A systematic review of patient reported outcome measures used to assess the effectiveness of opioid therapy in patients with chronic non-cancer pain

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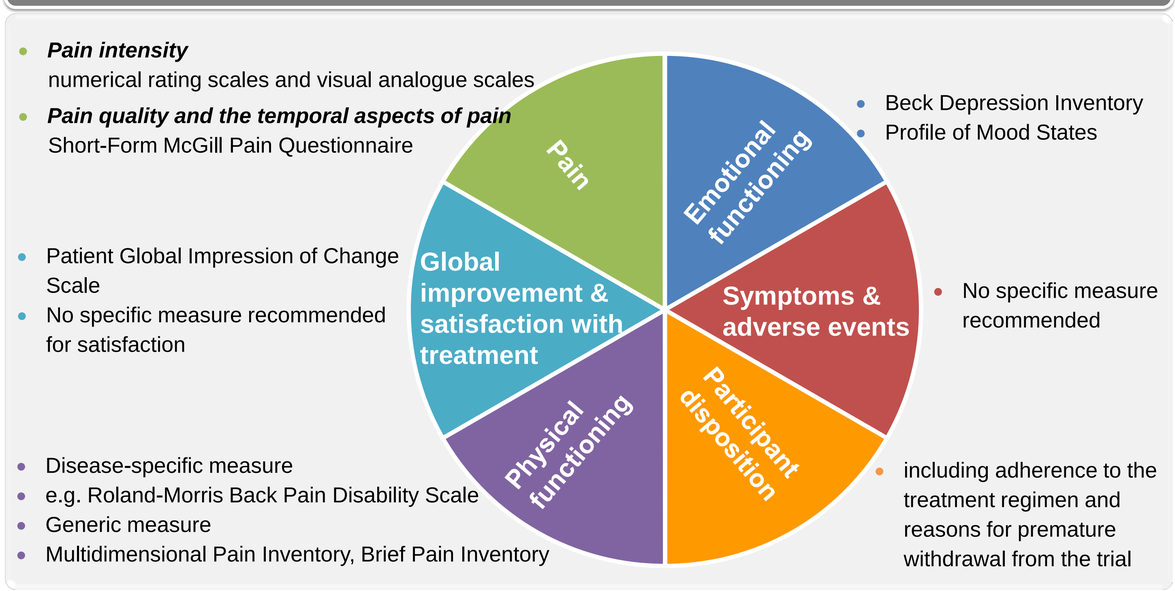
Introduction

Opioid utilisation for persistent non-cancer pain (PNCP) has increased worldwide over the past decade, however the long-term effectiveness of opioids for PNCP is still controversial. The efficacy of opioids was mostly assessed in short-term randomised controlled trials (RCTs) using complex measures following the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) recommendations (Figure 1). Patient reported outcome measures (PROMs) are predominantly used for assessing pain due to its subjective nature and the lack of biological markers, but they are rarely recorded in routine clinical practice.

Figure 1. Core domains for CNCP treatment efficacy and effectiveness in clinical trials



Aim

This systematic review aimed to summarise PROMs commonly used in RCTs and observational studies for evaluating opioid treatment in patients with CNCP, and to identify PROMs or domains that are feasible to be used in routine practice.

Methods

Search strategies

- An electronic database search was conducted using structured search strategies on EMBASE (1980 to Aug 2014), Ovid MEDLINE (1946 to Aug 2014), PubMed (Jan 1996 to Aug 2014) and Web of Science. The search strategies included search terms related to 'chronic pain' and 'opioid analgesics' as well as outcome measures.
- The searches were limited to English language, full text, human subjects and adults. Reference lists of identified articles were also reviewed to retrieve relevant studies.

Inclusion and exclusion criteria

- Full-published English original articles of prospective observational studies or RCTs that evaluated oral or transdermal opioids used in adult patients with CNCP and reported PROMs were included (Table 1). Reference lists of identified articles were also checked to include other eligible articles.

Outcome summary

- The identified PROMs and the domains of PROMs (including pain intensity, pain quality and temporal aspects of pain, physical functioning, emotional functioning, global improvement and satisfaction with treatment, symptoms and adverse events) were compared between RCTs and observational studies.
- The quality of selected studies was assessed by the Jadad Scale, Cochrane Collaboration's Risk of Bias tool, Newcastle-Ottawa Scale, and GRACE checklist.

