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 (1). The processes that lead to undertreatment of pain are complex (2). 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.(3)

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 (4). 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(5).

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. (6-8)

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.(9)

In addition to systemic factors the treatment of pain varies widely among clinicians in the same clinical settings, both in prehospital (10) and in the emergency department setting.(11)

**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.(12) 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, (13,14) 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.(15). These scales have been shown to be reproducible within patients(16), but in clinical practice different raters can elicit different pain scores from the same patient.(17).

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. (18,19) 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.(20)

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 improvement of 30%.(21). The findings were similar in a postoperative setting, (22), and in a rheumatology clinic.(23) 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,(23) 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. (24-26)

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(27,28), but does not relate this score to the proportion of patients that say they have been adequately treated for pain.

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

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

1. Wilson JE, Pendleton JM. Oligoanalgesia in the emergency department. American Journal of Emergency Medicine. 1989 Nov;7(6):620–3.

2. Rupp T, Delaney KA. Inadequate analgesia in emergency medicine. Ann Emerg Med. 2004 Apr;43(4):494–503.

3. Cope Z. The Prevention and Early Diagnosis of the Acute Abdomen. British Medical Journal. 1929 Jan 5;1(3548):6–9.

4. Tamayo-Sarver JH, Dawson NV, Cydulka RK, Wigton RS, Baker DW. Variability in emergency physician decisionmaking about prescribing opioid analgesics. Ann Emerg Med. 2004 Apr;43(4):483–93.

5. Miner JR, Todd KH. Pain Management in the Emergency Department. In: Practical Management of Pain. Elsevier; 2014. pp. 1009–1014.e2.

6. Poonai N, Paskar D, Konrad S-L, Rieder M, Joubert G, Lim R, et al. Opioid Analgesia for Acute Abdominal Pain in Children: A Systematic Review and Meta-analysis. Jones A, editor. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine [Internet]. 2014 Nov;21(11):1183–92. Available from: http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=25377394&retmode=ref&cmd=prlinks

7. Manterola C, Vial M, Moraga J, Astudillo P. Analgesia in patients with acute abdominal pain. Cochrane database of systematic reviews (Online). 2011;(1):CD005660.

8. Ranji SR, Goldman LE, Simel DL, Shojania KG. Do opiates affect the clinical evaluation of patients with acute abdominal pain? JAMA. American Medical Association; 2006 Oct 11;296(14):1764–74.

9. Ducharme J. Why is improving pain care so hard? Emerg Med Australas. 2013 Apr;25(2):110–1.

10. Albrecht E, Taffe P, Yersin B, Schoettker P, Decosterd I, Hugli O. Undertreatment of acute pain (oligoanalgesia) and medical practice variation in prehospital analgesia of adult trauma patients: a 10 yr retrospective study. British journal of anaesthesia [Internet]. 2013 Jan;110(1):96–106. Available from: http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=23059961&retmode=ref&cmd=prlinks

11. Heins JK, Heins A, Grammas M, Costello M, Huang K, Mishra S. Disparities in analgesia and opioid prescribing practices for patients with musculoskeletal pain in the emergency department. Journal of emergency nursing: JEN : official publication of the Emergency Department Nurses Association. 2006 Jun;32(3):219–24.

12. Campbell JN. APS 1995 Presidential address. Pain Forum. 1996;5(1):85–8.

13. Turk DC, Dworkin RH, Burke LB, Gershon R, Rothman M, Scott J, et al. Developing patient-reported outcome measures for pain clinical trials: IMMPACT recommendations. Vol. 125, Pain (03043959). 2006. pp. 208–15.

14. Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. 2008. pp. 105–21.

15. Marquié L, Duarte LR, Mariné C, Lauque D, Sorum PC. How patients and physicians rate patients’ pain in a French emergency department using a verbally administered numerical rating scale and a visual analog scale. Acute Pain. 2008;10(1):31–7.

16. Bijur PE, Silver W, Gallagher EJ. Reliability of the visual analog scale for measurement of acute pain. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2001 Dec;8(12):1153–7.

17. Harting B, Johnson T, Abrams R, Odwazny R, Hasler S, McNutt R, et al. An exploratory analysis of the correlation of pain scores, patient satisfaction with relief from pain, and a new measure of pain control on the total dose of opioids in pain care. Qual Manag Health Care. 2013 Oct;22(4):322–6.

18. Todd KH, Funk KG, Funk JP, Bonacci R. Clinical significance of reported changes in pain severity. Ann Emerg Med. 1996 Apr;27(4):485–9.

19. Kendrick DB, Strout TD. The minimum clinically significant difference in patient-assigned numeric scores for pain. American Journal of Emergency Medicine. 2005 Nov;23(7):828–32.

20. Barden J. Defining the Importance of Change in Clinical Trials of Acute Pain. In: McQuay HJ, Kalso E, Moore RA, editors. Systematic Reviews in Pain Research. International Assn for the Study of Pain; 2007. pp. 175–83.

21. Lee JS, Hobden E, Stiell IG, Wells GA. Clinically important change in the visual analog scale after adequate pain control. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2003 Oct;10(10):1128–30.

22. Cepeda MS, Africano JM, Polo R, Alcala R, Carr DB. What decline in pain intensity is meaningful to patients with acute pain? Pain. 2003 Sep;105(1-2):151–7.

23. Klooster ten PM, Drossaers-Bakker KW, Taal E, van de Laar MAFJ. Patient-perceived satisfactory improvement (PPSI): interpreting meaningful change in pain from the patient's perspective. Pain. 2006 Mar;121(1-2):151–7.

24. Bijur PE, Esses D, Chang AK, Gallagher EJ. Dosing and titration of intravenous opioid analgesics administered to ED patients in acute severe pain. The American Journal of Emergency Medicine. 2012 Sep;30(7):1241–4.

25. O'Connor AB, Zwemer FL, Hays DP, Feng C. Intravenous opioid dosing and outcomes in emergency patients: a prospective cohort analysis. The American Journal of Emergency Medicine. 2010 Nov;28(9):1041–6.

26. O'Connor AB, Lang VJ, Quill TE. Underdosing of morphine in comparison with other parenteral opioids in an acute hospital: a quality of care challenge. Pain Med. 2006 Jul;7(4):299–307.

27. MacKenzie M, Zed PJ, Ensom MHH. Opioid Pharmacokinetics-Pharmacodynamics: Clinical Implications in Acute Pain Management in Trauma. Ann Pharmacother [Internet]. 2016 Mar;50(3):209–18. Available from: http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=26739277&retmode=ref&cmd=prlinks

28. Patanwala AE, Keim SM, Erstad BL. Intravenous opioids for severe acute pain in the emergency department. Ann Pharmacother. 2010 Nov;44(11):1800–9.