthrotomy, osteotomy, amputation of limbs, pelvectomy, total shoulder arthroplasty, hand surgery, foot surgery.
Remainder of procedures	1,870	Hernia inguinalis, mastectomy, lumpectomy, laminectomy, spondylodesis, head or face surgery.

Table S2 Number of patients, number of unique, individual patients and the number of assessments of patients categorized per day or per combination of days

Pain assessment on	Day 1	Day 2	Day 3	Unique patients	Assessments
Only day 1	4,327	0	0	4,327	4,327
Only day 2	0	393	0	393	393
Only day 3	0	0	88	88	88
Day 1 & 2	1,748	1,748	0	1,748	3,496
Day 1 & 3	145	0	145	145	290
Day 2 & 3	0	343	343	343	686
Day 1 & 2 & 3	2,038	2,038	2,038	2,038	6,114
Total	**8,258**	**4,522**	**2,614**	**9,082**	**15,394**

Supplement S3 Results from logistic regression

Using the sample data, an iterative process (maximum likelihood) produces an estimated logistic regression equation of the form

$$logit(p) = log_e \frac{p}{1-p} = a + b_1 NRS + b_2 A + b_3 G + b_4 BMI \quad (1)$$

where:

- NRS, A, G and BMI are the explanatory variables (Table 1 in the Methods section);
- *p* is the estimated value of the true probability that a patient with a particular set of values for the explanatory variables has the outcome of interest, for example the patient moves appropriately;
- a is the estimated constant term;
- b_1, b_2, b_3, and b_4 are the estimated logistic regression coefficients.

We can manipulate equation (1) to estimate the probability that a patient has the outcome of interest. After simplifying (as A, G and BMI proved to be of no influence), we first calculate for a patient with a particular NRS,

$$S = a + b_1 NRS \quad (2)$$

Then, the probability that a patient has the outcome of interest is estimated as

$$p = \frac{e^S}{1+e^S} \quad (3)$$

and the probability that a patient does not have the outcome of interest as

$$1 - p = \frac{1}{1+e^S} \quad (4)$$

The probability p decreases from one to zero, for S decreasing from plus to minus infinity. Noticeably, equation (3) shows that the probability p=0.5 for S=0 or $NRS = -a/b_1$. Table S3.1 lists the estimated constant terms and logistic regression coefficients.

Table S3 Results from the logistic regression model using the 11--points Numerical Rating Scale for movement--evoked pain as explanatory variable for each of the three dependent variables PO, NO, and PONO. Listed are constant term α and logistic regression coefficient b_1 from equation (2), as well as the odds ratio (OR) with its 95 % Wald confidence interval

Day after surgery	Dependent variable	α (SE)	b_1 (SE)	OR (95 % CI)
1	PO	4.1156 (0.0943)	-0.6039 (0.0166)	0.547 (0.529-0.565)
	NO	4.7171 (0.1120)	-0.7773 (0.0197)	0.460 (0.442-0.478)
	PONO	3.5161 (0.0871)	-0.6805 (0.0169)	0.506 (0.490-0.523)
2	PO	3.8677 (0.1243)	-0.5303 (0.0224)	0.588 (0.563-0.615)
	NO	5.0953 (0.1651)	-0.7912 (0.0288)	0.453 (0.428-0.480)
	PONO	3.4504 (0.1156)	-0.6220 (0.0224)	0.537 (0.514-0.561)
3	PO	3.4035 (0.1430)	-0.4578 (0.0275)	0.633 (0.600-0.668)
	NO	5.3441 (0.2248)	-0.8378 (0.0402)	0.433 (0.400-0.468)
	PONO	3.1292 (0.1364)	-0.5719 (0.0280)	0.564 (0.534-0.596)

PO, patient's opinion on whether the pain is acceptable; NO, nurses' observation on the patient's ability to make appropriate movements; PONO, combined measure of PO and NO: is "acceptable pain" associated with "good appropriate movements" or not.

The values in Table S3 can be used to calculate S (eq. 2) and the probabilities given in equations (3) and (4). For example, a patient has NRS=4 on day 1. The probability that this patient moves appropriately is 0.833, whereas the probability of not moving appropriately is 0.167. The odds of moving appropriately is *p/(1-p)* = 0.833/0.167 = 4.99. Alternatively, combining equations (3) and (4) yields *p/(1-p)* = e^{S} = $e^{4.7171-0.7773x4}$ = 4.99.

Although mathematically correct, we should not apply estimates on the probability scale to individual subjects like we did in the example. Each individual subject reporting NRS=4 either does or does not move appropriately. The estimated probabilities from a logistic regression model are best viewed as estimates of proportions in the underlying population. As a result, we better express the result for the example as: the estimated proportion of patients that move appropriately at NRS=4 is 0.833. A confidence interval for an estimated proportion can be calculated. We therefore refer to Hosmer and Lemeshow.[†]

The odds ratio (OR) in the example is calculated as follows. For an *NRS*=4, it is the estimated odds of moving appropriately for *NRS*=5 relative to the estimated odds of moving appropriately for *NRS*=4. As the odds with *NRS*=5 is $e^{4.7171-0.7773x5}$ = 2.30, the OR = 2.30/4.99 = 0.46. Alternatively, it can be shown that the OR = e^{b1} = $e^{-0.7773}$ = 0.46, as NRS increases by one unit. If the OR is equal to one, then the two odds are the same. An OR > 1 indicates an increased odds of moving appropriately, and an OR < 1 indicates a decreased odds of moving appropriately, as *NRS* increases by one unit.

A measure of the model's ability to discriminate between those subjects who experience the outcome of interest versus those who do not is provided by the area under the Receiver Operating Characteristic (ROC) curve (Figure S1).[††] It plots sensitivity (true positive fraction of subjects) *versus* 1-specificity (false positive fraction of subjects) at all possible cutoff points on the NRS.[§] The 'optimal' cutoff point is found where the vertical distance between the curve and the line of identity is maximal (Youden's J--statistic).

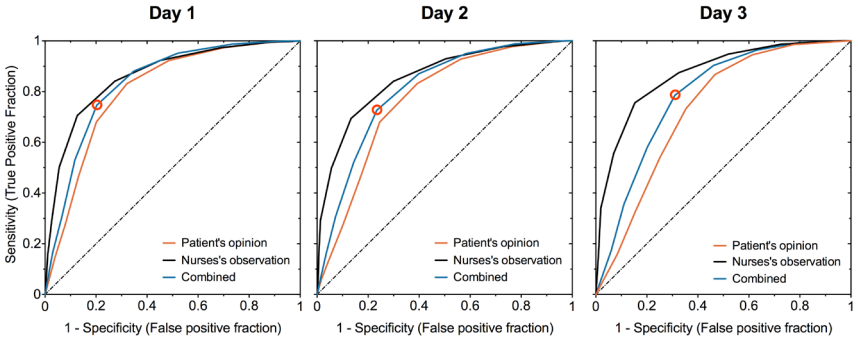

Figure S1

ROC curves for the dependent variables PO, NO and PONO for the three first postoperative days. The dashed line is the line of identity where the AUC = 0.5. The closer the ROC curve is to the upper left corner, the better NRS discriminates. Open circles are the points where Youden's J--statistic is maximal for PONO.

[†] Hosmer DW and Lemeshow S. In: Applied Logistic Regression, 2nd Ed, Chapter 1, p.17--21. ISBN 0--471--35632--8.

[††] Hosmer DW and Lemeshow S. In: Applied Logistic Regression, 2nd Ed, Chapter 5, p.160--164.

[§] Galley H. Solid as a ROC. Editorial II. Br J Anaesth 2004; 93: 623--6. doi: 10.1093/bja/aeh247

Relationship between postoperative pain and overall 30-day complications in a broad surgical population: an observational study

6

Submitted

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Abstract

Objective: The aim of this study was to establish the relationship between postoperative pain and 30-day postoperative complications.
Background: Only scarce data are available on the association between postoperative pain and a broad range of postoperative complications in a large heterogeneous surgical population.

Methods: Having postoperative pain was assessed in two ways: the movement-evoked pain score on the Numerical Rating Scale (NRS-MEP) and the patients' opinion whether the pain was acceptable or not. Outcome was the presence of a complication within 30 days after surgery. Additionally, outcome was the occurrence of one of three healthcare-associated infections (HAIs): lung infection, urinary tract infection, and surgical site infection. Multivariable logistic regression was used.

Results: In 1,014 patients the overall complication rate was 34%. The proportion of patients experiencing postoperative complications increased from 0.25 (95 % CI=0.21-0.31) for NRS-MEP=0 to 0.45 (95 % CI=0.36-0.55) for NRS-MEP=10. Patients who found their pain unacceptable had more complications (adjusted odds ratio = 2.17 (95 % CI=1.51-3.10; p<0.001)). Higher NRS-MEP scores and unacceptable pain on the first postoperative day were strongly associated with an increase in HAIs (adjusted odds ratio was 1.161 per NRS-point (95 % CI=1.055-1.279; p=0.002) and 2.49 (95 % CI=1.31-4.75; p=0.006) for unacceptable pain). Increasing age and a higher class of preoperatively expected pain independently contributed to the development of complications, including HAIs.

Conclusions: Higher actual postoperative pain scores and unacceptable pain, even on the first postoperative day, are associated with more postoperative complications, including HAIs. Further research should focus on the precise relationship between postoperative pain and the occurrence of complications per type of surgery.

Introduction

Lack of consensus on the method of reporting may have contributed to the widely varying incidence rates of adverse postoperative events [1]. For general surgery reported overall incidences vary between 3.9 % and 53.0 % [1-6]. Such a wide range is hard to interpret, thus impeding its direct use in quality assessment. Given the lack of consensus it is hardly surprising that the general relationship between the occurrence of postoperative complications and potentially contributing factors, such as postoperative pain, remains unclear [7-12]. This contrasts with the perception that perioperative pain management becomes increasingly important to the quality of surgical care [13]. Postoperative pain reduction is therefore one of the key elements of Enhanced Recovery After Surgery (ERAS) programs [14-16].
Comparing outcomes across the literature may be ameliorated by using the Clavien-Dindo Classification (CDC) of Surgical Complications, which systematically scores postoperative complications in grades [17, 18]. Notwithstanding, only scarce data were obtained on the putative association between a broad range of postoperative complications and postoperative pain in a large, heterogeneous surgical population. Meaningful data are only available for specific surgeries and major complications. Recently, it has been shown that hospitals where patients reported low pain scores after colorectal resection had significantly lower rates of pulmonary complications, including pneumonia [13].
Therefore, the aim of the current study was to establish the relationship between postoperative pain, defined by its intensity and its acceptability, and 30-day postoperative complications in real-world practice.

Methods

Approval - ethical considerations

The Institutional Review Board of the Radboud University Medical Center (Nijmegen, The Netherlands) ethically approved the study (authorization number: 2012/430). The Radboud University Medical Center is a large regional academic hospital where all patient data are systematically gathered in an electronic medical record system. Informed consent was obtained from the participants. Prior to data handling, data were de-identified. All participating patients received the routine care customary for each of the surgical procedures and specialties. Research-related interventions were not introduced.

Study design – Inclusion and exclusion criteria

Step 1. We performed a prospective patient questionnaire study in the Radboud University Medical Center. All patients who underwent scheduled surgery between

November 2012 and April 2015 were considered eligible for participation in our study. No preselection of to be included patients was performed. Although all patients of all surgical specialties were considered eligible, exclusion criteria were: 1) younger than 18 years of age; 2) procedures outside the operation room. The method of recruitment automatically excluded emergency surgery or surgery on intensive care patients. Recruitment of patients occurred after their visit to the anesthesia preoperative evaluation clinic of the Department of Anesthesiology, Pain and Palliative Medicine. Once every two weeks, medical research assistants sequentially called these patients over the telephone, using a randomized list. They asked them to participate and to return a questionnaire including a written informed consent. When patients did so, they were enrolled in the study.
Step 2. Three months after the planned surgery we retrospectively searched the electronic medical record of each participating patient for complications that had occurred within the first 30 days after surgery.

Pain assessment

On the day before surgery, each participant received a journal to record data. Preoperatively, participants entered their gender, age, weight, height, personal view on the surgical procedure and a preoperative pain score. Postoperatively, the journal was used to enter the results of the assessment of their pain. Pain was assessed on the morning of the first, second and third day after surgery in two ways. Pain intensity was measured with a numerical rating scale (NRS). Pain acceptability was determined by asking the patient whether the pain was acceptable or not.
The NRS is an 11-points numerical rating scale with end points representing the extremes of the pain experience: 0 = “no pain at all” and 10 = “worst possible pain”. Patients were asked to rate their movement-evoked postoperative pain with the NRS in the morning after bathing and getting dressed [19-21]. Since movement-evoked pain (MEP) has a negative effect on recovery after surgery [22], NRS-MEP was used in this study to answer our research question, and not a pain score measuring pain at rest.
Pain acceptability was added because the patient’s appreciation of the pain is clinically important for making the patient comfortable [23, 24]. Patient’s opinion on the acceptability of the pain is a binary categorical variable as the answer to the question whether the pain was acceptable was only yes or no [25].

Surgical procedures

We retrieved the surgical specialty and the exact type of surgery from the hospital electronic medical record system. Regarding the specialty, we distinguished ten categories: general surgery, orthopedic surgery, urology, gynecology, ear-nose-throat surgery, eye surgery, plastic surgery, neurosurgery (including herniated disc surgery), oral and maxillofacial surgery and other surgeries. Other surgeries were, for example, cardiac surgery, cardiac procedures and chronic pain

surgery.
Using the exact type of surgery, we classified the surgical procedures into three categories of expected postoperative pain. We therefore used the model of Janssen and co-workers [26]. They developed a classification of type of surgery to be used for predicting severe acute postoperative pain with the aid of a prediction rule. First they identified 27 groups of surgical procedures based on clinical experience, current practice and interviews with surgeons and anesthesiologists. Then, the univariate association between each surgical group and early severe acute postoperative pain was estimated in a cohort of patients. Groups with similar associations were further combined. The original table of the authors is given as Table S1 in the Supplemental Digital Content. It shows five classes of surgical procedures ordered by increasing incidence of severe acute postoperative pain (NRS≥6) occurring within the first hour after surgery. For our study, we reduced these five categories of expected pain into three categories: lowest and low expected pain, moderate expected pain, and high and highest expected pain, hereafter referred to as the Janssen 3C-classification of expected pain.

Postoperative complications

A medical researcher first searched for complications and then classified them according to strict guidelines, including the CDC grades (see Figure S2 in the Supplemental Digital Content, which contains the original Table 1 of the authors) [17, 18, 27, 28]. To prevent bias, the medical researcher was not involved in the patient's care. We define a postoperative complication as any medical adverse outcome occurring between admission and 30 days after operation [29]. Grade l complications were defined as "mild complications" and grade ll-V complications as "severe".
A second medical researcher, who also was not involved in the patient's care, checked the records to ensure completeness of data.
Complications occurring in the operation room and complications directly related to anesthesia (e.g. nausea which resolves immediately after medication in the operation room) were not included in the CDC. Each complication was evaluated separately and categorized into cardiovascular, pulmonary, gastro-intestinal, thrombo-embolic, musculoskeletal, neurological, urinary tract, infectional and other complications.

Statistical analysis

Descriptive analysis of the observed population preceded formal statistical analysis. To that end, age and BMI were summarized as mean (SD) [minimum-maximum], whereas relative frequencies were calculated for gender, specialty and type of surgery according to the Janssen 3C-classification of expected pain. For the specialties with N>60, frequencies of the specific surgical procedures, averaged NRS-MEP and complication rates were calculated. The incidence of postoperative pain, operationalized as moderate pain (NRS-MEP 4-7) and severe pain (NRS-MEP

8-10), was calculated. All postoperative complications were counted to calculate the incidence. Per patient, only the complication with the highest grade in the CDC was considered to count the number of complications for each of the grades of the CDC [17, 18, 28].

To quantify the relationship between having postoperative pain and complications after surgery, two logistic regression models were estimated. In both models the dependent binary variable was the presence of a complication with a CDC of I-V. In the first model, the independent explanatory variable was postoperative pain identified as the average of the three NRS-MEP scores for the first three days after surgery. In the second model, the independent explanatory variable was a binary variable representing the acceptability of the pain. The pain was defined 'unacceptable' if the patient had found the pain unacceptable at least once in the course of the first three days after surgery. We performed the same analyses with the presence of a complication defined as a CDC of ll-V to ascertain that findings were not driven by mild complications (CDC Grade l).

Additional logistic models were estimated to identify possible differences between the three postoperative days. A logistic model was therefore estimated, for each of the three postoperative days, with an appropriate independent variable, i.e. the actual NRS-MEP or the binary variable representing the acceptability of the pain for the day under study.

Univariate logistic regression models yielded crude estimates. Multivariable logistic regression models were used to obtain adjusted estimates after controlling for six covariates known for their potential influence on results.26, 30-38 Age and BMI were introduced as continuous covariates. Gender and having a preoperative pain score higher than seven were introduced as dichotomous covariates. Surgical specialty and the Janssen 3C-classification of expected pain were introduced as categorical covariates.