Table 1. Inclusion and exclusion criteria

Criteria	Inclusion	Exclusion
Population	• Adult patients aged ≥18 years old with CNCP.	• Patients with cancer pain, pre-operative, post-operative or acute pain with duration < 3 months. • Duration of pain < 3 months.
Intervention	• Any opioids listed in the BNF and opioid agonists. • Opioids administered orally or transdermally.	• Opioids administered via intravenous, intrathecal or intramuscular routes. • Opioids prescribed < 120 days or opioids taken < 90 days or < 11 opioids prescriptions a year. • Opioids taken for purposes other than CNCP (i.e. addiction). • Patients only receive non-opioids therapy. • No intervention
Outcomes	• Patient-reported outcomes including: • Pain intensity (pain score) • Physical function (walk, exercise, ability to carry out normal daily activities) • Psychological/Mental condition (depression) • Quality of life	• Reported outcomes that focus on drug interactions, pharmacodynamics, pharmacology and pharmacokinetic. • No patient-reported outcome measures reported

Results

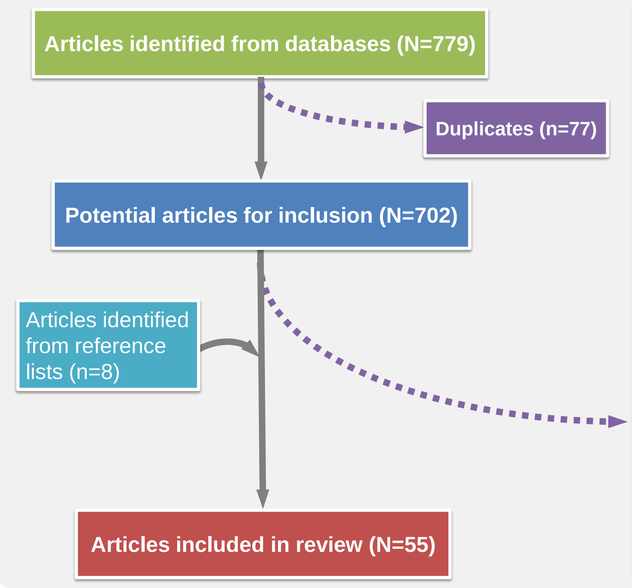
Selection of studies

- Overall, 55 studies including RCTs (n=19), pooled analysis of two RCTs (n=1), and observational studies (n=35), were selected and 59 different PROMs were identified (Figure 2).

Characteristics of included studies

- The duration of included studies ranged from 2 weeks to 3 years, although some articles did not state study duration. Majority of the studies were conducted in the US (n=29). Number of participants ranged from 18 to 6496.
- The majority of included studies included patients with various CNCP conditions (n=35). Where studies focused on a specific CNCP condition the most frequency condition examined was osteoarthritis (n=8). The most frequently studied opioids were fentanyl, morphine, tramadol, hydromorphone and oxycodone in oral or transdermal forms.

Figure 2. Selection of RCTs and observational studies



Frequency of PROM used in RCTs and observational studies

- The most frequently used PROMs in both RCTs and observational studies were numerical rating scales, Short-Form Health Survey-36, visual analogue scales and Brief Pain Inventory. The PROM most frequently used in observational studies that was not used in RCTs was the Patient Health Questionniare-8 (n=6) (Table 2).

Domains of PROMs used in RCTs vs. observational studies

- Unsurprisingly, pain intensity was the most frequently assessed outcome domain in both RCTs and observational studies. Compared with RCTs that mainly focused on pain intensity and physical functioning, observational studies tended to include more outcome domains than the RCTs, particularly pain quality and temporal aspects of pain, and emotional functioning.

Table 2. Top 10 PROMs most frequently used in RCTs and observational studies

Used in RCTs only		Used in both RCTs and observational studies			Used in observational studies only	
PROM	**frequency**	**PROM**	**frequency RCT**	**frequency observational studies**	**PROM**	**frequency**
Patient Assessment of Constipation Symptoms	2	Numerical Rating Scale for Pain Intensity	8	9	Patient Health Questionnaire-8	6
Profile of Mood States	2	Brief Pain Inventory	3	10	Chronic Pain Grade Scale	4
Subjective Opioid Withdrawal Scale	2	Visual Analog Scale for Pain Intensity	6	4	Pain Impact Scale (from Chronic Pain Grade)	3
Activities of Daily Living	1	Short-Form Health Survey-36	4	6	Prescribed Opioids Difficulties Scale	3
Arthritis Pain Intensity Visual Analog Scale	1	Beck's Depression Index	1	4	Pain Catastrophizing Scale	2
Chronic Pain Sleep Inventory	1	Center for Epidemiological studies - Depression Scale	1	4	State-Trait Anxiety Inventory	2
Depression and Anxiety and Stress Scale-21	1	McGill Pain Questionnaire	2	3	WMH - CIDI	2
Drug Effects Questionnaire	1	Multidimentional Pain Inventory	1	4	Addiction Severity Index	1
Drug Liking Index	1	Pain Diability Index	3	2	DN4	1
Opiate Withdrawal Scale	1	WOMAC Osteoarthritis Index	4	1	EQ-5D	1

Conclusion

The PROMs for assessing opioid treatment in patients with CNCP are complex. In addition to pain intensity, there was general agreement between RCTs and observational studies that pain quality, temporal aspects of pain, emotional and physical functioning are critical domains to be measured. However, the results are limited by selection and reporting bias due to only selecting English articles, and the poorly reported details of outcome measures in abstracts or published articles. To apply those measures in routine clinical practice, ensuring the value to patients and the utility to healthcare professionals, a simple and easily accessed platform to collect and integrate information into clinical decision making is still needed.

Poster presentation, 23rd HSRPP Conference, University of Nottingham, April 10th-11th 2017, Email: li-chia.chen@manchester.ac.uk