Thesis proposal

**Patients in emergencies are not consistently well-treated for pain.**

Oligoanalgesia is the inadequate treatment of pain, and in the emergency setting the term is usually reserved for the experience of patients with acutely painful conditions who present for emergency care, and who do not get adequate analgesia {Wilson:1989da}. The processes that lead to undertreatment of pain are complex {Rupp:2004bk}. It has been traditional to think that the administration of opioid analgesia may lead to complications. Sir Vincent Zachary Cope, the author of \*Cope's Early Diagnosis of the Acute Abdomen\*, a standard text of general surgery, said in 1929:

>There are many acute abdominal pains for which a dose of

morphine is the correct treatment—such, for example, as

renal and biliary colic, gastric crises, diaphragmatic

pleurisy with pain referred to the abdomen—but there are

other conditions of an apparently similar nature for which

to give a dose of morphine is, to say the least, an unwise

and, to say the most, a possibly fatal, procedure.{Cope:1929we}

This fairly nuanced expression was taken as a prohibition against giving opioids to patients with acute abdominal pain.

Different physicians presented with the same clinical presentation may decide to give widely varying treatments for acute pain {TamayoSarver:2004jw}. Factors such as lack of clinician education about the management of pain; treatment of pain not being included in quality improvement initiatives; fears of addiction and abuse of opioids; concerns over side effects, such as nausea, vomiting, respiratory depression, or hypotension; and differential treatment to members of racial and ethnic groups contribute to the undertreatment of pain{Miner:2014ht}.

The concern that treating acute pain may delay diagnosis and surgical treatment and lead to subsequent complications had been addressed: reviews addressing these concerns are summarized below.{Poonai:2014hv}{Manterola:2011fk}{Ranji:2006ki}

Caregivers’ attitudes such as the belief that pain is an accepted part of the process of disease and that patients pain experience is not valid also contribute to oligoanalgesia.{Ducharme:2013bp}

In addition to systemic factors the treatment of pain varies widely among clinicians in the same clinical settings, both in prehospital {Albrecht:2013dv} and in the emergency department setting.{Heins:2006gb}

**The best outcome for research and clinical use is patient oriented: “enough pain treatment”.**

Pain is a subjective experience that, unlike temperature, pulse, blood pressure and oxygen saturation, cannot be measured by an external instrument; yet it has considered to be the "Fifth Vital Sign" in medicine.{Campbell:1996gb} The intent behind designating pain this way is to promote the treatment of pain by recognizing significant abnormalities and taking action to bring these abnormalities back into an acceptable range; and to prioritize the treatment of patients in pain.

As pain is a patient reported outcome (PRO), based on self report of symptoms, pain researchers have developed methods of measuring pain so as to make an individual patient's symptoms reproducible from one time to the next, and to measure and aggregate multiple patients' intensity of pain. The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT)] group has published recommendations for PROs in clinical trials for chronic pain,{Turk:2006kf}{Dworkin:2008ej} but so far have not published recommendations for acute pain. The most commonly used measurements in emergency research are a visual analogue scale (VAS)that goes from 0 mm to 100 mm, and an eleven point verbal numerical rating scale (VNRS) that goes from 0 to 10. these two scales do not seem to differ significantly when compared to each other.{Marquie:2008bq}. These scales have been shown to be reproducible within patients{Bijur:2001uo}, but in clinical practice different raters can elicit different pain scores from the same patient.{Harting:2013cd}.

The score a patient gives on a pain scale is not consistently related to their desire to be treated for the pain. In the emergency setting there have been multiple studies that analysed pain scales to find the minimally detectible pain score difference (sometimes called the minimally important difference (MID) or the minimally clinically important difference (MCID)), which usually works out to be an improvement between than 1 and 2 cm on a VAS.{Todd:1996uv}{Kendrick:2005gf} This is the amount of change on a VAS that is associated with patients saying that they feel a little better. These changes are averaged over the group in the study and then reported. There are two problems with this measure: first, the detection of a minimal difference is not the same as adequate control of pain, and second, the studies report a group average but an individual patient in the study may have a change in pain scale that is not near the group average, some patients may record an increase in their VAS and still report feeling a little better! Feeling "a little better" is not the same as having the amount of pain medicine that you wanted.{Barden:2007uw}