Additionally we performed an analysis testing the potential association between having pain on the first postoperative day and the occurrence of one of three major healthcare-associated infections (HAI): lung infection (LI), urinary tract infection (UTI) and surgical site infection (SSI) [39]. Multivariable logistic regression models included only those covariates that were found statistically significant in the procedures described above.

Data were analyzed using SPSS (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. IBM Corporation, Armonk, NY, USA). In all analyses a P-value < 0.05 was considered statistically significant.

Results

Patient characteristics

In total, 1,393 consenting patients entered the study (Figure 1). Retrospective data on postoperative pain scores and the occurrence of complications, whether

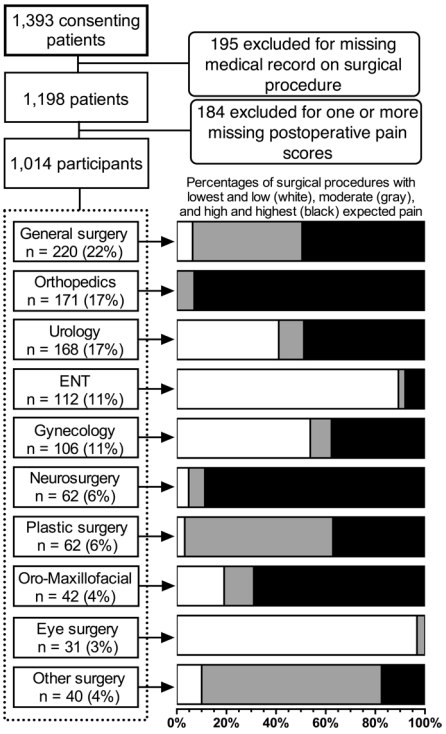

Figure 1 Selection and classification of participating patients

The number of participants (percentage of n=1,014) is given per surgical specialty. For each specialty, the relative frequencies of the surgical procedures with lowest and low expected pain (white), moderate expected pain (gray), and high and highest expected pain (black) are shown as stacked bars. The categories of expected pain are those from Janssen and coworkers[26] (Table S1). Medical records were missing (N=195) because surgery was postponed, performed in another hospital, or not performed at all. ENT = Ear, Nose, Throat surgery.

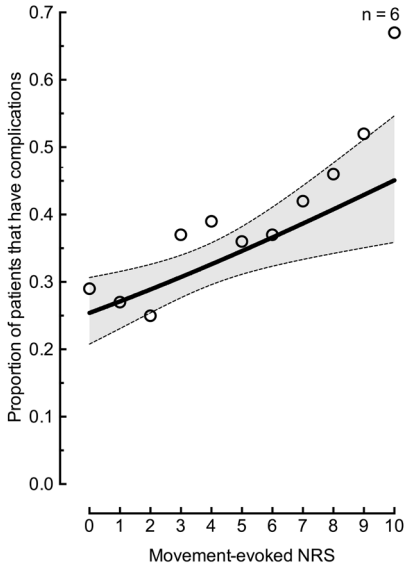

Figure 2 Estimated proportion of patients that have complications as a function of NRS-MEP averaged across day 1, 2 and 3 after surgery

The solid curve is obtained from the fully adjusted logistic regression model. The gray area is the 95% confidence interval for the estimated proportion. The circles represent groups of observed proportions of patients at each of the 11 points of the NRS-MEP; groups were made by rounding fractional numbers for NRS-MEP to the nearest whole numbers. There were only six patients with an average NRS-MEP=10.

present or not, were available for 1,014 patients (48.3 % male). Their mean age was 55 (SD=15) [18-90] years. Their mean Body Mass Index was 26.1 (SD=4.5) [17.3-50.4] kg m^{-2}. Figure 1 shows the study sample categorized per surgical specialty and class of expected pain according to the Janssen 3C-classification. The group of patients excluded for missing pain scores did not differ from the cohort of included patients with regard to age, gender, body mass index, medical specialty, complication rate and severity of complications.

Table 1 Number of patients, gender (M(ale)/F(emale)), Numerical Rating Scale for movement-evoked pain (NRS-MEP) and incidence of complications for specific surgical procedures from surgical specialties with N>60. Procedures occurring <10 times were classified as 'miscellaneous'. NRS-MEP is the average NRS-MEP in the first three days after surgery

Specialty	Procedure type	N (M/F)	NRS-MEP (mean(SD))	Complications (%)
General surgery	Hernia	31 (27/ 4)	4.2 (2.1)	19.4
	Upper gastro-intestinal	30 (11/19)	4.5 (2.4)	63.3
	Lower gastro-intestinal	17 (12/ 5)	3.8 (2.3)	76.5
	Skin and soft tissue	19 (11/ 8)	3.5 (2.0)	36.8
	Thyroid and parathyroid	13 (2/11)	2.8 (1.9)	61.5
	Miscellaneous general surgery	110 (51/59)	3.7 (2.3)	27.3
	Total general surgery	220 (114/106)	3.8 (2.3)	37.7
Orthopedics	Hip	54 (25/29)	4.0 (2.2)	44.4
	Knee	42 (13/29)	4.7 (2.1)	28.6
	Miscellaneous orthopedics	75 (35/40)	3.9 (2.4)	26.7
	Total orthopedics	171 (73/98)	4.1 (2.2)	32.7
Urology	Prostate and/or bladder	50 (49/ 1)	2.9 (2.4)	48.0
	Kidney and adrenal	34 (17/17)	3.8 (2.0)	41.2
	Miscellaneous urology	84 (63/21)	3.9 (2.5)	39.3
	Total urology	168 (129/39)	3.6 (2.4)	42.3
Ear-nose-throat surgery	Cochlear implant	17 (7/10)	2.1 (1.7)	17.7
	Laryngoscopy	14 (10/ 4)	2.1 (2.2)	21.4
	Miscellaneous ear-nose-throat surgery	81 (39/42)	3.2 (2.7)	28.4
	Total ear-nose-throat surgery	112 (56/56)	2.9 (2.6)	25.9
Gynecology	Uterus	23 (0 /23)	3.4 (2.6)	21.7
	Adnexa	13 (0 /13)	3.5 (1.8)	23.1
	Miscellaneous gynecology	70 (0 /70)	3.6 (2.4)	41.4
	Total gynecology	106 (0 /106)	3.5 (2.4)	34.9
Neurosurgery	Lumbar spinal cord decompression	31 (17/14)	4.9 (2.1)	29.0
	Miscellaneous neurosurgery	31 (20/11)	4.0 (3.0)	58.1
	Total neurosurgery	62 (37/25)	4.5 (2.6)	43.5
Plastic surgery	Breast reconstruction	19 (0 /19)	3.6 (1.9)	36.8
	Miscellaneous plastic surgery	43 (14/29)	4.1 (2.4)	25.6
	Total plastic surgery	62 (14/48)	4.0 (2.3)	29.0

Surgical procedures

Table 1 provides insight in the type of surgical procedures. The rate of complications varies widely among surgical procedures. Between surgical specialties the complication rate varies between 26 % and 44 %.

Pain intensity

Moderate pain (NRS-MEP 4-7) occurred in 39 %, 37 % and 32 % of the patients on postoperative day one, two and three, respectively. Severe pain (NRS-MEP

Table 2 Number and incidence, expressed as percentage of the total number of patients, of complications in each category as well as individual complications

Category of Complications	Number[a]	Incidence %[b]	Type of complication
Gastro-intestinal	156	15.4	nausea (76), constipation (26), vomiting (25), ileus (13), diarrhea (9), malaise and weight loss (4), gastroparesis (3).
Neurological	105	10.4	lightheadedness (31), persistent pain (25), sensibility dysfunction (15), paresthesia (7), transient confusion (6), headache (5), neuropraxia (4), facial paresis (2), delirium (2), hallucinations (2), tinnitus (2), ataxia (1), hypoesthesia (1), neurinoma (1), globus sensation (1).
Infectional	95	9.4	infections without evident cause (36), surgical site infection (28), fungal infection (8), erysipelas (5), abscess (4), phlebitis (4), sepsis (2), pyelonephritis (2), cholangitis (2), herpes zoster (1), empyema (1), endophthalmitis (1), osteitis pubii (1).
Urinary tract	57	5.6	urinary retention (27), urinary tract infection (24), elevated creatinine (6).
Thrombo-embolic	51	5.0	hematoma (27), bleeding (20), thrombosis (2), omental infarction (1), stroke (1).
Pulmonary	28	2.8	pneumonia (18), atelectasis (6), respiratory insufficiency (4).
Cardiovascular	19	1.9	atrial fibrillation or flutter (7), tachycardia (7), ischemia (3), conduction disorder (1), repolarization disorder (1).
Musculoskeletal	10	1.0	stiffness (5), muscle pain (4), muscle weakness (1).
Other	95	9.4	wound dehiscence (24), anemia (13), hypokalemia (10), hoarseness (10), seroma (5), hyperkalemia (5), chest pain without ischemia (4), hyponatremia (3), chylous leakage (3), incisional hernia (3), decubitus ulcer (3), adhesion (2), hypocalcemia (2), lymphocele (2), hypophosphatemia (2), new onset Diabetes Mellitus (2), erectile dysfunction (1), mastocytosis (1).
Total	616	n/a	

[a] Consulting 1,014 medical records yielded 616 complications in 343 patients in the first 30 days after surgery. Multiple complications per patient were added.
[b] Expressed as a percentage of the 1,014 patients. n/a means “not applicable”.

Table 3 Number and relative frequencies of complications graded by the Clavien-Dindo classification of Surgical Complications in those 343 patients who suffered from at least one complication within 30 days after surgery (total N=1,014)
Only the complications with the highest grade in the Clavien-Dindo classification were counted.

	Number	(%)
Grade I	189	(55.1)
Grade II	123	(35.9)
Grade III	24	(7.0)
Grade IV	7	(2.0)
Grade V	0	(0.0)
Total	343	(100.0)

8-10) occurred in 16 %, 10 % and 6 % of the patients on day one, two and three, respectively. Overall, 16.8 % of the patients reported unacceptable pain at least once in the course of the first three postoperative days.

Complications

A total of 616 postoperative complications occurred within 30 days after surgery. Table 2 shows the specific complications found in each of the ten categories. As these 616 complications occurred in 343 patients, more than one third of the patients (33.8 %) suffered from at least one postoperative complication. Using the complication with the highest value in the CDC for each of the 343 patients, Table 3 further specifies the different grades of severity.
Overall, 55.1 % were mild complications (Grade I), which occurred in 18.6 % of the patients. These complications consisted mainly of nausea and light-headedness (Table 2). Severe complications (Grade II-V) occurred in 15.2 % of the patients. These complications consisted mainly of infections and urinary tract complications. The most common infection was an infection without evident cause. Seventy patients experienced a HAI. The most common urinary tract complication was urinary retention (Table 2).

The association between postoperative pain and complications after surgery

Table 4 shows that a statistically significant association exists between having postoperative pain and the occurrence of postoperative complications, even after adjusting for potential confounders.

When having postoperative pain is operationalized as the NRS-MEP averaged across the first three postoperative days, the crude odds ratio associated with a one-point increase in NRS-MEP is 1.113 (95 % CI=1.054-1.174; $p<0.001$). The adjusted odds ratio is smaller and equals 1.092 (Table 4). This may mean, for example, that patients who score an average NRS-MEP=9 have two times the odds of suffering from one or more complications as those who score an average NRS-MEP=1, other factors

Table 4 Odds ratios obtained from multivariable binary logistic regressions estimating the association between pain and complications*

The presence of a complication is the dependent variable. The Numerical Rating Scale (NRS-MEP) or the patient's opinion whether the pain is unacceptable is the primary independent variable. NRS-MEP is the average NRS of movement-evoked pain in the first three days after surgery. Unacceptable pain means having unacceptable pain at least once in the course of the first three days after surgery. Secondary independent variables are potential confounders.

		Relationship NRS-MEP — Complications			Relationship Unacceptable pain — Complications		
Independent variables		**Odds Ratio**	**(95% CI)**	**P-value**	**Odds Ratio**	**(95% CI)**	**P-value**
Primary variable							
Average NRS-MEP‡		1.092	(1.027-1.161)	0.005	n/a		
Unacceptable pain		n/a			2.17	(1.51-3.10)	<0.001
Secondary variables							
Continuous							
Age‡		1.019	(1.009-1.030)	<0.001	1.019	(1.009-1.030)	<0.001
Body Mass Index‡		1.022	(0.991-1.055)	0.166	1.022	(0.990-1.055)	0.176
Dichotomous							
Female gender		0.83	(0.61-1.13)	0.228	0.84	(0.61-1.15)	0.266
Preoperative NRS > 7		1.30	(0.82-2.06)	0.258	1.38	(0.88-2.17)	0.164
Categorical							
Medical specialty	Other surgeries	1.00	(reference category)		1.00	(reference category)	
	General surgery	1.39	(0.65-2.99)	0.397	1.50	(0.70-3.22)	0.301
	Orthopedics	0.84	(0.37-1.91)	0.685	0.92	(0.40-2.08)	0.834
	Urology	2.03	(0.90-4.55)	0.088	2.16	(0.96-4.86)	0.062
	Gynecology	2.09	(0.86-5.11)	0.106	2.14	(0.88-5.25)	0.095
	ENT	1.79	(0.71-4.50)	0.214	1.85	(0.74-4.65)	0.190
	Eye surgery	0.47	(0.09-2.46)	0.368	0.50	(0.09-2.61)	0.409
	Plastic surgery	1.04	(0.42-2.58)	0.939	1.12	(0.45-2.78)	0.815
	Neurosurgery	1.09	(0.43-2.74)	0.859	1.16	(0.46-2.93)	0.753
	Oro-maxillofacial surgery	0.66	(0.22-1.93)	0.443	0.65	(0.22-1.92)	0.437
Category expected pain	Lowest and low	1.00	(reference category)		1.00	(reference category)	
	Moderate	2.14	(1.26-3.64)	0.005	2.16	(1.27-3.67)	0.005
	High and highest§	2.82	(1.79-4.42)	<0.001	2.90	(1.86-4.55)	<0.001

* Here N was 988 because of 26 missings for the covariate 'preoperative NRS > 7'.

‡ Three decimals are given for the odds ratio of a continuous variable because such an odds ratio is calculated per unit of the variable.

§ The categories of expected pain are those from Janssen and coworkers[26] (Figure S1 in the supplementary information).

CI means confidence interval. n/a means not applicable. Hosmer-Lemeshow Chi-square test for NRS-MEP=4.901, P-value=0.768; for unacceptable pain: 2.734, P-value=0.950.

being equal (1.0928 = 2.022, where the exponent 8 is the difference between 9 and 1). A clinically meaningful interpretation of these results is shown in Figure 2. It displays the estimated positive relationship, adjusted for all confounders, between the intensity of postoperative pain identified by the average NRS-MEP and the proportion of patients that suffer from postoperative complications. The latter proportion increases from 0.25 (95 % CI=0.21-0.31) for NRS-MEP=0 to 0.45 (95 % CI=0.36-0.55) for NRS-MEP=10.

When having postoperative pain is operationalized as unacceptable pain at least once in the first three days after surgery, a positive relationship with having complications is also evident. The crude odds ratio for unacceptable pain is 2.27 (95 % CI=1.63-3.17; p<0.001). The adjusted odds ratio of 2.17 (Table 4) estimates that patients who found their pain unacceptable, even if only once, have more than two times the odds of suffering from one or more complications as those who found their pain acceptable across three successive days, other factors being equal.
The results in Table 4 indicate that age and category of expected pain according to the Janssen 3C-classification are strongly associated with the occurrence of postoperative complications, after adjusting for the other covariates.
The adjusted odds ratio associated with a one-year increase in age is 1.019 for the relationship between NRS-MEP and complications as well as the relationship between unacceptable pain and complications (Table 4). Since age was introduced in the model as a continuous variable, this means for example that compared with a 20-year-old patient a patient of 70 years of age has increased odds of 156 % for developing complications, other factors being equal, such as NRS-MEP or unacceptability of pain and class of expected pain (odds ratio for a difference of 50 years is 1.01950 = 2·56).
The adjusted odds ratios estimated for expected pain show that the higher the category of expected pain the higher the chance on complications, other factors kept equal. As these odds ratios range from 2.14 to 2.90, patients who undergo surgery where the pain is expected to be at least moderate have a considerably larger chance to suffer from postoperative complications as those where the expected pain is low at the most.
The covariates BMI, gender, preoperative NRS>7 and specialty do not contribute significantly to the relationships between postoperative pain and complications (Table 4).
The results are not driven by mild (CDC Grade l) complications. Results from extra analyses with the presence of a complication defined as a CDC of ll-V do not differ significantly from the original results (Tables S3a and S3b in the Supplemental Digital Content).
The additional logistic models for each of the three postoperative days did not show any relevant difference between the days (Tables S4a, S4b, S4c in the Supplemental Digital Content). Noteworthy, the statistically significant association between having postoperative pain and the occurrence of postoperative complications already exists on the first postoperative day (Table S4a).

