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# Targeting pro-nociceptive mechanisms to prevent chronic pain after whiplash injury - a randomised controlled trial

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Investigators:

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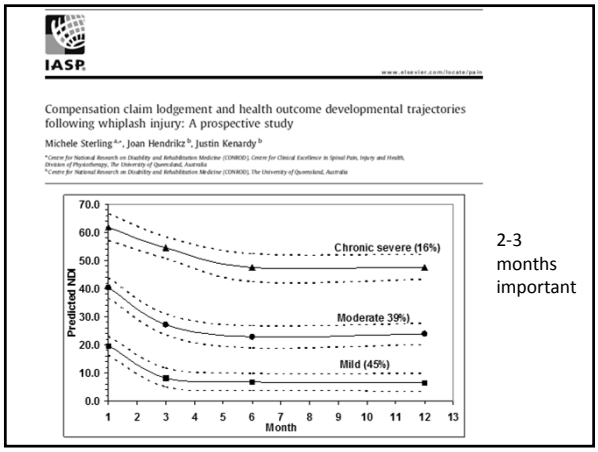
## Whiplash Associated Disorders

- MSK disorders are the second most common cause of disability worldwide, measured by years lived with disability (YLDs). LBP – 1st; neck pain – 4th (Global Burden of Disease Study,2010)
- Whiplash is costly – greater costs than SCI and TBI (MAIC, 2012)
- 50% of people don't recover – have chronic pain & disability (Sterling et al 2005, 2010, 2011)
- Most recovery if it occurs takes place in the first 2-3 months (Sterling et al 2005, 2010, 2011)
- Current treatments aren't very effective – advice/exercise/activity
- Initial pain levels are the strongest predictor of poor outcome – strong evidence – 5 systematic reviews
- The early presence of pro-nociception is predictive of poor recovery – moderate evidence (Goldsmith et al 2012; Sterling et al 2012)
- There have been NO high quality medication trials conducted




2-3 months important

## Why Pregabalin?

- Pregabalin acts to block the development of central sensitisation
- Shows promise to prevent chronic post-surgical pain (Clarke et al, 2012; Mishriky et al, 2015; Eipe et al, 2015)
- Has effects on anxiety
- Use of opioids is a concern
  - Can cause hyperalgesia
  - Opioids at the time of traumatic stress such as a road traffic injury worsen pain outcomes (Beaudoin et al, 2017)
  - Potential for misuse

## Why do this study?

- *Can pregabalin, if given early in acute whiplash, prevent chronic pain that develops in 50% of people after a whiplash injury?*
- Enormous implications for health outcomes, costs, productivity etc.

## Hypotheses

Can pregabalin prevent the development of chronic pain after whiplash injury?

Hypotheses:

1. Pregabalin and evidence-based advice will be more effective than placebo and the same advice in reducing neck pain intensity.
2. Pregabalin and evidence-based advice will be more effective than placebo and the same advice in reducing disability, depression, posttraumatic stress symptoms, pain catastrophizing and pro-nociception.
3. Pregabalin and advice will be cost-effective

## Methodology

Double blind, randomised, placebo-controlled trial comparing

- *pregabalin and evidence-based advice* (intervention) to
- *placebo and evidence-based advice* (control)

for patients with neck pain and VAS of 5 or more.


- Intervention will commence within 12 hours of injury and continue for 5 weeks – monitored by trial GP

## Interventions

**Active group**

- Pregabalin 5 weeks
- Initial dose of 75 mg (x 2 day) titrated over 28 days based on patient response and then weaned (up to max 300mg – 2xday)
- Advice booklet

**Control group**

- Placebo at same dose titration based on response
- Advice booklet


## Inclusion Criteria

- Individuals with neck pain and decreased range of motion and tenderness (WAD II) following road traffic crash
- VAS ≥ 5/10 on arrival without fractures or neurological compromise
- Age 18-65
- Proficient in written and spoken English

## Exclusion Criteria

- Known or suspected serious spinal pathology
- Confirmed fracture or dislocation at the time of the injury (WAD IV)
- WAD III (neurological compromise)
- Previous whiplash injury or neck pain condition requiring treatment
- Patient Health Questionnaire-2 score of 3 or more
- Patients using gabapentin/pregabalin
- Patients with known peripheral neuropathy
- Known sensitivity to pregabalin use
- History of renal insufficiency
- Women who are pregnant or breast feeding
- History of psychiatric illness or substance abuse
- Inability to speak or write in English

## Outcome measurement

- Will be performed by blinded assessor

***Primary Outcome***

- neck pain intensity (NRS) at 3 months post randomization

***Secondary Outcomes:***

- Neck Disability Index
- Pain Catastrophising Scale
- Posttraumatic Stress Diagnostic Scale
- DASS
- Measures of pro-nociception - conditioned pain modulation, temporal summation
- S-LANSS
- SF-12*
- Proportion of participants who lodge a claim

**Follow-ups:** 5 weeks, 6 & 12 months

Sample size : The primary outcome is change in neck pain intensity at 3 months post randomisation. A sample size of 180 participants (90/group) will provide 90% power to detect a difference of 1.5 out of 10 units of pain on the NRS, assuming a standard deviation of 2.5, at 5% type 1 error level, and allowing for the possibility of dropout of 30%. We have based the sample-size calculation on a between-group difference of 1.5/10 on the NRS on IMMPACT recommendations for clinical trials of chronic pain prevention

Data analysis: Intention to treat, blinded statistician, linear mixed models

Economic analysis: MBS, PBS and diary data, Sf-12

Progress to date

- Trial registered
- Protocol publication near finalisation
- ANZMusc review for NHMRC submission
- Ethics, procedures, protocols established at GCUH
- Trial commenced GCUH
- Ipswich Hospital to be added soon

Issues to date:

| Issue | Plan |
|---|---|
| Recruitment | Add additional site/s – Ipswich, elsewhere |
| Patient after hours/weekend presentations | Funding issue, some funding for nurses/physios to identify patients<br>Pay/patient<br>RA flexibility with hours |
| Declined consent – don't want drugs | Intern doctors to now employed to explain trial |
| Not meeting inclusion criteria | ? Extend time frame post injury |
| Doctors onside | Doing ED audit of presentations<br>In service talks – Sterling, McLean |