Other studies have looked at a different measure, confusingly also called the minimally clinically important difference, which is the change in VAS associated with adequate relief of pain. The amount of change on a pain scale that is associated with adequate relief of pain varies with the initial severity of the pain, and some studies have associated the change with a certain distance on the scale, others with a percentage change from an initial value. In the emergency department setting the group average MCID associated with adequate pain relief was an improvement of 3 cm on the VAS, and the average change in pre-treatment pain score was an decrease of 30% from the initial score.{Lee:2003wl}. The findings were similar in a postoperative setting, {Cepeda:2003bo}, and in a rheumatology clinic.{tenKlooster:2006je} This is again problematic as it is a group average rather than a measure that applies to every patient. The relationship between a patient's experience of having a sufficient relief of pain and a change in a pain score is inconsistent: some people can say they have had a sufficient relief of pain even though their final pain score is higher than their initial score. The rheumatology study reported sensitivities and specificities of close to 70% for their 3 cm cutoffs,{tenKlooster:2006je} which leads to substantial misclassification of whether or not an individual patient had adequate pain relief.

**The standard pain treatment for pain is morphine and the doses in clinical use vary considerably.**

Morphine is the “gold standard” opioid which is often used as a comparison in studies of other analgesics, yet the dose of morphine that is used in clinical practice is lower than the equivalent doses of other opioids.{Bijur:2012jy}{OConnor:2010hu}{OConnor:2006gk}

Education about pain management and protocols for analgesia have the possibility to improve the treatment of pain. In order to effectively treat pain we need to know the optimal doses of morphine for analgesia, and that is the purpose of this thesis.

**Research on morphine dosing often uses outcomes that are not patient-oriented.**

Research on morphine dosing most often uses a change in pain score as the outcome of interest{MacKenzie:2016gx}{Patanwala:2010er}, but does not relate this score to the proportion of patients that say they have been adequately treated for pain. Some research has used overall patient satisfaction as an outcome, but overall satisfaction does not correlate with pain relief, as patients may be satisfied with their care while continuing to be in severe pain,{DeLaney:2015fj} or patient satisfaction may go up after an intervention even though no more analgesia is given.{Taylor:2015bm}

**A systematic review that links “enough pain treatment” to other outcomes will make research easier to interpret**.

The PICO for this review is “In patients presenting to the emergency department with acute painful and receiving a treatment for pain; does an lowering the pain score below a threshold, or reaching an absolute or relative change in pain score, best predict the patient’s expressed statement that they have had enough pain treatment?”

**A systematic review of morphine dosing that translates other outcomes to “enough pain treatment” will be a better guide to morphine dosing.**

The PICO for this second review is “In patients presenting to the emergency department with acute pain what standardised dosing regimen of morphine, compared with usual care, will relieve the acute pain as judged by the patient expressed goal of enough pain treatment?”

**Methods.**

There will be two systematic reviews, addressing the two PICO questions. Each review will be registered in the PROSPERO database (<http://www.crd.york.ac.uk/PROSPERO/)> and will be prepared following the checklist in the PRISMA-P statement.{Moher:2015dh} The search strategies will be developed with a librarian. The databases searched will be MEDLINE, EMBASE, and CINAHL. The included studies will be randomised controlled trials and cohort studies that address the PICO questions. Articles will be excluded if they are case reports, reviews, abstracts or editorials. Two authors will independently review the articles found by the search and rate their relevance. Any conflicts will be resolves by discussion until the reviewers reach consensus. Following selection of articles two reviewers will review independently rate the methodological quality of the articles using a form that will be developed based on the Cochrane risk of bias tools for randomised{Higgins:2011cg} and non-radomised{Sterne:2016jn} and GRADE guidelines. Data from the articles will be summarized in tables. The will be a qualitative synthesis of the results. If the studies contain sufficient detail and are judged to be homogenous enough after the qualitative synthesis then a meta-analysis will be included.