Table 5 Odds ratios obtained from multivariable binary logistic regressions estimating the association between pain on the first postoperative day and the occurrence of a healthcare-associated infection (HAI)*

The presence of a HAI is the dependent variable. HAISs are lung infections, surgical site infections or urinary tract infections. The Numerical Rating Scale (NRS-MEP) or the patient's opinion whether the pain is unacceptable is the primary independent variable. NRS-MEP is the NRS score for movement-evoked pain on day 1 after surgery. Unacceptable pain means having unacceptable pain on day 1 after surgery. Secondary independent variables are potential confounders

		Relationship NRS-MEP — HAIs			Relationship Unacceptable pain — HAIs		
Independent variables		**Odds Ratio**	**(95% CI)**	**P-value**	**Odds Ratio**	**(95% CI)**	**P-value**
Primary variable							
Day 1 NRS-MEP‡		1.161	(1.055-1.279)	0.002	n/a		
Day 1 Unacceptable pain		n/a			2.49	(1.31-4.75)	0.006
Secondary variables							
Continuous							
Age‡		1.036	(1.015-1.057)	0.001	1.035	(1.015-1.056)	0.001
Categorical							
Category expected pain	Lowest and low	1.00	(reference category)		1.00	(reference category)	
	Moderate	4.06	(1.58-10.47)	0.004	4.55	(1.77-11.68)	0.002
	High and highest§	2.97	(1.22-7.24)	0.016	3.61	(1.50-8.68)	0.004

* Here N was 64 because of 6 missings for the NRS or acceptability score.

‡ Three decimals are given for the odds ratio of a continuous variable because such an odds ratio is calculated per unit of the variable.

§ The categories of expected pain are those from Janssen and coworkers (Figure S1 in the Supplemental Digital Content).

CI means confidence interval. n/a means not applicable. Hosmer-Lemeshow Chi-square test for NRS-MEP=4.112, P-value=0.847; for unacceptable pain: 9.184, P-value=0.327.

Having postoperative pain on the first postoperative day, age and class of expected pain are strongly associated with the occurrence of one of three major HAIs: lung infection (N=18), surgical site infection (N=28) and urinary tract infection (N=24) (Table 5). For example, the adjusted odds ratio of 2.49 estimates that patients who found their pain unacceptable on day one have two and a half times the odds of suffering from a HAI as those who found their pain acceptable, age and expected pain being equal.

Discussion

This study suggests that the presence of postoperative pain may contribute to the occurrence of complications after surgery. Our study has four main findings: 1) a considerable part of the patients experienced moderate to severe pain; 2) one third of patients experienced some type of complication within 30 days; 3)

complications were positively associated with the actual postoperative pain as well as with the expected pain as well as age; 4) healthcare-associated infections after surgery were positively associated with the actual pain on the first postoperative day, the expected pain and age.

The incidence of moderate to severe pain after surgery has not improved in recent decades [13]. In 2002, the overall incidence of moderate and severe pain after major surgery was 30 % and 11 %, respectively [40]. In 2008, 41 % of 1,490 inpatients reported moderate or severe pain on day 0, and 30 %, 19 %, 16 % and 14 % on day 1, 2, 3 and 4, respectively [41]. We found that moderate and severe pain occurred in 39 % and 16 % of the patients on the first day after surgery, and that 17 % had unacceptable pain at any moment in the first three days. Although figures vary among studies because of methodological differences, such as the definition of moderate or severe pain, they strongly suggest that there is room for improving postoperative pain management.

The complication rate of 34 % we found is similar to that in studies on colorectal surgery (37.0 %) [42], major operations (36.4 %) [2], and frailty and complications (up to 44 %) [4]. However, it is much higher than the 11 % to 16 % found in studies including all types of surgery [17, 43, 44]. There may be three reasons. First, our study was conducted in a university hospital where more patients needing more complex care tend to be treated than in general hospitals. Moreover, indications for inpatient surgery have been extended to increasingly older patients who are more likely to have more complex medical needs [45]. Our study sample with an average age of 55 (SD=15) years was thus at even higher risk [45]. Second, we retrieved complications from electronic medical records in which the whole hospital-based medical history of a patient is filed. Third, methodological differences, such as definitions, quantity or methods of documentation, hamper comparisons among studies [46, 47]. We used the CDC to retrieve and classify complications. Roughly one half of them were grade I; the other half was grade ll-V, mostly grade ll. The latter findings are in accordance with those of others [1, 17, 48].

Although we found an association between the occurrence of complications after surgery and having postoperative pain, an association does not prove causation [49]. Patients may even have more pain just because a complication is present [50]. However, we doubt whether it is feasible to prove a causal relationship in any other study in humans. As the ERAS program is most successful using an interdisciplinary multifaceted approach, complications may have multifactorial causes. We investigated only one of them, i.e. postoperative pain. Nonetheless, a growing amount of arguments obeying the Bradford Hill criteria [49] lends weight to a potentially causative role of postoperative pain.

First, a plausible mechanism may be responsible for the contribution of pain (cause) to the occurrence of complications (effect). Pain stimulates the neuro-humoral stress response, including an increase in protein catabolism, autonomic activity and levels of cortisol, catecholamines and glucagon [11, 51]. These increased responses may have metabolic, hemodynamic, hemostatic, gastro-intestinal and immune-related consequences [11, 51]. Second, previous studies show that movement-evoked pain has

a negative effect on recovery after surgery [22]. Adequate regional analgesia after major surgery appears to improve outcome [52]. Third, Figure 2 can be regarded as a dose-response relationship, i.e. higher levels of pain lead to more complications [49]. Fourth, the association between having pain on the very first postoperative day and the occurrence of complications somewhere in the postoperative period (Table S4a), suggests that early pain may contribute to the later development of complications. This finding is supported by others who found that adverse postoperative outcomes were less common in hospitals with lowest pain scores on the first postoperative day after colorectal resection [13].

The association we found between having postoperative pain on the morning of the first postoperative day and the occurrence of HAIs strongly supports the theory that postoperative pain may cause complications. It is unlikely that HAIs present themselves on the first morning after surgery. Also, it would be illogical to suppose that the HAI, and not surgery, caused such early-experienced pain. A recent study showed that ERAS and fast track surgery pathways, which advocate excellent postoperative pain management as part of the program, are associated with significant reductions in postoperative HAIs (LI, UTI and SSI) [39]. Therefore we analyzed the data of patients who experienced one of these three major HAIs. Doing so, we even found stronger associations between pain and HAIs (Table 5) than between pain and all sorts of complications (Table 4).

We found that even expected pain may directly and proportionally predict the occurrence of complications (Table 4). This also suggests that the severity of the actual postoperative pain could directly contribute to the number of postoperative complications. However, the expected pain covariate may be correlated with the complexity and operative risk of different procedures. The order of increasing incidence of early severe postoperative pain coincides, to a certain degree, with an order of increasing case complexity (Table S1). However, there are exceptions. If we number the classes from 1 (Lowest) to 5 (Highest expected pain), a tonsillectomy is classified in class 5, whereas upper abdominal surgery with epidural is in class 3. Class 5 for a tonsillectomy is also noteworthy because “Ear nose throat surgery” is class 1. Abdominal surgery without epidural is classified as class 5 (80 %), but abdominal surgery with epidural as class 3 (63 % early severe postoperative pain). This classification therefore reflects, to some extent, pain management. In accordance with Janssen’s work, Gerbershagen and co-workers found that several common minor- to medium-level surgical procedures, including some with laparoscopic approaches, resulted in unexpectedly high levels of postoperative pain. In many surgical procedures, the incision size and extent of tissue trauma were not related to postoperative pain intensity, depending on pain treatment [53].

A limitation of our study is that the study population is too heterogeneous and too small to completely separate the contribution of case complexity to the occurrence of postoperative complications from that of other factors (Table 1). Residual confounding by case complexity and/or operative risk cannot be excluded entirely, despite the use of surgical specialty and Janssen’s classification as covariates. However, to our knowledge, there is no peer-reviewed validated classification of

operative complexity and/or operative risk.
Another limitation of this study was the retrospective grading of complications because of potentially incomplete reporting of complications during routine clinical care. Complications may have remained unnoticed in patients discharged early, but this hypothetical bias is known to every study with in-hospital follow-up [54]. Especially grade I complications may have been under-reported because patients will not always name them, or health care professionals may not record them because of their relatively small therapeutic consequences. We think under-reporting had only a minor effect because, very probably, patients discharged early underwent minor surgery with low expected pain or recovered fast. Results also did not differ significantly between the analyses with or without the mild CDC I complications.
A strong point of the study was that the medical researchers searching for and grading complications could not be involved with the care for the patient because of the retrospective character of their activities. It is thinkable that, in a prospective study, the ongoing research and the researchers' activities could improve the quality of patient's care. Monitoring complications should ideally be performed independently of patient care.

Conclusions

Complications after surgery occurred more often in patients with postoperative pain. Especially, healthcare-associated infections were linked to pain on the first day after surgery. Expected pain and higher age directly predicted the occurrence of 30-day complications. A proactive approach in systematic recording and analysis of postoperative complications, independent of patient care, is important to untangle all relevant causal factors, leading to more personalized risk estimations. Our data strongly support the paradigm that high pain scores in the early postoperative phase may lead to an increased risk of postoperative complications. However, the precise relationship between postoperative pain and the occurrence of complications per type of surgery is still to be determined in future studies.

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Table S1 Surgical Procedures Conducted in Patients of the Amsterdam Cohort, Ordered by Increasing Incidence of Severe Acute Postoperative Pain (Defined as >6 on a Numerical Rating Scale)

Surgical procedure	Incidence %	Severe pain N (total N)
Lowest expected pain		
Endospopic urology	26	7 (27)
Testical surgery (including orchidopexy, biopsy, prosthesis implantation, vasoepididymostomy, testis-scrotum exploration)	27	3 (11)
Eye surgery (including strabismus)	37	43 (116)
Low expected pain		
Pharyngo- and laryngoscopy plus biopsy	40	8 (20)
Ear nose throat surgery	47	130 (277)
Diagnostic laparascopy	48	50 (105)
Gynecologic surgery (nonabdominal nonlaparoscopic)	49	34 (69)
Minor rectal surgery	49	18 (37)
Oral soft tissue surgery	55	21 (38)
Carotid endarterectomy	56	5 (9)
Moderate expected pain		
Skin surgery or lymph node biopsy	58	43 (74)
Peripheral vascular procedures (including varicose veins)	59	26 (44)
Minor breast surgery	61	39 (64)
Procedures on muscle and / or ligaments of extremities	63	75 (119)
Upper abdominal surgery with epidural, including hepato-billiary, esophageal, pancreatic and intestinal surgery	63	19 (30)
High expected pain		
Major breast surgery	67	45 (67
Bone procedures, including cranial / facial, oral, spine, orthopedic / traumatology procedures on clavicle, extremities, hip and pelvis	68	255 (377)
Instrumentation or removal of instrumentation, including spine, hip, jaw / denture, hand / wrist, clavicle, elbow, ankle / foot or knee Arthroscopy of shoulder, hip / pelvis and extremities		
Procedures for abdominal wall herniation	69	42 (61)
Nefrectomy	69	9 (13)
Highest expected pain		
Therapeutic laparoscopic procedures, including laparoscopic cholecystectomy, gynecologic laparoscopy and other therapeutically laparoscopy	76	94 (123)
Intaabdominal surgery without epidural, including colon, bladder, prostate, vascular, and gynecologic surgery	80	49 (61)
Tonsillectomy (in patients over 16 years)	80	37 (46)
Herniated disc surgery	84	16 (19)
Bone procedures including shoulder, thoracotomies, elbow, ankle / foot (exluding instrumentation or removal of instrumentation)	85	86 (101)
Thyroid procedures	86	12 (14)
Peripheral nerve reconstruction	92	12 (13)
Vaginal hysterectomy	100	7 (7)

Surgical procedures ordered by increasing incidence of severe acute postoperative pain (NRS MEP ≥ 6) from: Janssen KJ, Kalkman CJ, Grobbee DE, Bonsel GJ, Moons KG, Vergouwe Y. The risk of severe postoperative pain: modification and validation of a clinical prediction rule. Anesthesia and analgesia. 2008;107(4):1330-9.

Table S2 Classification of surgical complications

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, and radiological interventions Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IIIa	Intervention not under general anesthesia
Grade IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management
Grade IVa	Single organ dysfunction
Grade IVb	Multi organ dysfunction
Grade V	Death of a patient
Suffix "d"	If the patient suffers from a complication at the time of discharge (see examples in Table 2), the suffix "d" (for "disability") is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication

* Brain hemorrhage, ischemic stroke, subarrachnoidal bleeding, but excluding transient ischemic attacks. CNS, central nervous system; IC, intermediate care; ICU, intensive care unit. Classification of Surgical Complications from Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Annals of surgery. 2004;240(2):205-13.

Table S3a Odds ratios obtained from multivariable binary logistic regressions estimating the association between NRS-MEP and complications*

The "extra relationship" uses only CD2-CD4 as complications. The presence of a complication is the dependent variable. The Numerical Rating Scale (NRS-MEP) is the primary independent variable. NRS-MEP is the average NRS of movement-evoked pain in the first three days after surgery. Secondary independent variables are potential confounders.

		Relationship from manuscript NRS-MEP — Complications			Extra relationship Unacceptable pain — Complications		
Independent variables		**Odds Ratio**	**(95% CI)**	**P-value**	**Odds Ratio**	**(95% CI)**	**P-value**
Primary variable							
Average NRS-MEP‡		1.092	(1.027-1.161)	0.005	1.192	(1.101-1.292)	<0.001
Secondary variables							
Continuous							
Age‡		1.019	(1.009-1.030)	<0.001	1.025	(1.010-1.040)	0.002
Body Mass Index‡		1.022	(0.991-1.055)	0.166	1.036	(0.994-1.079)	0.094
Dichotomous							
Female gender		0.83	(0.61-1.13)	0.228	0.62	(0.40-0.94)	0.024
Preoperative NRS > 7		1.30	(0.82-2.06)	0.258	0.80	(0.42-1.53)	0.497
Categorical							
Medical specialty	Other surgeries	1.00	(reference category)		1.00	(reference category)	
	General surgery	1.39	(0.65-2.99)	0.397	2.15	(0.70-6.62)	0.182
	Orthopedics	0.84	(0.37-1.91)	0.685	1.09	(0.33-3.64)	0.886
	Urology	2.03	(0.90-4.55)	0.088	3.53	(1.11-11.22)	0.032
	Gynecology	2.09	(0.86-5.11)	0.106	2.29	(0.62-8.42)	0.211
	ENT	1.79	(0.71-4.50)	0.214	1.25	(0.32-4.98)	0.748
	Eye surgery	0.47	(0.09-2.46)	0.368	0.75	(0.07-7.73)	0.808
	Plastic surgery	1.04	(0.42-2.58)	0.939	1.88	(0.51-6.89)	0.343
	Neurosurgery	1.09	(0.43-2.74)	0.859	1.15	(0.30-4.44)	0.838
	Oro-maxillofacial surgery	0.66	(0.22-1.93)	0.443	0.61	(0.10-3,73)	0.594
Category expected pain	Lowest and low	1.00	(reference category)		1.00	(reference category)	
	Moderate	2.14	(1.26-3.64)	0.005	1.63	(0.83-3.20)	0.160
	High and highest§	2.82	(1.79-4.42)	<0.001	1.75	(0.99-3.09)	0.055

*Here N was 988 because of 26 missings for the covariate 'preoperative NRS > 7'.

‡ Three decimals are given for the odds ratio of a continuous variable because such an odds ratio is calculated per unit of the variable.

§ The categories of expected pain are those from Janssen and coworkers (Tabel S1).

CI means confidence interval.

Table S3b Odds ratios obtained from multivariable binary logistic regressions estimating the association between unacceptable pain and complications*

The "extra relationship" uses only CD2-CD4 as complications. The presence of a complication is the dependent variable. The patient's opinion whether the pain is unacceptable is the primary independent variable. Secondary independent variables are potential confounders.

		Relationship from manuscript NRS-MEP — Complications			Extra relationship Unacceptable pain — Complications		
Independent variables		**Odds Ratio**	**(95% CI)**	**P-value**	**Odds Ratio**	**(95% CI)**	**P-value**
Primary variable							
Unacceptable pain		2.17	(1.51-3.10)	<0.001	2.48	(1.62-3.79)	<0.001
Secondary variables							
Continuous							
Age‡		1.019	(1.009-1.030)	<0.001	1.023	(1.008-1.037)	0.002
Body Mass Index‡		1.022	(0.990-1.055)	0.176	1.035	(0.993-1.078)	0.104
Dichotomous							
Female gender		0.84	(0.61-1.15)	0.266	0.63	(0.42-0.97)	0.033
Preoperative NRS > 7		1.38	(0.88-2.17)	0.164	0.93	(0.49-1.77)	0.835
Categorical							
Medical specialty	Other surgeries	1.00	(reference category)		1.00	(reference category)	
	General surgery	1.50	(0.70-3.22)	0.301	2.55	(0.83-7.82)	0.102
	Orthopedics	0.92	(0.40-2.08)	0.834	1.31	(0.39-4.36)	0.660
	Urology	2.16	(0.96-4.86)	0.062	4.23	(1.34-13.40)	0.014
	Gynecology	2.14	(0.88-5.25)	0.095	2.54	(0.69-9.31)	0.159
	ENT	1.85	(0.74-4.65)	0.190	1.42	(0.36-5.62)	0.615
	Eye surgery	0.50	(0.09-2.61)	0.409	0.83	(0.08-8.48)	0.872
	Plastic surgery	1.12	(0.45-2.78)	0.815	2.18	(0.59-8.00)	0.240
	Neurosurgery	1.16	(0.46-2.93)	0.753	1.39	(0.36-5.36)	0.629
	Oro-maxillofacial surgery	0.65	(0.22-1.92)	0.437	0.66	(0.11-4.00)	0.650
Category expected pain	Lowest and low	1.00	(reference category)		1.00	(reference category)	
	Moderate	2.16	(1.27-3.67)	0.005	1.80	(0.92-3.52)	0.085
	High and highest§	2.90	(1.86-4.55)	<0.001	1.95	(1.11-3.43)	0.020

*Here N was 988 because of 26 missings for the covariate 'preoperative NRS > 7'.

‡ Three decimals are given for the odds ratio of a continuous variable because such an odds ratio is calculated per unit of the variable.

§ The categories of expected pain are those from Janssen and coworkers (Tabel S1).

CI means confidence interval.

Table S4a Day one after surgery: odds ratios obtained from multivariable binary logistic regressions*

The presence of a complication is the dependent variable. The Numerical Rating Scale (NRS-MEP) or the patient's opinion whether the pain is unacceptable is the primary independent variables. NRS-MEP is the NRS of movement-evoked pain of day one after surgery. Unacceptable pain means having unacceptable pain on that particular day. Secondary independent variables are potential confounders.

		Relationship NRS-MEP — Complications			Relationship Unacceptable pain — Complications		
Independent variables		**Odds Ratio**	**(95% CI)**	**P-value**	**Odds Ratio**	**(95% CI)**	**P-value**
Primary variable							
Average NRS-MEP‡		1.062	(1.007-1.121)	0.028	n/a		
Unacceptable pain		n/a			2.05	(1.34-3.15)	0.001
Secondary variables							
Continuous							
Age‡		1.019	(1.008-1.029)	<0.001	1.018	(1.008-1.029)	0.001
Body Mass Index‡		1.022	(0.990-1.054)	0.177	1.023	(0.991-1.055)	0.164
Dichotomous							
Female gender		0.83	(0.61-1.13)	0.225	0.84	(0.61-1.14)	0.257
Preoperative NRS > 7		1.37	(0.87-2.16)	0.174	1.41	(0.90-2.21)	0.133
Categorical							
Medical specialty	Other surgeries	1.00	(reference category)		1.00	(reference category)	
	General surgery	1.45	(0.68-3.11)	0.339	1.59	(0.74-3.41)	0.236
	Orthopedics	0.87	(0.38-1.96)	0.733	0.94	(0.41-2.12)	0.873
	Urology	2.13	(0.95-4.78)	0.067	2.36	(1.05-5.29)	0.038
	Gynecology	2.13	(0.87-5.21)	0.097	2.30	(0.94-5.62)	0.068
	ENT	1.85	(0.74-4.65)	0.189	1.92	(0.76-4.82)	0.165
	Eye surgery	0.47	(0.09-2.49)	0.376	0.51	(0.10-2.66)	0.420
	Plastic surgery	1.09	(0.44-2.69)	0.860	1.16	(0.47-2.90)	0.743
	Neurosurgery	1.13	(0.45-2.84)	0.794	1.26	(0.50-3.17)	0.623
	Oro-maxillofacial surgery	0.68	(0.23-2.01)	0.488	0.69	(0.23-2.02)	0.495
Category expected pain	Lowest and low	1.00	(reference category)		1.00	(reference category)	
	Moderate	2.18	(1.28-3.71)	0.004	2.21	(1.30-3.76)	0.003
	High and highest§	2.85	(1.81-4.48)	<0.001	2.97	(1.90-4.64)	<0.001

*Here N was 988 because of 26 missings for the covariate 'preoperative NRS > 7'.

‡ Three decimals are given for the odds ratio of a continuous variable because such an odds ratio is calculated per unit of the variable.

§ The categories of expected pain are those from Janssen and coworkers (Table S1).

CI means confidence interval. n/a means not applicable. Hosmer-Lemeshow Chi-square test for NRS-MEP=3.134, P-value=0.926; for unacceptable pain: 3.228, P-value=0.919.

Table S4b Day two after surgery: odds ratios obtained from multivariable binary logistic regressions*

The presence of a complication is the dependent variable. The Numerical Rating Scale (NRS-MEP) or the patient's opinion whether the pain is unacceptable is the primary independent variables. NRS-MEP is the NRS of movement-evoked pain of day two after surgery. Unacceptable pain means having unacceptable pain on that particular day. Secondary independent variables are potential confounders.

		Relationship NRS-MEP — Complications			Relationship Unacceptable pain — Complications		
Independent variables		**Odds Ratio**	**(95% CI)**	**P-value**	**Odds Ratio**	**(95% CI)**	**P-value**
Primary variable							
Average NRS-MEP‡		1.071	(1.013-1.133)	0.016	n/a		
Unacceptable pain		n/a			1.62	(1.03-2.55)	0.035
Secondary variables							
Continuous							
Age‡		1.019	(1.009-1.030)	<0.001	1.018	(1.007-1.028)	0.001
Body Mass Index‡		1.022	(0.991-1.055)	0.163	1.022	(0.991-1.055)	0.167
Dichotomous							
Female gender		0.83	(0.61-1.13)	0.244	0.83	(0.61-1.13)	0.227
Preoperative NRS > 7		1.34	(0.85-2.11)	0.215	1.43	(0.91-2.24)	0.119
Categorical							
Medical specialty	Other surgeries	1.00	(reference category)		1.00	(reference category)	
	General surgery	1.40	(0.65-3.01)	0.384	1.54	(0.72-3.30)	0.267
	Orthopedics	0.86	(0.38-1.94)	0.712	0.94	(0.42-2.12)	0.879
	Urology	2.04	(0.91-4.58)	0.085	2.24	(1.00-5.01)	0.050
	Gynecology	2.13	(0.87-5.19)	0.098	2.37	(0.97-5.79)	0.059
	ENT	1.81	(0.72-4.54)	0.206	1.95	(0.78-4.89)	0.154
	Eye surgery	0.46	(0.09-2.44)	0.364	0.49	(0.09-2.60)	0.404
	Plastic surgery	1.04	(0.42-2.57)	0.940	1.14	(0.46-2.83)	0.777
	Neurosurgery	1.11	(0.44-2.79)	0.830	1.21	(0.48-3.04)	0.684
	Oro-maxillofacial surgery	0.65	(0.22-1.92)	0.438	0.69	(0.24-2.03)	0.500
Category expected pain	Lowest and low	1.00	(reference category)		1.00	(reference category)	
	Moderate	2.17	(1.28-3.69)	0.004	2.29	(1.35-3.88)	0.002
	High and highest§	2.88	(1.84-4.52)	<0.001	3.07	(1.96-4.80)	<0.001

*Here N was 988 because of 26 missings for the covariate 'preoperative NRS > 7'.

‡ Three decimals are given for the odds ratio of a continuous variable because such an odds ratio is calculated per unit of the variable.

§ The categories of expected pain are those from Janssen and coworkers (Tabel S1).

CI means confidence interval. n/a means not applicable. Hosmer-Lemeshow Chi-square test for NRS-MEP=5.827, P-value=0.667; for unacceptable pain: 5.357, P-value=0.719.

Table S4c Day three after surgery: odds ratios obtained from multivariable binary logistic regressions*

The presence of a complication is the dependent variable. The Numerical Rating Scale (NRS-MEP) or the patient's opinion whether the pain is unacceptable is the primary independent variables. NRS-MEP is the NRS of movement- evoked pain of day three after surgery. Unacceptable pain means having unacceptable pain on that particular day. Secondary independent variables are potential confounders.

		Relationship NRS-MEP — Complications			Relationship Unacceptable pain — Complications		
Independent variables		**Odds Ratio**	**(95% CI)**	**P-value**	**Odds Ratio**	**(95% CI)**	**P-value**
Primary variable							
Average NRS-MEP‡		1.098	(1.035-1.165)	0.002	n/a		
Unacceptable pain		n/a			2.03	(1.26-3.27)	0.003
Secondary variables							
Continuous							
Age‡		1.020	(1.009-1.030)	<0.001	1.019	(1.008-1.029)	<0.001
Body Mass Index‡		1.023	(0.992-1.056)	0.149	1.023	(0.991-1.055)	0.164
Dichotomous							
Female gender		0.83	(0.61-1.13)	0.234	0.83	(0.61-1.14)	0.245
Preoperative NRS > 7		1.30	(0.82-2.05)	0.261	1.45	(0.93-2.27)	0.104
Categorical							
Medical specialty	Other surgeries	1.00	(reference category)		1.00	(reference category)	
	General surgery	1.37	(0.64-2.95)	0.421	1.50	(0.70-3.21)	0.300
	Orthopedics	0.83	(0.37-1.88)	0.654	0.90	(0.40-2.03)	0.790
	Urology	1.99	(0.88-4.48)	0.096	2.12	(0.95-4.77)	0.068
	Gynecology	2.09	(0.85-5.11)	0.107	2.18	(0.89-5.33)	0.088
	ENT	1.76	(0.70-4.41)	0.231	1.85	(0.74-4.65)	0.190
	Eye surgery	0.46	(0.09-2.43)	0.361	0.47	(0.09-2.46)	0.370
	Plastic surgery	1.03	(0.41-2.55)	0.957	1.11	(0.45-2.75)	0.830
	Neurosurgery	1.17	(0.42-2.70)	0.887	1.15	(0.46-2.90)	0.764
	Oro-maxillofacial surgery	0.64	(0.22-1.90)	0.421	0.69	(0.23-2.02)	0.496
Category expected pain	Lowest and low	1.00	(reference category)		1.00	(reference category)	
	Moderate	2.13	(1.25-3.63)	0.005	2.17	(1.28-3.70)	0.004
	High and highest§	2.86	(1.83-4.49)	<0.001	2.98	(1.90-4.66)	<0.001

*Here N was 988 because of 26 missings for the covariate 'preoperative NRS > 7'.

‡ Three decimals are given for the odds ratio of a continuous variable because such an odds ratio is calculated per unit of the variable.

§ The categories of expected pain are those from Janssen and coworkers (Table S1).

CI means confidence interval. n/a means not applicable. Hosmer-Lemeshow Chi-square test for NRS-MEP=3.530, P-value=0.897; for unacceptable pain: 0.889, P-value=0.999.

General discussion

7

Adequate postoperative pain management is essential to keep patients comfortable, help them to quickly recover, and to prevent postoperative complications. Several authors have reported on insufficient postsurgical pain management, concluding that there is room for improvement [1, 2].
The foremost aim of the work presented in this thesis was to explore the quality of postoperative pain management in hospitals. To achieve this, we used the Donabedian model, selecting a set of factors from each of its three categories: structure, process and outcome [3].

In the discussion, we summarize our findings of seven separate studies in relation to the current situation regarding postoperative pain care, and relate these to the findings from other international research groups, providing directions for future research. We have formulated several recommendations to improve clinical practice, education and research.

Quality of care of postoperative pain management

APS teams in Dutch hospitals

The presence of an APS team in a hospital is mandatory and requested until 2006 by annual reports to the Health Care Inspectorate*. To date, no studies have been published on the organization and procedures of APS teams in the Netherlands. We therefore set up and conducted a survey, using an online questionnaire sent to all 96 Dutch hospitals performing surgical procedures (Chapter 2).
We found that 90 % of Dutch hospitals reported having an APS. The majority of APS teams are nurse based and supervised by an anesthesiologist. APS members standardly visit postoperative patients with complex pain management therapies such as regional analgesia or patient-controlled analgesia. All APS teams have educational tasks. However, 13 % of the APS teams did not participate in quality improvement projects, and nearly no APS teams were involved in pain research.
As in other countries, most APS teams in the Netherlands consist of anesthesiologists and nurses [4-6]. Patient-related activities in the Dutch APS teams are comparable with activities in APS teams in other countries. In our study sample, we found a division into two main forms of APS teams: specially dedicated and integrated dedicated teams. The first solely have duties related to APS, the latter combine APS with other duties. This second group therefore may spend less time on non-patient-related activities such as education, research and quality improvement by evaluating pain scores and making protocol adjustments; all these are generally considered important components of the APS [7-13]. These data from the Dutch hospitals indicate that most APS teams focus on direct individual patient care

* Dutch Health Care Inspectorate. Basic set for quality indicators for hospitals 2011 [cited 2012 19 May]. Available from: www.ziekenhuizentransparant.nl

without evaluating service provision at a group level. Our data also suggest that organization and procedures of APS teams in Dutch hospitals differ greatly. We note that this is similar to the situation in Germany and in the UK, where APS teams show a wide structural variation in both organization and procedures. In Germany, a recent report on the structure and processes of APS teams noted that APS teams in many hospitals are still "catheter- service" teams, like those once initiated by Ready and co-authors in 1988 [14]. In the UK, Duncan and co-workers set up the National InPatient Pain Study (NIPPS) project in 2009 [15, 16]. In this project, data from all admissions to the acute pain service of different national hospitals were digitally collected in a database. Their study revealed the wide variation in service provision of acute pain services in the UK, and related this to complex organizational and cultural barriers as well as a lack of service evaluation [15, 16].
In theory, optimally functioning APS teams should perform all patient-related and non-patient-related tasks as described by a number of authors, e.g. Rawal and co-workers and Breivik and co-workers [7-13]. Whether or not organizational differences in APS teams regarding performing these tasks influence the outcome of postoperative patients is unknown.
Now that APS teams are common in the Netherlands, further studies are needed to specify in what way these organizational differences (special versus integrated dedicated and exclusively patient-related versus non-patient-related activities included) relate to quality of care and patient outcome measures, i.e. postoperative pain intensity and complications.

Dutch Hospital Patient Safety Program: pain assessments

In 2010, the Dutch Hospital Patient Safety Program (DHPSP) was introduced in almost all Dutch Hospitals providing practice guidelines on pain assessment and pain treatment. One of the guidelines prescribed that pain should be assessed at least every eight hours and consistently documented in a patient's medical record. A few years after the program started, the question arose with regards to the extent that the DHPSP had been implemented, so we conducted two studies (Chapter 2 and 3) using different methods to answer this question. Our first study was an online survey among hospital contact persons asking for their opinion on the implementation of the DHPSP guidelines, especially with regard to pain assessment in their hospital. In the second study, we evaluated 3,895 patient records from 16 hospitals regarding the frequency of documented standardized pain assessments.

Hospitals: compliance with pain assessment is good!

In our first survey, we achieved a response rate of 83 % (Chapter 2). The hospital contact respondents indicated that almost all hospitals had pain protocols in place and that they assessed pain in surgical patients. They also reported that the DHPSP guidelines on pain assessment had been almost fully implemented. The majority of hospitals assessed movement evoked pain (MEP) as well as pain at rest (PAR)

at least three times a day. Almost half of the responding hospitals assessed pain during the entire hospitalization of the patient.
The extent of bias in self-reported outcomes of guideline implementation is known to be substantial and may produce an overestimation of performance [17]. One of the reasons is social desirability: to report socially desirable behavior when questioned even when the adherence to a social norm is not optimal. In the Netherlands, the need to adhere to the norm of the DHPSP may be great, possibly biasing the results in our study. Therefore, in the second study, we evaluated patient records concerning the frequency of documented standardized pain assessments.

Patient records: compliance with pain assessment is inadequate!

In the second study, we analyzed secondary data on the compliance with DHPSP guidelines, based on two data sources: (1) data from an evaluation study of the DHPSP, based on evaluation of patient records performed by the Netherlands Institute for Health Services Research (NIVEL); and (2) data from the digital questionnaire survey described in chapter 3. In this study, we matched data from hospitals included in both data sources. Our results show that the process indicators of DHPSP (percentage postoperative patients with ≥3 pain assessments a day, all 3 full days after surgery: 12 %), and the process indicator of the Health Care Inspectorate based on patient records (percentage postoperative patients with ≥1 pain assessment a day, all 3 full days after surgery: 53 %) and the process indicator of the Health Care Inspectorate as reported by the included hospitals (78 %), were not in line with each other.
In other countries like Canada [18] and Scotland [19], Safety Programs have been installed, however, limited or no data is available on specific themes, such as pain. Additionally, differences in assessments and the data collection method make it impossible to compare our results with those of other national programs. Therefore, we were only able to evaluate the situation in the Netherlands on this topic.
The discrepancy between reported and observed proportions of pain assessments may be partly explained by different interpretations of the definition of the process indicator of the Health Care Inspectorate. Furthermore, if pain was assessed or documented but not in a standardized manner (NRS or VAS), it was not included as an assessment in this second study, yet it could be reported as assessment to the Health Care Inspectorate. Another explanation may be the external pressure to publish the process indicator, which determines the position of the hospital on various ranking lists [20].
Our two different study designs yielded different results. Up to now, the optimal frequency of pain assessments is unclear and depends on the needs of an individual patient. Frequent assessment of pain in patients provides information enabling a decision to be made on interventions enhancing optimal pain relief [21] It is important that pain intensity is assessed regularly, using a standardized instrument [22]. Compliance with the process indicator asking for ≥1 pain assessments a day was not higher than 53 %, so this is not in line with the definition ‘assessed regularly’.

Thus there is scope to improve the nurses' adherence to pain assessment recommendations.
To develop implementation strategies, we analyzed whether hospital characteristics or APS characteristics influenced the compliance of health professionals with the guidelines on pain assessment. The analysis is discussed in the following section.
To conclude from both studies, we were able to show that it is not sufficient only to ask for implementation progression, but that data on the exact methods of pain assessment and documentation is also necessary. Feedback on these processes may help further improve adherence to pain assessment. Further research should focus on a multifaceted implementation strategy, addressing good education on the importance of pain assessment itself, the disappearance of organizational barriers, and feedback on personal performance of nurses [23].

Surgery shows best compliance with pain assessment!

In our second study, we also investigated whether hospital characteristics or APS characteristics influence the compliance of health professionals with the pain assessment guidelines (Chapter 3). We found that type of hospital and type of department influenced the compliance with postoperative pain assessment. Based on patient records, general hospitals reported a better compliance with pain assessments, both regarding ≥3 pain assessments a day and ≥1 pain assessment a day (11 % and 59 % respectively) compared to tertiary teaching (2 % and 27 % respectively) and academic hospitals (7 % and 56 % respectively). Between departments, compliance was relatively high for patients admitted to the surgical oncology department and to the surgery and orthopedics departments, compared to other departments.
APS factors were not associated with the compliance with pain assessment, except for the presence of a training program by the APS for nurses and/or physicians. Those hospitals had a lower compliance with pain assessment.
Studies on compliance with pain assessment are scarce. In a study by Nicholas and co-workers investigating hospital process compliance and surgical outcomes, the researchers determined whether high rates of compliance with perioperative process of care measures used for public reporting and pay-for-performance were associated with lower rates of risk-adjusted mortality and complications with high-risk surgery [24]. They found that process compliance ranged from 54 % in low compliance hospitals to 91 % in the highest, supporting differences between hospitals in compliance with perioperative process indicators [24]. Other factors, however, might play a role in the varying compliance, for example hospital or department culture, priorities of the organization, education possibilities or research; these were not studied [25].
The higher compliance for assessing pain in patients admitted to the surgical oncology department and to the surgery and orthopedics departments compared to the other departments may be explained by the relatively high percentage of patients with pain in these departments [26, 27]. It is likely that assessing pain in these

departments has greater priority, be part of the daily routine, and embedded in ward-specific protocols of these medical specialties. This finding is supported by a study by Chang and co-workers investigating pain management in medical wards in the United Kingdom. They found that pain was assessed in the medical wards in only 18 % of the hospitals [28]. One of the reasons was that time and staff shortages in some hospitals meant that many APS teams were only just coping with the management of acute pain in surgical patients, leaving few resources for medical patients. In another study on pain assessment in different wards of a tertiary care hospital, Anwar-ul-Huda and co-workers showed that regular pain assessment was performed for all the patients in the surgical ward and was also reasonably good in the emergency room (60 %) but much lower (24 %) in the medical ward. The authors concluded that this was probably because the surgical ward was managed by a team of the Acute Pain Management Service [29].

Since the presence of APS teams may enhance postoperative pain management, it is not clear why hospitals with an APS training program for nurses and/or physicians in our study had a lower compliance on pain assessment. Education of nurses in pain management has been shown to improve nurses' knowledge of pain, leading to a better compliance to guidelines on pain management [30]. Additionally, pain education may be organized in various ways. Hospitals with no APS training programs could have a hospital-wide program whereby the hospital takes responsibility for the training course, and possibly more personnel could therefore be trained in pain management. Successful use of guideline recommendations in clinical practice not only depends on education alone, but on the availability of staff and time, cooperation with other professionals, and attitudes of personnel [31-33]. Implementation is influenced by the attitude of nurses and doctors, so that a negative attitude toward pain assessment and treatment forms a barrier to implementing practice change [34]. Compliance may also decrease if the interval between periodical training is too long [35]. In our studies, we did not record information about participation, experiences with, and duration of the training.

A high compliance to postoperative pain guidelines is often seen as the way to improve the outcome of pain management after surgery [36]. However, a study by Nicholas and co-workers showed that a high compliance with perioperative process indicators did not automatically mean that the chance of complications after surgery was reduced [24]. Nevertheless, as discussed earlier, future research should focus on multifaceted implementation strategies to improve the nurses' adherence to pain assessment while taking into account different influencing factors. Furthermore, the role of APS teams in medical wards should be investigated and the relationship between the compliance with pain assessment and patient outcomes needs to be addressed.

High prevalence of moderate to severe postoperative pain in surgical patients!

Several studies describe a high overall prevalence of moderate to severe postoperative pain in surgical patients, also in the Netherlands [1, 2, 37-39]. These figures range from 41 %-65 % patients, and are more or less constant over time [15, 40].
We therefore conducted two studies to investigate the prevalence of pain in our hospital, as well as the incidence of complications. The first study was performed on prospectively collected pain assessments of patients following major surgery (Chapter 4). The second study was performed on data of a prospectively recruited cohort of patients undergoing a broad range of surgical procedures (Chapter 6).
Our first study showed that the overall percentage of patients with moderate to severe pain on day 1-4 after surgery based on movement evoked numerical rating scale pain (NRS-MEP) scores were 50.3 % and 9.2 % respectively. In the second study, 39.2 % and 15.8 % of the patients reported moderate to severe pain respectively on day one after surgery; 37.0 % and 10.2 % on day two; and 32.1 % and 6.3 % on day 3. Overall, 16.8 % of the patients reported unacceptable pain on one of the first three postoperative days. In a Dutch study conducted in 2008, moderate or severe pain after surgery was reported by 41 % of the patients on day 0, 30 % on day 1, 19 % on day 2, 16 % on day 3, and 14 % on day 4 [2]. These percentages are comparable with other studies on the prevalence of postoperative pain [1, 37, 41].
Although studies differ in research methodology, such as the choice of pain measurement tool, the definition of moderate or severe pain and the time frame of observation, all studies show that the number of patients experiencing moderate to severe pain remains high. This suggests that there is great room for improvement. We need to find out more about the differences between those patients who recover quickly and without any complications and those who, after a number of days, still have moderate or severe pain and those who develop complications.
Reducing the prevalence of moderate to severe postoperative pain may be possible by implementing personalized procedure specific pain treatment. Several risk factors for the development of postoperative pain have been identified, such as gender, age, type of surgery, anxiety, pain catastrophizing and preoperative chronic pain intensity [42-44]. In a recent multicenter study, Guntinas-Lichius and co-workers noted inter-hospital variability of pain after tonsillectomy, claiming that other extrinsic factors influence the pain experience [45]. These may include hospital-related parameters like availability of APS teams and protocols, staff training, environmental influences, and factors like dedication and empathy of doctors and nurses. Personalized procedure specific pain treatment may be possible when all known risk factors contributing to the patient's personal pain experience are taken into account preoperatively and used to balance treatment options [46, 47].
Another patient-related factor is the patients' ability to accept pain. In our second study, only 16.8 % of patient found the pain to be unacceptable on day 1-3 after surgery, despite the high prevalence based on NRS-MEP scores. Therefore, inter-individual and inter-hospital variability in postoperative pain experience need

to be further explored in order to improve postoperative pain management for the individual patient.

Regional anesthesia superior to PCIA!

One factor of hospital variability is the hospital protocol on pain treatment after different surgical procedures. We performed a study on prospectively collected pain data of patients after major surgery to investigate whether regional anesthesia provided superior pain relief compared to patient-controlled intravenous analgesia in patients undergoing abdominal surgery, thoracotomy, and extremity surgery (Chapter 4). Although there was a great variation in pain scores, results showed that those patients who received regional anesthesia reported lower pain scores than those who received patient controlled intravenous analgesia (PCIA), after undergoing the same surgical procedures. Additionally, pain at rest (PAR) scores were significantly lower than MEP scores.

Srikandarajah and co-workers estimated the frequency of reported MEP scores versus reported PAR scores in postsurgical clinical trials and meta-analyses [48]. They found that MEP is generally more severe in intensity than PAR [48]. Furthermore, MEP has an adverse impact on surgical site-related physiological function [49], and that interventions resulting in less severe MEP were associated with fewer postoperative thrombo-embolic and pulmonary complications [50, 51]. MEP adversely impacts upon patient ambulation and functional recovery in the early postoperative period [52]. They recommended that MEP should be assessed and reported as outcome in every postsurgical trial. We also noted the difference between MEP scores and PAR scores in our study, so we strongly support this statement and used the NRS-MEP in our next studies.

Although there were large variations in pain scores, results of our study showed that patients who received regional anesthesia reported lower pain scores than those who received PCIA. Pöpping and co-workers reviewed the data of 18,925 patients who had undergone major surgery on the quality of pain relief, major complications, and adverse effects [53]. They also reported that regional anesthesia was superior to PCIA. Furthermore, they noted that close supervision of these techniques by an APS team in the postoperative period is mandatory, as they are potentially dangerous if not applied professionally. In a study by Guntinas-Lichius and co-workers, inter-hospital variability of postoperative pain scores was reported. As shown in our study, different pain treatment techniques for the same surgical procedures in different hospitals may be one of the causes of this variation [45].

The large variability on pain scores highlights the personal experience of pain as being something greater than tissue damage triggering a response from the nervous system, and that it is influenced by several other factors. Therefore, as stated in the previous section, future research should focus on personalized pain assessment and pain treatment to improve clinical practice for the individual patient.

One in five patients accept their pain and show normal physical activities even with high pain scores!

In the clinical setting, patients may report a high MEP, yet claim their pain is acceptable. Van Dijk and co-workers showed that some patients and pain professionals interpret pain scores differently [54]. We therefore conducted a study to quantify relationships between NRS and other methods of pain assessment, such as the patients' willingness to accept pain and the functional capacity.
In this study (Chapter 5) we found that low pain scores do not always mean that patients find their pain acceptable. Nor do high pain scores necessarily mean that patients find their pain unacceptable. Approximately one in ten patients reported a low NRS-MEP of 0, 1, 2, 3 or 4, but had unacceptable pain. Despite a high pain score of NRS-MEP=7, at least one in five patients were willing to accept their pain and, at the same time, perform the required physical activities. Therefore, we can conclude that caregivers, in order to make adequate clinical decisions, should use multidimensional assessments of pain, and move beyond the sole use of cut-off points on the NRS.
Although ours was the first study to quantify the relationships between NRS-MEP and acceptability of pain, functional impact of pain, and a measure combining the two as a clinically desirable situation, other authors have found similar results.
Van Dijk and co-workers reported that many patients with a high pain score did not want to use opioids when having a high pain score, because they considered their pain "tolerable" [55]. They concluded that patients have a different view on NRS cut-off scores; many patients consider NRS scores 4, 5 and 6 as bearable, and prefer not to take analgesics [21]. Maroney and co-workers observed that 31 % of 1,249 patients who reported severe pain on a four-item scale, found their pain acceptable [56].
To fully estimate patients' experience of pain, a single NRS score alone is not sufficient for decision-making. To balance treatment options, other dimensions of pain should be assessed [57, 58]. A combination of patient opinion and nurse observation is a requirement when communicating with the patient, as this results in a better understanding of the particular pain score without being judgmental [21].
Our study did not include outcome data, so no effect could be measured of the multidimensional pain assessment. Future research should therefore focus on pain-related outcomes in relation to multidimensional pain assessment and treatment decisions.

Postoperative complications directly related to postoperative pain!

In recent years, reports of inadequate management of acute postoperative pain have suggested that postoperative pain is associated with severe effects on patient outcomes, delaying the patients' physical recovery after surgery, as well as reducing quality of life [38, 59].
Results from our study on the relationship between postoperative pain and

complications after surgery (Chapter 6) show that postoperative pain may contribute to the occurrence of complications after surgery. We showed that one third (33.8 %) of postoperative patients experienced some type of complication. Additionally, complications after surgery were positively associated with the actual postoperative pain, the expected pain, as well as with age. Furthermore, subgroup analysis showed that healthcare-associated infections after surgery were positively associated with the actual pain on the first postoperative day, the expected pain and age.

We found a relatively high complication rate. This overall complication rate is comparable with several other studies in this field, for example Mayo and co-workers reported on colorectal surgery (37.0 %) [60], Ghaferi and co-workers on major operations (36.4 %) [61] and Makary and co-workers on frailty and complications (up to 43.5 %) [62]. However, the complication rate in our study is much higher than that found in three other studies in which all surgery was included (10.8 % [63], 11.0 % [64], and 16.4 % [65]. We propose three reasons for our high complication rate: (1) our study was conducted at a university hospital where patients with more complex diagnoses requiring more complex care are treated compared to general hospitals, (2) complications were retrieved from full digital medical records in which all hospital- based medical history of the patients was filed, and (3) it is difficult to compare complication rates between studies due to methodological differences such as definitions, quantity or methods of documentation [66, 67].

We showed an association between the occurrence of complications after surgery and having postoperative pain, with analyses of NRS-MEP, as well as with a separate acceptability question on whether the postoperative pain was acceptable or not. We argue that there is a causal relationship however this is not proven; in theory, patients may simply have more pain because a complication is present [68]. However, the association we found between having postoperative pain on the morning of the first postoperative day and the occurrence of healthcare-associated infections (HAIs) strongly supports the theory that postoperative pain contributes to developing complications. It is unlikely that HAIs present themselves on the first morning after surgery. However, we can state that both less postoperative pain and/or less complications after surgery would be beneficial for patients.

Our results suggest that the quality of acute postoperative pain management can be improved by the awareness of early detection and treatment of postoperative pain. Even though we do not understand the exact relationship between postoperative pain intensity and complications, and whether adequate postoperative pain management prevents HAIs, we can state that postoperative pain is a good indicator of future complications.

One limitation of our study was the retrospective grading of complications because of potentially incomplete reporting during routine clinical care. Future research should focus on the early detection of pain and complications in a full prospective study.

Critical analysis of the research methodology

A great strength of our studies on APS teams presented in Chapters 2 and 3 was the high response rate of the national survey (83 %), resulting in an accurate overview of the Dutch APS teams. The two studies performed using the consecutive patient data gathered during five years of clinical practice of the APS, the study on regional anesthesia versus patient controlled intravenous analgesia presented in Chapter 4, and the study on the relationship between NRS and other methods of pain assessment reported in Chapter 5, were based on clinically collected real-time documentation of patient consultations of more than 9,000 patients who underwent major surgery. These data give a realistic valuable reflection of clinical practice.
A strong point of our study on the relationship between postoperative pain and complications noted in Chapter 6 was the inclusion of a patient mix of many surgical specialties and types of surgery, with or without co-morbidities, as a representation of real-world clinical practice. Another strong point was that the medical researchers searching for and grading complications were not involved with the care of the patient because of the retrospective character of their activities. It is conceivable that in a prospective study, the ongoing research and the researchers' activities could lead to improvements in the quality of patient care.

However, we have to address a number of limitations with regard to the research we conducted. In chapter 2, we report on an investigation of the existence, structure and responsibilities of the Dutch APS teams in hospitals and the degree of implementation of the Dutch Hospital Patient Safety Program. All hospitals in the Netherlands were approached with a survey about acute pain management in their hospital. Although this research design is frequently used, when using self-completion questionnaires it is not entirely clear if the answers reflect the real clinical situation in a hospital.
In our study presented in chapter 3, we noted a difference in the number of pain measurements observed in patient files compared to the number of pain assessments that the contact persons claimed to be executed in their hospitals. This difference seems to imply that the information provided by the contact persons was not reliable. In the future, research evaluations of the quality of acute pain management in hospitals should ideally be performed by site visits instead of surveys [17].
Furthermore, when investigating quality of pain management after surgery, preferably all characteristics of patients, hospitals and APS teams as well as outcome measures need to be considered in order to draw reliable conclusions.
In chapter 6, we reported on our study on the association of postoperative pain and complications after surgery. Prospective randomized controlled trials on this topic confirming causality are neither possible or ethically approved. Therefore, we retrospectively collected complications after surgery from the patient files.

Depending on the administration of clinical findings, we found that patient reports were not filled in consistently. In order to reduce costs and improve clinical value, we suggest performing large prospective observational studies of clinically collected data. In order to do so, we need to introduce uniform reporting methods and digital patient files, with the ability to retrieve data easily. Therefore, in the future, a study on uniform reporting of complications in digital patient files should be conducted.

General conclusions and recommendations

General conclusions

In this thesis we present the results of seven separate studies: (1) a description of the Dutch APS teams in hospitals, (2) an analysis of the compliance with pain assessment in postoperative patients after implementation of the Dutch Hospital Patient Safety Program and influencing factors, based on information of hospital contact respondents and based on patient records, (3) a description of the prevalence of acute postoperative pain in a tertiary high academic hospital setting in the Netherlands, (4) an analysis of the outcome of different pain management techniques after major surgery, (5) an analysis of the association between several components of pain assessment, and (6) an analysis of the association between unacceptable postoperative pain and complications after surgery.

This has led to a description of factors that determine the quality of care of postoperative pain management. Currently, there is a good understanding of the interrelationship between the factors in the three categories: “structure,” “process,” and “outcome” [3] as shown in the quality circle of postoperative pain management derived from Donabedian’s quality of care framework [22, 39, 59].

Our results demonstrate that postoperative pain management can be improved by (1) optimizing APS teams, (2) performing frequent multidimensional pain assessments and by (3) evaluating outcome measures including postoperative complications. Using the Donabedian model, we have shown that the structure, the process, as well as the outcome of postoperative pain management are interrelated factors. In order to improve postoperative pain management, all the influencing factors need to be addressed. Therefore, a hospital-wide improvement program is necessary which reviews the role of APS teams and other professionals, and focuses on the improvement of adherence to multidimensional pain assessment and the evaluation of pain treatment according to the Plan-Check-Do-Act cycle (PDCA cycle) [69]. The program evaluation should include measures of the intensity of the pain, the patient’s opinion on the acceptability of the pain, the observation of physical function, and the development of complications after surgery.
In addition to the recommendations made in this thesis, some conditions are inseparably connected with quality improvement. The Board of Directors of

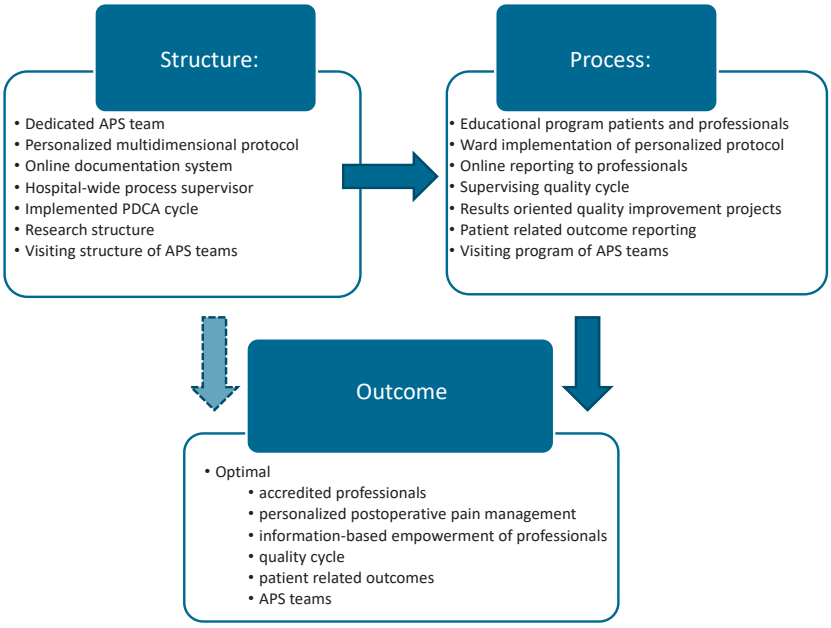

Figure 1 Donabedian's quality of care framework of postoperative pain
Donabedian's quality of care framework of postoperative pain management shows the recommendations for improving the quality of pain management after surgery, classified under three categories "structure", "process", and "outcome".

a hospital needs to approve investments in a dedicated APS team, in ICT with possibilities for adequate data analyses, and in a hospital-wide process coordinator for the supervision of the implementation and maintenance of multidimensional pain assessment and pain treatment by quality improvement projects.
The conclusions and recommendations presented in this thesis can be used to assess the situation in the reader's own hospital to improve the organization of postoperative pain management.

Connecting our results to the Donabedian model

By completing the Donabedian framework for postoperative pain management, we connected our findings with those from previous studies, as shown in Figure 1 of the Introduction. This has enabled us to make several recommendations and to develop a comprehensive overview to be used as a quality cycle for improving the quality of postoperative pain management.

In Figure 1, we have summarized the recommendations in Donabedian's quality of care framework of postoperative pain management. The detailed recommendations are described in Tables 1-3.

Recommendations for clinical practice

Acute Pain Service

Although there is currently no consensus on the organization, staffing or requirements for qualitative APS teams [70], the main components of an APS should include the following: (1) designated personnel responsible for 24-hour APS (in small hospitals 1 or 2 individuals may suffice), (2) regular multidimensional pain assessment at rest and movement, maintaining pain scores below predetermined individual threshold level, and documentation ("make pain visible"), with appropriate scales for children and patients with cognitive impairment, (3) active cooperation with physicians and ward nurses for developing protocols and critical pathways to achieve preset goals for mobilization and rehabilitation, (4) ongoing teaching programs for ward nurses and physicians for the provision of safe and cost-effective analgesic techniques, (5) patient education regarding pain monitoring and treatment options, goals, benefits and adverse effects, and (6) regular analysis of pain intensity and complications and an audit of cost-effectiveness of analgesic techniques on surgical and medical wards and patient satisfaction of both inpatients and day case patients [12].

We propose that APS teams should invest in patient care as well as in non-patient-related activities as recommended above, enhancing organizational postoperative pain management. It would be ideal for all APS teams to evaluate the outcome of all postoperative patients in their hospital for procedure-specific optimized pain management. Creating the research structure, time and ambiance to analyze patient data is essential. Evaluating real patient data collected on every patient visit is important for further improvement of the quality of postoperative pain management, because this information is crucial to identifying problems in the implementation process [15]. APS teams should take the lead in a multifaceted implementation strategy to advance pain assessment and pain treatment. To avoid high costs and workload, the large datasets should be created as part of the clinical process. Tailored educational programs for ward personnel as well as patients are also important and need to be organized by APS teams. The way forward may require organizational changes to the APS teams so that they can fulfil all tasks appropriately. Site visits by well-functioning APS teams may be valuable in initiating the upgrading of other APS teams.

Pain assessment

Frequent assessment of pain in patients provides information enabling decisions to be made on interventions enhancing optimal pain relief [21]. It is important that pain intensity is assessed regularly, using a standardized instrument [22]. Studies conducted in this thesis have shown that pain is not assessed regularly in all hospitals; adherence to pain assessment in hospital needs improving. Therefore, result-oriented quality improvement projects addressing pain assessment are recommended. A hospital-wide process supervisor, connected with the APS team needs to implement and maintain improvements and facilitate organizational changes. When assessing pain, health professionals need to be aware of the

multidimensional aspect of postoperative pain and thus use a multidimensional instrument. The combination of NRS pain score and the patients' opinion on the acceptability of the pain as well as the nurses' observation of the functional impact of the pain can be used for this purpose. Furthermore, decisions on pain treatment need to be taken based on the multidimensional pain assessment and in accordance with multidimensional personalized protocols, set up with the patient.

Pain intensity and complications

Complications after surgery occurred more often in patients with postoperative pain. Whether or not a causal relationship is present, postoperative complications developed need to be evaluated in order to identify barriers and limitations in perioperative care, including postoperative pain management. After surgery, every patient should be closely monitored and data registered in an easily accessible

Table 1 Recommendations for clinical practice following the results presented in this thesis

A:	**Concerning the organization and responsibilities of APS teams in hospitals**
1.	Install dedicated APS team outreaching from the Department of Anesthesiology with hospital-wide responsibilities.
2.	Stipulate that this APS team has patient-related and non-patient-related tasks.
3.	Organize a multifaceted implementation project concerning pain assessment and pain treatment, addressing good education on the importance of pain assessment itself, the disappearance of organizational barriers, and feedback on personal performance of health professionals.
B:	**Concerning pain assessment in hospitals**
1.	Make a preoperative pain treatment plan accounting for known risk factors for the development of postoperative pain.
2.	Assess pain in patients using a multidimensional assessment tool which includes a pain score at rest and in movement, a question on the acceptability of the pain, and a tool to observe physical functioning.
3.	Define a personal treatment threshold with the patient.
4.	Assess pain in patients regularly, preferably three times but at least once every day during admission time.
5.	Make pain treatment decisions based on a multidimensional pain assessment including the patient's perception.
6.	Avoid using a predefined cut-off point to decide on pain treatment.
7.	Evaluate and adjust pain treatment including the patient's perception.
C:	**Concerning postoperative pain intensity and complications after surgery in hospitals**
1.	Evaluate pain intensity, acceptability of pain and functional capacity in individual patients as well as in groups of patients to identify obstacles concerning adequate analgesia.
2.	Evaluate complications in individual patients as well as in groups of patients to identify obstacles concerning adequate analgesia.
3.	Set up quality improvement projects to solve identified obstacles.
4.	Adjust current pain practices to achieve excellent postoperative pain management.

electronic patient file regarding the development of postoperative pain and complications. Evaluations should be performed at patient and group level to identify the barriers to and limitations of excellent pain management. Quality improvement projects should be developed to overcome these problems to improve the quality of care for current as well as for future patients.
Table 1 summarizes the recommendations for clinical practice.

Recommendations for education

As we have described several recommendations for clinical practice in the previous section, it will be necessary to provide education programs for all health professionals working with patients perioperatively. This may start directly from when patients are referred to surgical specialists by the general practitioner. Very little or fragmented education on pain management is given at medical school or even in basic nursing education.
Physicians and nurses working with surgical patients may need regular updates on patient education, and on how to perform pain assessment adequately in order to balance treatment options, including patient perceptions.
APS teams play an important role in educating other health professionals in pain management. The APS teams themselves should invest in expanding their role according to the recommended patient-related and non-patient-related tasks of APS teams, and to ensure they acquire the competencies needed to fulfil this role.

Table 2 Recommendations for education following the results presented in this thesis

A:	**Concerning the organization and responsibilities of APS teams in hospitals**
1.	Educate members of APS teams to fulfil APS activities in accordance with the recommended patient-related and non-patient-related tasks.
2.	Educate all health professionals working with surgical patients to digitally document patient data concerning postoperative pain management in the corresponding system.
B:	**Concerning pain assessment in hospitals**
1.	Educate patients in pain and pain assessment and the importance of treating postoperative pain.
2.	Educate all health professionals involved in peri-operative care in postoperative pain management, addressing patient education, known risk factors for the development of postoperative pain, and the importance of treating and evaluating postoperative pain based on regular multidimensional pain assessments, including the patient's perception.
C:	**Concerning postoperative pain intensity and complications after surgery in hospitals**
1.	Use data on pain intensity, acceptability of pain, functional capacity and complications on a patient level as well as aggregated data at group level to teach all health professionals involved in peri-operative care in postoperative pain management.
2.	Teach all health professionals involved in peri-operative pain assessment to look beyond a predefined protocol cut-off score for pain treatment, and define a personal treatment threshold with the patient.

Table 2 summarizes the recommendations for education.

Recommendations for research

Research should be conducted on the organizational process of postoperative pain management in the reader's own hospital, for example analysis of patient-reported outcomes, the online reporting of these findings to professionals, as well as organizing a visiting program of APS teams.
Our findings have led to several new research questions. First, some APS characteristics need to be investigated for their influence on the adherence to pain assessment. More research is needed to explore which APS characteristics allow the best pain intensity and functional outcome in patients. Second, we

Table 3 Recommendations for research following the results presented in this thesis

A:	**Concerning the organization and responsibilities of APS teams in hospitals**
1.	Create a research structure, time and awareness in APS teams and the Department of Anesthesiology, hosting APS teams.
2.	Organize a system, including a research structure in which prospective clinically collected digital real-time documentation of postoperative pain management, including complications after surgery is facilitated.
3.	Organize a visiting program of APS teams.
4.	Investigate which patient-related and non-patient-related activities of APS teams influence the pain intensity, acceptability of pain, and functional capacity of postoperative patients, and their recovery by site visits, including all known influential factors.
5.	Investigate the role of APS teams in medical wards.
B:	**Concerning pain assessment in hospitals**
1.	Organize a regular data-analysis process.
2.	Set up new quality improvement projects based on results of data-analysis of hospital-wide patient-related outcome.
3.	Evaluate and adjust the multifaceted implementation strategy concerning pain assessment and pain treatment based on results of data-analysis.
4.	Report results of data-analysis to health care professionals.
5.	Investigate pain-related outcomes in relation to multidimensional pain assessment and treatment decisions.
C:	**Concerning postoperative pain intensity and complications after surgery in hospitals**
1.	Investigate the outcome of all postoperative patients in the hospital to optimize procedure-specific pain management.
2.	Investigate the inter-individual and inter-hospital variability in postoperative pain experience of patients, with the ultimate goal of personalized pain management.
3.	Create a system in which outcome data are reported regularly to clinicians, based on patient-related outcomes.

show that the adherence to pain assessment needs to be improved and that multidimensional pain assessment is important. More research is needed on a multi-faceted implementation strategy for multidimensional pain assessment. Third, the inter-individual and inter-hospital variability in postoperative pain experience of patients and pain-related outcomes should be investigated in order to perform personalized pain management.

Table 3 summarizes our recommendations for research.
To conclude: to improve the quality of current postoperative pain management, it is imperative for hospitals and APS teams to increase the attention paid to postoperative pain in patients and the implementation of the recommendations made above, according to Donabedian's quality of care framework of postoperative pain management.

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8

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Summary

Postoperative pain is a common occurrence following surgery. Inadequate postoperative pain management is associated with several negative consequences, patient discomfort, and is linked to increased healthcare costs. The prevalence of moderate to severe postoperative pain in the Netherlands and in the rest of the world is high, varying between 41 % and 65 %.

In this thesis, our focus is on postoperative pain experienced by inpatients in an academic hospital setting in the Netherlands. The overall aim of this thesis was to explore the quality of postoperative pain management in hospitals. We used the Donabedian model to assess the quality of postoperative pain management, selecting a set of factors from each of the three categories: structure, process and outcome. In the category "structure", we investigated the presence and responsibilities of acute pain service (APS) teams in hospitals. Pain assessment was studied for the category "process". As "outcome", we explored pain assessment including pain scores, complications, and relationships between these two outcome variables.

This thesis is organized in three main parts based on the three factors of Donabedian's framework for modeling the quality of care. ***Chapter 1*** provides a general introduction.

Chapter 2, the first part of the thesis, describes a study on the organizational structure of postoperative pain management. We aimed to report on the current state, structure and responsibilities of the APS teams in Dutch hospitals and to review the implementation of the Dutch Hospital Patient Safety Program (DHPSP). Therefore, we conducted a digital questionnaire survey, sent to all 96 Dutch hospitals performing surgical procedures. Ninety percent of Dutch hospitals reported having an APS, which are predominantly nurse based and mostly supervised by an anesthesiologist. The majority of team members are nurses. APS teams differ in both the way they are locally organized, and in the activities they employ, divided into patient-related and non-patient-related activities. All APS members make daily rounds to evaluate surgical patients with complex pain treatments like epidural, loco-regional analgesia or patient controlled analgesia. All APS teams have educational tasks and some participate in quality improvement projects of pain management. Research by APS teams is not common. Furthermore, the hospital contact respondents indicated that almost all hospitals had pain protocols in place and that they assessed pain in surgical patients. They also reported that the DHPSP guidelines on pain assessment had been almost fully implemented. The majority of hospitals assessed pain at least three times a day, however 46 % offer no access to regular in hospital pain training and 13 % do not inform patients about pain after surgery. We concluded that for more effective APS, APS teams should invest in patient care as well as non-patient-related activities enhancing organizational

improvement of postoperative pain management.
In ***Chapter 3***, the second part of the thesis, we describe a study on the process of pain assessment in hospitals. The aim of this study was to examine the compliance with pain assessment in postoperative patients after implementation of the DHPSP, according to the national quality indicators for pain assessment in postoperative patients. Furthermore, organizational factors associated with this compliance were determined. We used two data sources: 1) data from an evaluation study of the Dutch Hospital Patient Safety Program; and 2) data from our study in Chapter 2. Data of 3,895 patient records from 16 hospitals showed a low compliance with pain assessment in postoperative patients. In 53 % of the postoperative patients, pain was assessed at least once a day on all three full days after surgery. In only 12 % of the postoperative patients was pain assessed at least three times a day, all three full days after surgery. Compliance was highest in general hospitals compared to tertiary teaching and academic hospitals, and was higher at the surgery and surgical oncology department compared to the other departments. We concluded that the implementation of pain assessment in hospitals is still insufficient, based on data from patient records.

In the third part of the thesis, we present three studies on the outcome of postoperative pain management in hospitals. In ***Chapter 4***, we examined if neuraxial or regional analgesia provide superior pain relief compared to patient controlled intravenous analgesia (PCIA) in three different procedures. We also identified the incidence of minor and major adverse effects or complications of these techniques. Prospectively collected data of postoperative patients from an online data registration system of a special dedicated nurse based APS were analyzed. The overall percentage of patients with moderate to severe pain on day 1-4 after surgery based on movement evoked numerical rating scale pain (NRS-MEP) scores were 50.3 % and 9.2 % respectively. We found that patients who received epidural analgesia and continuous peripheral nerve blocks reported lower pain scores than those who received PCIA, after undergoing the same procedures. Additionally, pain at rest scores were significantly lower than movement evoked pain scores. The incidence of severe nausea was mostly observed in patients with PCIA and itching was most common in patients with epidural analgesia. A major adverse effect, i.e. opioid induced respiratory depression was found in five patients with PCIA. Since pain scores may vary widely between patients with similar surgical procedures we recommended personalized pain measurement and pain management, in order to improve clinical practice.

In ***Chapter 5***, we described the relationships between pain scores and other methods of pain assessment, e.g. acceptability of pain or its interference with physical functioning. Therefore, we conducted a cross-sectional study on patients who underwent major surgery. 15,394 assessments in 9,082 patients in the first three postoperative days showed that the unidimensional NRS-MEP score does not entirely reflect the multidimensional aspects of postoperative pain. Low pain scores

do not guarantee that patients find their pain acceptable. Nor do high pain scores invariably mean that patients are not satisfied by their pain levels. Approximately one out of ten patients had unacceptable pain but reported a low NRS-MEP score of 0-4. Despite a high NRS-MEP score of 7, at least one in five patients were willing to accept their pain and, at the same time, performed the required physical activities. We concluded that pain management should be guided by the many dimensions of the patient's pain experience, not solely by cut-off points of a numerical pain score. We encouraged health professionals to use a multi-source pain evaluation by assessing a numerical pain score, the acceptability of the pain and physical functioning in order to balance pain treatment options and possible complications.

In ***Chapter 6***, we report on the relationship between postoperative pain and 30-day postoperative complications. Having postoperative pain was assessed in two ways: the movement-evoked pain score on the Numerical Rating Scale (NRS-MEP) and the patients' opinion whether the pain was acceptable or not. Outcome was the presence of a complication within 30 days after surgery. Additionally, outcome was the occurrence of one of three healthcare-associated infections (HAIs): lung infection, urinary tract infection, and surgical site infection. 39.2 % and 15.8 % of the patients reported moderate to severe pain respectively on day one after surgery; 37.0 % and 10.2 % on day two; and 32.1 % and 6.3 % on day 3. Overall, 16.8 % of the patients reported unacceptable pain on one of the first three postoperative days. We found that complications after surgery occurred more often in patients with postoperative pain. Especially, healthcare-associated infections were linked to pain on the first day after surgery. Expected pain and higher age directly predicted the occurrence of 30-day complications. Our data strongly supported the paradigm that insufficient pain control in the early postoperative phase leads to an increased risk of postoperative complications. Consequently, an early detection of pain to avoid complications after surgery is important.

In ***Chapter 7***, the main findings of the thesis are discussed. In addition, we presented recommendations to improve clinical practice, education and research. The results of our studies demonstrated that postoperative pain management can be improved by 1) optimizing APS teams, 2) performing frequent multidimensional pain assessments and by 3) evaluating outcome measures including postoperative complications. Using the Donabedian model, we have shown that the structure, the process, as well as the outcome of postoperative pain management are interrelated factors. In order to improve postoperative pain management, all the influencing factors need to be addressed. Therefore, a hospital-wide improvement program is necessary which reviews the role of APS teams and other professionals, and focuses on the improvement of adherence to multidimensional pain assessment and the evaluation of pain treatment according to the Plan-Do-Check-Act cycle (PDCA cycle). The program evaluation should include measures of the intensity of the pain, the patient's opinion on the acceptability of the pain, the observation of physical function, and the development of complications after surgery.

Samenvatting

Postoperatieve pijn is een veel voorkomende gebeurtenis na de operatie. Onvoldoende postoperatieve pijnbehandeling is geassocieerd met verschillende negatieve gevolgen, ongemak van de patiënt en is geassocieerd aan hogere kosten voor de gezondheidszorg. De prevalentie van matige tot ernstige postoperatieve pijn in Nederland en in de rest van de wereld is hoog, variërend tussen 41 % en 65 %.

In dit proefschrift ligt de focus op postoperatieve pijn die wordt ervaren door patiënten in een academisch ziekenhuis in Nederland. Het algemene doel van dit proefschrift was om de kwaliteit van postoperatieve pijnbehandeling in ziekenhuizen te onderzoeken. We hebben het model van Donabedian gebruikt om de kwaliteit van postoperatieve pijnbehandeling te beoordelen en een reeks factoren uit elk van de drie categorieën te selecteren: structuur, proces en uitkomst. In de categorie "structuur" hebben we de aanwezigheid en verantwoordelijkheden van acute pijn service (APS) teams in ziekenhuizen onderzocht. Pijnmeting werd bestudeerd voor de categorie "proces". Als 'uitkomst' hebben we pijnmeting waaronder pijnscores onderzocht, complicaties en de relaties tussen deze twee uitkomstvariabelen.

Dit proefschrift is georganiseerd in drie onderdelen, gebaseerd op de drie factoren van het model van Donabedian voor het beschrijven van de kwaliteit van de zorg. ***Hoofdstuk 1*** geeft een algemene inleiding. ***Hoofdstuk 2***, het eerste onderdeel van het proefschrift, beschrijft een studie over de organisatiestructuur van postoperatief pijnmanagement. We beoogden verslag te doen over de huidige status, structuur en verantwoordelijkheden van de APS-teams in Nederlandse ziekenhuizen en om de implementatie van het Nederlandse Veiligheidsmanagementsysteem (VMS) Veiligheidsprogramma te beoordelen. Daarom hebben we dwarsdoorsnede onderzoek gedaan via een digitale vragenlijst, uitgestuurd naar alle 96 Nederlandse ziekenhuizen die chirurgische procedures uitvoeren. Negentig procent van de Nederlandse ziekenhuizen meldde dat ze een APS hebben, die overwegend het "nurse based anesthesiologist supervised" model heeft. De meerderheid van de teamleden zijn verpleegkundigen. APS-teams verschillen zowel in de manier waarop ze lokaal georganiseerd zijn als in de activiteiten die zij verrichten, onderverdeeld in patiëntgerelateerde en niet-patiëntgerelateerde activiteiten. Alle APS-leden maken dagelijkse consultrondes om chirurgische patiënten te evalueren die complexe pijnbehandelingen zoals epidurale, loco-regionale of patiënt- gecontroleerde analgesie krijgen. Alle APS-teams hebben educatieve taken en sommige nemen deel aan kwaliteitsverbeteringsprojecten ten aanzien van pijnmeting of pijnbehandeling. Het uitvoeren van (wetenschappelijk) onderzoek door APS-teams is niet gebruikelijk. Bovendien hebben de aangeschreven contactpersonen van de ziekenhuizen aangegeven dat bijna alle ziekenhuizen pijnprotocollen hadden en dat zij gestructureerd pijn meten bij chirurgische patiënten. Zij hebben ook gemeld dat de richtlijnen van het VMS Veiligheidsprogramma ten aanzien van pijnmeting bijna

volledig zijn geïmplementeerd. De meerderheid van de ziekenhuizen zou drie keer per dag pijn meten bij patiënten, maar 46 % biedt geen toegang tot regelmatige bijscholing over pijn en 13 % informeert de patiënten niet over pijn na de operatie. We concluderen dat APS-teams voor effectievere APS zouden moeten investeren in zowel directe patiëntenzorg als in niet-patiëntgerelateerde activiteiten die de organisatie van postoperatief pijnmanagement kunnen verbeteren.

In ***hoofdstuk 3***, het tweede onderdeel van het proefschrift, beschrijven we een studie over het proces van pijnmeting in ziekenhuizen. Het doel van deze studie was te onderzoeken of de richtlijnen van het VMS Veiligheidsprogramma na diens implementatie wat betreft pijnmeting bij postoperatieve patiënten worden opgevolgd, volgens de nationale kwaliteitsindicatoren voor het meten van pijn bij postoperatieve patiënten. Bovendien werden organisatorische factoren die verband houden met deze opvolging bekeken. We hebben twee databronnen gebruikt: 1) gegevens uit een studie ter evaluatie van het VMS Veiligheidsprogramma; en 2) gegevens uit onze studie die in hoofdstuk 2 beschreven staat. Gegevens van 3.895 patiëntendossiers van 16 ziekenhuizen lieten een lage opvolging zien van de richtlijnen ten aanzien van pijnmeting bij postoperatieve patiënten. Bij 53 % van de postoperatieve patiënten werd pijn minstens één maal per dag gemeten op alle drie de dagen na de operatie. Bij slechts 12 % van de postoperatieve patiënten werd pijn ten minste drie keer per dag gemeten, alle drie de dagen na de operatie. De opvolging was het hoogst in algemene ziekenhuizen in vergelijking met academische ziekenhuizen, en was hoger bij de chirurgische en chirurgisch oncologische afdelingen in vergelijking met de andere afdelingen. Wij concludeerden dat de implementatie van pijnmeting in ziekenhuizen nog steeds onvoldoende is, gebaseerd op gegevens uit de patiëntdossiers.

In het derde onderdeel van het proefschrift presenteren we drie studies over het resultaat van postoperatief pijnmanagement in ziekenhuizen. In ***hoofdstuk 4*** presenteren we een studie waarin de vraag wordt gesteld of neuraxiale of regionale analgesie superieure pijnbehandeling biedt in vergelijking met patiënt gecontroleerde intraveneuze analgesie (PCIA) in drie verschillende chirurgische procedures. Ook identificeerden we de incidentie van ernstige en minder ernstige bijwerkingen of complicaties van deze technieken. Prospectief verzamelde gegevens van postoperatieve patiënten uit een online data registratiesysteem van een “special dedicated nurse based” APS werden geanalyseerd. Het algehele percentage patiënten met matige tot ernstige pijn op dag 1-4 na de operatie op basis van numerieke pijnscores bij bewegen (NRS-MEP) waren respectievelijk 50,3 % en 9,2 %. We stelden vast dat patiënten die epidurale of loco-regionale analgesie kregen, lagere pijnscores meldden dan patiënten die PCIA kregen, in groepen die dezelfde procedures ondergingen. Daarnaast waren pijn in rust scores significant lager dan de pijn bij bewegen scores. De incidentie van ernstige misselijkheid werd meestal waargenomen bij patiënten met PCIA , terwijl jeuk het meest voorkwam bij patiënten met epidurale analgesie. Een belangrijk negatief effect, een opioïd

geïnduceerde ademhalingsdepressie, werd gevonden bij vijf patiënten met PCIA. Aangezien de pijnscores erg varieerden tussen patiënten met soortgelijke chirurgische procedures, hebben we de aanbeveling gedaan dat bij het meten van pijn een meer gepersonaliseerde benadering moet worden aangehouden, alsook bij de behandeling van pijn.

In ***hoofdstuk 5*** beschrijven we de relaties tussen pijnscores en andere methoden van pijnbeoordeling, zoals het wel of niet acceptabel zijn van pijn voor patiënten en de impact die de pijn heeft op het fysiek functioneren. Daarom hebben we een dwarsdoorsnede onderzoek uitgevoerd aan de hand van standaard pijnmetingen die gedaan waren door de APS bij patiënten die een grote operatie hadden ondergaan. 15.394 standaard pijnmetingen bij 9.082 patiënten in de eerste drie dagen na de operatie toonden aan dat de unidimensionale pijnscore bij bewegen niet de multidimensionele aspecten van postoperatieve pijn weerspiegelt. Lage pijnscores garanderen niet dat patiënten hun pijn acceptabel vinden. Ook betekenen hoge pijnscores niet altijd dat patiënten ontevreden zijn met hun pijnniveau. Ongeveer één op de tien patiënten had onacceptabele pijn maar meldde een lage pijnscore bij bewegen van 0-4. Ondanks een hoge pijnscore bij bewegen van 7, was minstens één op de vijf patiënten bereid de pijn te accepteren en tegelijkertijd de vereiste fysieke activiteiten uit te voeren. Wij concludeerden dat pijnbehandeling moet worden geleid door de vele dimensies van de pijnervaring van de patiënt, en niet alleen door het overschrijden van een afkappunt van een numerieke pijnscore. We moedigden gezondheidswerkers aan om een multidimensionele pijnmeting te gebruiken voor het beoordelen van de pijnbeleving bij patiënten. Dit kan door minimaal een aantal zaken uit te vragen, zoals een numerieke pijnscore, het wel of niet acceptabel zijn van de pijn en het fysieke functioneren van de patiënt te observeren ter overweging van mogelijke pijnbehandelopties en eventuele complicaties.

In ***hoofdstuk 6*** rapporteren we over een studie naar de relatie tussen postoperatieve pijn en complicaties binnen 30 dagen na een operatie. Postoperatieve pijn werd op twee manieren gedefinieerd: de numerieke pijnscore bij bewegen (NRS-MEP) en de mening van de patiënt of de pijn acceptabel was of niet. De uitkomst was de aanwezigheid van een complicatie binnen 30 dagen na de operatie. Een andere uitkomst was de aanwezigheid van één van de drie gezondheidszorg-geassocieerde infecties (HAI's): longinfectie, urineweginfectie en wondinfectie. 39,2 % en 15,8 % van de patiënten meldden matige tot ernstige pijn op dag één na de operatie; 37,0 % en 10,2 % op dag twee; en 32,1 % en 6,3 % op dag 3. Over het algemeen meldde 16,8 % van de patiënten onacceptabele pijn op één van de eerste drie dagen na de operatie. Het ontstaan van complicaties na een operatie kwam vaker voor bij patiënten met postoperatieve pijn. Vooral ook de gezondheidszorg-geassocieerde infecties waren geassocieerd met pijn op de eerste dag na de operatie. Verwachte pijn en hogere leeftijd voorspelden direct het optreden van complicaties binnen 30 dagen na de operatie. Onze gegevens ondersteunen het paradigma

dat onvoldoende pijnbehandeling in de vroege postoperatieve fase leidt tot een verhoogd risico op postoperatieve complicaties. Bijgevolg is een vroege detectie van pijn om complicaties na de operatie te vermijden belangrijk.

In ***hoofdstuk 7*** worden de belangrijkste bevindingen van het proefschrift besproken. Daarnaast hebben we aanbevelingen gedaan om de klinische praktijk, het onderwijs en het onderzoek te verbeteren. De resultaten van onze studies hebben aangetoond dat postoperatieve pijnbehandeling kan worden verbeterd door 1) het optimaliseren van APS-teams, 2) het uitvoeren van regelmatige multidimensionele pijnbeoordelingen en 3) de evaluatie van uitkomsten van pijnbehandeling, inclusief postoperatieve complicaties. Met behulp van het Donabedian model hebben we aangetoond dat de structuur, het proces, evenals de uitkomst van postoperatief pijnmanagement factoren zijn die onderling met elkaar verbonden zijn. Om postoperatief pijnmanagement te verbeteren, moeten alle beïnvloedende factoren worden aangepakt. Daarom is een ziekenhuisbreed verbeterprogramma nodig dat de rol van APS-teams en andere gezondheidswerkers evalueert en zich richt op de verbetering van de naleving van multidimensionele pijnmetingen en de evaluatie van pijnbehandeling volgens de Plan-Do-Check-Act-cyclus (PDCA cyclus). De evaluatie van het verbeterprogramma moet in ieder geval de meting van de intensiteit van de pijn bevatten, alsook het oordeel van de patiënt over het wel of niet acceptabel zijn van de pijn, de observatie van het fysiek functioneren en de ontwikkeling van complicaties na de operatie.

Epilogue

Now I have finished my thesis. I am very grateful that I was given the opportunity to immerse myself in postoperative pain management. Some of the questions I had before starting my research have been answered. However some of them have not been answered. During my research, more questions arose on certain topics, resulting in perspectives for future research.

Pain is a personal, subjective experience that arises in the conscious brain, typically associated with actual or potential tissue damage, or described in terms of such damage. As it is a subjective emotional sensation, reliable tools are required to facilitate the diagnosis and treatment of pain in clinical practice. Evaluation of whether pain therapy is effective should account for patients' experience and sensation.

My goal is to prevent patients from unnecessary suffering caused by postoperative pain. I believe that postoperative pain management can be improved by optimizing APS teams, optimizing frequent pain assessments, and by analyzing patient outcomes. But we need to work together with our patients in achieving this goal. We need to empower them and embrace shared decision-making. Because our patients are the ones actually feeling the pain. Without their cooperation and consent, pain management can never be optimal. In my work as the hospital-wide process supervisor patient empowerment is my first priority.

I will continue advocating the importance of adequate assessment and treatment of postoperative pain, in the clinic in individual patients as well as during education and training sessions for health care professionals. Additionally, I will continue advocating the analysis of pain data and facilitate quality improvement projects. Finally I will continue my research on postoperative pain management, with the help of our patients.

I have finished my thesis, but I have not yet finished my work. I believe that somewhere in the future postoperative pain will be managed adequately in all patients.

Rianne van Boekel

Dankwoord / Words of gratitude

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Curriculum Vitae

Rianne van Boekel was born in Oss and grew up in Schaijk, a small village on the countryside of The Netherlands. After primary school, she went to secondary school, the gymnasium in Oss, a city just 10 kilometres away. Six years later she passed for gymnasium. She continued with Nursing on the higher professional educational level, being a student nurse in the Radboud university medical center when she was 19 years old. At the age of 23, she received her Bachelor of Nursing. Her job was offered immediately after her graduation in the department of General Internal Medicine and then at the Thorax / Heart Surgery department. After three years, she started nursing education specializing in intensive care nursing. After four years at the Intensive Care department, she accepted the position of clinical pain nursing consultant at the Department of Anesthesiology, Pain and Palliative Medicine. She is still working at this department and has since been employed as a nursing expert and is the hospital leader for the theme "Early Recognition and Treatment of Pain". In this function, she is responsible for all aspects of pain in patients, such as protocols, work instructions, patient education, training programs, reports and quality improvement programs of individual departments.

In addition to clinical work, Rianne initiated the two-year post-graduate program for pain nursing consultant at the HAN University of Applied Sciences in 2011. She still coordinates this training and some other courses related to pain and palliative care at the HAN. Furthermore, she has accepted the assignment to promote research and evidence based practice and give these topics a more prominent place in the courses within HAN VDO. In 2013 she won a personal scholarship, "NWO Promotion Grant for Teachers", to start her PhD study on acute postoperative pain management in collaboration with the Radboud University Medical Center and HAN.

In 2014, Rianne successfully completed the Master Epidemiology at the EMGO Institute for Health and Care Research (EMGO +), the Interfaculty Research Institute of the VU Medical Center and the VU University in Amsterdam. She is an active member of the research department of Anesthesiology, Pain and Palliative Medicine of Radboud University Medical Center, and participated in various research projects, aiming to bring research closer to the public society, such as the Radboud research team at Lowlands 2016 and the Great National Research on the Sensitivity of Pain in The Netherlands.

Supporting the development of pain nursing consultants, Rianne became the president of the Dutch Association of Pain nurses in 2015, an association that she founded with other colleagues in 2006. In this association, she has taken care of, among other things, the establishment of the area of expertise

of Pain Nursing, as well as the Pain Nursing domain in the Nurses' Quality Register. She is also the president of the multidisciplinary Working Group that prepares the new quality indicator Hospital-wide Pain Management for the Healthcare Inspectorate's Basic set of Quality Indicators of hospitals. She also served as a board member of the Dutch Pain Society and has been in Pain Alliance in the Netherlands (P.A.I.N.), established since April 2017.

Rianne is married to Marcel Eikholt. Together they have three children, Lucas, Emma and Sophie, respectively, 14, 12 and 9 years old.

Publications

- **van Boekel RLM**, Nielen RGC, Vissers KCP, van de Sande R, Lerou JGC, Steegers MAH. Relationship between postoperative pain and adverse events in a broad surgical population. Submitted in Annals of Surgery.

- **van Boekel RL**, Vissers KC, van der Sande R, Bronkhorst E, Lerou JG, Steegers MA. Moving beyond pain scores: Multidimensional pain assessment is essential for adequate pain management after surgery. PloS one. 2017;12(5):e0177345.

- Hoogervorst-Schilp J, **van Boekel RL**, de Blok C, Steegers MA, Spreeuwenberg P, Wagner C. Postoperative pain assessment in hospitalised patients: National survey and secondary data analysis. International Journal of Nursing Studies. 2016;63:124-131.

- **van Boekel RL**, Vissers KC, van de Vossenberg G, de Baat-Ananta M, van der Sande R, Scheffer GJ, Steegers MA. Comparison of Epidural or Regional Analgesia and Patient-controlled Analgesia: A Critical Analysis of Patient Data by the Acute Pain Service in a University Hospital. Clinical Journal of Pain. 2016; 32: 681-688

- **van Boekel R**. Pijn bij kanker: verpleegkundige zorg in alle facetten. Kankerbreed.2015;7(2): 13-16.

- **van Boekel RL**, Steegers MA, de Blok C, Schilp J. [Pain registration: for the benefit of the inspectorate or the patient?]. Nederlands Tijdschrift voor Geneeskunde. 2014;158:A7723

- Houweling PL, Molag ML, **van Boekel RLM**, Verbrugge SJC, van Haelst IMM, Hollmann MW.['Postoperative pain treatment' practice guideline revised]. Nederlands Tijdschrift voor Geneeskunde. 2013;157: A7005.

- **van Boekel RL**, Steegers MA, Verbeek-van Noord I, van der Sande R, Vissers KC. Acute Pain Services and Postsurgical Pain Management in the Netherlands: A Survey. Pain Practice. 2015; 15(5):447–454.

- **Boekel RLM**, Steegers MAH, van der Sande R, Vissers KCP. Postoperative pain assessment should not be solely based on numeric ratings! Commentary on Van Dijk et al. (2011). International Journal of Nursing Studies. 2012;49(5):631–633.

- **van Boekel R**. Werkgroep onderwijs is klaar voor de toekomst! Pijnperiodiek. 2012;2(6):20-21.

- **van Boekel R**. Hoogwaardige pijnzorg van verantwoord niveau. Pijnperiodiek. 2012;3(6):12-15.

- **Boekel R van**, Steegers M, Vissers K. Week van de pijn in Radboudumc: bewustwording en borging. Nederlandstalig Tijdschrift Pijnbestrijding. 2012;31(51):3-9.

- **Boekel R van**. Implementatie. TvZ Tijdschrift voor verpleegkundigen. 2010;120(7):65-68.

- **Boekel R van**. Voor een optimale postoperatieve pijnbehandeling: De Acute Pijn Service. TvZ Tijdschrift voor verpleegkundigen. 2010;120(6):30-33.

- **Boekel R van**. Postoperatieve pijnbehandeling. TvZ Tijdschrift voor verpleegkundigen. 2010;120(6):40-45.

- **Boekel R van**, Giesberts MG, Roode E de; Snel herstellen na uw operatie? Blijf de pijn de baas!; NTVA; jaargang 26, nr 3, mei 2009.

- **Boekel R van**, Complicaties van postoperatieve pijnbehandeling; NTVA; 2006.

- **Boekel R van**, Giesberts MG; Pijnbehandeling kan effectiever en veiliger; Verpleegkunde Nieuws 03;2005:27-29.

- Giesberts M, **Boekel R van**; Minder pijn voor de patiënt: de rol van de pijnverpleegkundige; Kwaliteit in Beeld 2004;6:8-9.

- Vroom M, **Boekel R van**, Giesberts M; Postoperatieve pijnbehandeling kan nog beter; TVZ nr 9, september 2004.

PhD Portfolio

Name PhD student:	RLM van Boekel RN MSc
Period:	2013-2017
Radboudumc Department:	Anesthesiology Pain and Palliative Medicine
Promotor:	Prof. dr. KCP Vissers
Co-promotors:	dr. MAH Steegers, dr. R van der Sande
Research School:	Radboud Institute for Health Sciences

1. PhD training

General academic skills

Introductie Nijmeegse curricula (startkwalificatie onderwijs)	2017	(0.2 ECTS)
Mediatraining	2017	(0.2 ECTS)
Scientific Integrity for RIHS and RIMLS PhD students	2015	(0.4 ECTS)
Academic Writing	2015	(3.0 ECTS)

Research skills

NWO Inspiratiedag promotiebeurs voor leraren	2017	(0.3 ECTS)
Basiscursus regelgeving en organisatie voor klinisch onderzoekers (BROK)	2016	(1.0 ECTS)
Summercourse HAN University of Applied Sciences	2016	(0.3 ECTS)
Summercourse HAN University of Applied Sciences	2015	(0.3 ECTS)
Radboud Institute for Health Sciences Introduction Course for PhD students	2014	(0.6 ECTS)
Longitudinale data-analyse	2014	(3.0 ECTS)
Master epidemiologie (EMGO/VU)	2014	(60.0 ECTS)

Oral Presentations

Societal Impact of Pain (SIP) congress Malta	2017	(1.0 ECTS)
7e nationaal pijn Congres V&VN Pijnverpleegkundigen	2016	(0.3 ECTS)
Avondsymposium Pijn bij kanker: meten en begeleiden	2016	(0.1 ECTS)
Avondsymposium Pijn bij dementie	2015	(0.1 ECTS)
Refereeravond “Pijn in al zijn facetten” Ziekenhuis Rivierenland Tiel	2015	(0.1 ECTS)
Minisymposium “Pijn en palliatieve zorg; zorg ondersteund door netwerken”	2015	(0.1 ECTS)
Radboud Research Rounds	2015	(0.1 ECTS)
Nederlandse OK dagen	2014	(0.2 ECTS)
Invitational conference Acute Pain Service	2013	(0.1 ECTS)
XXIX Annual ESRA congress	2010	(1.0 ECTS)

Poster Presentations

World Institute of Pain (WIP) 8th World congress	2016	(1.0 ECTS)
European Federation of IASP Chapters (EFIC) 9th Congress	2015	(1.0 ECTS)
World Institute of Pain (WIP) 7th World congress	2014	(1.0 ECTS)
Congres NVA/VAP/V&VN Pijnverpleegkundigen "Pijndagen"	2012	(0.2 ECTS)
IASP 14th World Congress on Pain	2012	(1.0 ECTS)

Seminars and workshops

Nederlandse OK-dagen	2015	(0.2 ECTS)
6e nationaal congres V&VN Pijnverpleegkundigen	2014	(0.3 ECTS)
Admiraal de Ruyter ziekenhuis Goes/Vlissingen	2014	(0.2 ECTS)
Studiedag Palliatieve zorg; voor en door elkaar. (3x)	2014	(0.3 ECTS)
Verpleegkundige Adviesraad. Passie voor pijn	2013	(0.1 ECTS)
Lectoraat acute intensieve zorg	2013	(0.1 ECTS)
Congres NVA/VAP/V&VN Pijnverpleegkundigen	2012	(0.2 ECTS)
5e nationaal congres V&VN Pijnverpleegkundigen	2012	(0.3 ECTS)
Venticare	2010	(0.2 ECTS)
4e nationaal congres LVP	2010	(0.2 ECTS)
Expeditie Patientveiligheid (VMS programma)	2010	(0.2 ECTS)

International conferences

Societal Impact of Pain (SIP) congress Malta	2017	(1.0 ECTS)
World Institute of Pain (WIP) 8th World congress	2016	(1.0 ECTS)
European Federation of IASP Chapters (EFIC) 9th Congress	2015	(1.0 ECTS)
World Institute of Pain (WIP) 7th World congress	2014	(1.0 ECTS)
IASP 14th World Congress on Pain	2012	(1.0 ECTS)
XXIX Annual ESRA congress	2010	(1.0 ECTS)

2. Teaching activities

Lecturing

Cursus Postoperatieve Pijn Radboud Health Academy	2017	(0.5 ECTS)
Keuzeblok 5KVZ5 Geneeskunde	2016-2017	(0.1 ECTS)
Incompany cursus Acute pijn service medewerker ZRT	2015	(0.5 ECTS)
St Martins' home White-Yellow Cross Foundation	2015	(2.0 ECTS)
Minor Pijn multidisciplinair HAN	2014-2017	(0.4 ECTS)
ZZG Zorggroep	2012	(0.4 ECTS)
Minor Oncologie HBOV HAN	2011-2013	(0.3 ECTS)
Opleiding Pijnconsulent HAN VDO	2011-2017	(200 ECTS)
Cursus Assistent Pijnbehandeling HAN VDO	2010-2017	(60 ECTS)
Keuzeblok KNW7 Geneeskunde	2010-2017	(0.5 ECTS)
Specialistische verpleegkundige vervolgopleiding Snijdende Specialismen Radboud Health Academy	2010-2017	(1.2 ECTS)

Specialistische verpleegkundige vervolgopleiding Maag Darm Lever-verpleegkunde	2010-2017 (1.2 ECTS)
Specialistische verpleegkundige vervolgopleiding Longverpleegkunde	2010-2011 (0.3 ECTS)

Supervising students on research projects

Verpleegkunde (HBOV):	
Mandy Wiggers en Nina Vermaas (APS UMCN)	2010
Marianne Hollestelle en Marianne Hogendoorn (APS UMCN)	2011
Karin van der Heijden en Lieve van Dalen (verpleegkundige interventies acute postoperatieve pijn)	2011
Yvonne de Bruin en Jet Brinks (verpleegkundige interventies preventie chronische pijn)	2011
Carmen Garraud en Rosan van der Wijst (APS)	2011
Sylvia Luijten en Anouk van Betteraij (zorgpad chronische pijnpatiënt)	2012
Aniek Verheggen en Maruschka Seegers (APS)	2012
Juul Altinga en Cecile Buurman: (Pijnpredict: preoperatieve pijn)	2013
Luuk Aarts en Karin Matser (Pijnpredict: geslacht)	2013
Tom Bik en Anne-Marit Kort (Pijnpredict: chronische pijn)	2013
Lonneke Kuipers en Merit Struik (Pijnpredict: catastroferen)	2015
Kim van Woezik en Noor Nusselder (Pijnpredict: PSQ)	2013
Frank Vermeer en Sandra Maas (Pijnpredict: angst)	2015
Bas Altstadt en Niek Vlekken (Pijnpredict: postoperatieve complicaties)	2015
Danique Mulder en Judith Raaijmakers (Pijnpredict: preoperatieve pijn)	2015
Kim Hermans en Tamara Verstraten (palliatie onderwijs NPZZG)	2015
Vanity Looyschelder (Pijnpredict: preoperatieve pijn)	2016
Mariëlle Heusinkveld en Sanne Verheijen (Pijnpredict: postoperatieve complicaties)	2016
Maureen Tittse, Nicole Roelofs en Bas van Uden (Pijnpredict: postoperatieve complicaties)	2017
Deli Ahoud en Seyenna Vink (Pijnpredict: Janssen indeling)	2017
Alyssa Misseyer en Anne Aarts (Pijnpredict: postoperatieve complicaties)	2017

Bachelor medische hulpverlening (BMH):	
Kimberley Geven en Michelle Peperkamp (Pijnpredict: regel)	2012
Mirjam Schakenbos en Sanne Schakenbos (Pijnpredict: angst)	2014
Terry van Grunsven en Lisa van Bergen (Pijnpredict: leeftijd)	2014
Cynthia Bosman en Jeroen Takke (Pijnpredict: angst)	2014
Jesse Liebrand en Rossy Scharbaay (Pijnpredict: complicaties)	2014
Anne van Lamoen, Carlijn Smits, Willem Vincken (Pijnpredict: complicaties)	2015
Geneeskunde:	
BOWO blok:	
Nicole van Vlijmen en Karin ter Weele	2012-2013
Jedda Eppink en Maarten te Groen, Jelmer van Dijk en Lizzy Harmsen	2013-2014
Alexander Janssen en Joris Drossaers, Lara van der Schoot en Hielke Markerink	2014-2015
Mathijs Weijers en Hugo Aarts, Robin Ros en Stef Schoenmakers	2015-2016
Eerstejaars Geneeskunde met innovatieproject:	
Matthijs, Thomas, Lars en Casper Tacke (PONV)	2016
Tweedejaars Geneeskunde met onderzoeksproject:	
Maaike Kampshoff en Marly Habets (preoperatieve chronische pijn)	2016
Biomedische wetenschappen (BMW):	
Frederique Vermeulen (Janssen categorieën)	2015
Renske Nielen (postoperatieve complicaties)	2015
Roderick van Oudenaerde (postoperatieve outcome)	2015
Daan van den Nieuwenhof, Leah Jacobs en Bart Sloot (postoperatieve complicaties)	2016
Master Advanced Nursing Practice (MANP)	
Ingeborg de Booij-Liewes-Thelosen (thuisbloeddrukmeting)	2015
Jantine Boerrigter- van Ginkel (preoperatieve informatie)	2015

3. Awards

X2 Ambition Award The best leadership in combining patient care, education and research, and having a societal impact	2017
TOPP stuk-award The best scientific output in 2013	2014
NWO Grant: Netherlands Organization for Scientific Research PhD Grant for teachers Five year financial support for PhD research	2013