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A systematic review and qualitative evidence synthesis of the experiences of people taking opioid medication for chronic non-malignant pain: a meta-ethnography

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-032988
Article Type:	Research
Date Submitted by the Author:	15-Jul-2019
Complete List of Authors:	Nichols, Vivien; University of Warwick, Warwick Clinical Trials Unit, Warwick Medical School Toye, Francine; Oxford University Hospitals NHS Trust, Nuffield Orthopaedic Centre Physiotherapy Research Unit Eldabe, Sam; The James Cook University Hospital Sandhu, Harbinder; University of Warwick, Warwick Clinical Trials Unit, Warwick Medical School Underwood, Martin; University of Warwick, Warwick Clinical Trials Unit, Warwick Medical School; University Hospitals of Coventry and Warwickshire Seers, Kate; University of Warwick, Warwick Research in Nursing, Division of Health Sciences, Warwick Medical School
Keywords:	opioid, patients' views, QUALITATIVE RESEARCH, chronic non-malignant pain, meta-ethnography, qualitative evidence synthesis

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A systematic review and qualitative evidence synthesis of the experiences of people taking opioid medication for chronic non-malignant pain: a meta-ethnography

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Abstract

Objective To review qualitative studies of the experience of taking opioid medication for Chronic Non-Malignant Pain (CNMP)

Design A qualitative evidence synthesis using meta-ethnography.

Methods We used a seven step approach from the methods of meta-ethnography. We searched selected databases for qualitative studies which gave patients' views of taking opioid medication for CNMP. Papers were quality appraised using a CASP tool and GRADE-CERQual guidelines were applied. We identified concepts and iteratively abstracted these concepts into a line of argument.

Results We screened 2129 unique citations, checked 153 full texts and 31 met our review criteria. We identified five themes: 1) Reluctant users with little choice; 2) Understanding opioids: the good and the bad; 3) A therapeutic alliance: not always on the same page; 4) Stigma: feeling scared and secretive but needing support; and 5) The challenge of tapering or withdrawal. A new overarching theme of 'constantly balancing' emerged from the data.

Conclusions People taking opioids are constantly balancing tensions, not always wanting to take opioids, but feeling they have no choice because of the pain. They frequently feel judged, were not always 'on the same page' as their health care professional and changes in opioid use were often challenging.

Key words: Opioid, patients' views, qualitative research, chronic non-malignant pain, meta-ethnography, qualitative evidence synthesis.

Word count 4,863

Strengths and Limitations

- To our knowledge this is the first qualitative evidence synthesis of patients' experiences of taking opioid medications.
- Meta-ethnography provides a thorough, systematic way of synthesising qualitative findings across multiple studies and gives the reviewer's interpretation of the data.
- Using a GRADE-CERQual approach can assist in rating confidence in the review findings.
- Qualitative research that illuminates patients' perspectives can help to shape future approaches to opioid management.

Introduction

Chronic non-malignant pain (CNMP) affects an estimated 11 to 20% of the population in Europe and US respectively and can impact heavily on people's quality of life ^{1,2}. Opioid medications are strong painkillers which have a well-established role in the treatment of acute and cancer pain; they have also been advocated for CNMP. Opioids can have distressing side effects as dosages increase such as; constipation, sedation, drowsiness, nausea, decreased concentration and memory, or mood changes ³. Most people who use opioids develop tolerance to the painkilling effect of opioids, and some become dependent on them. Studies have shown that high opioid usage can also put people's lives at risk ⁴. Despite this, the prescription of opioid medication for CNMP has risen sharply in the higher income countries. Few studies of opioids have shown effectiveness beyond 12 weeks follow up. Population

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2
3 surveys have shown long-term use to be associated with increased side effects and
4
5 limited pain relief^{3 5 6}.

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8 This synthesis of qualitative research was undertaken to underpin a process evaluation
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10 for the Improving the Wellbeing of people with Opioid Treated Chronic pain (I-
11
12 WOTCH) study funded by the National Institute for Health Research. I-WOTCH is a
13
14 randomised controlled trial evaluating a multi-component education and patient
15
16 centred group intervention with tapering programme against a control of an advice
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18 booklet with a relaxation CD. More information can be found in the main study
19
20 protocol (in press) and process evaluation protocol (under review) (references to be
21
22 added).
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26 This qualitative evidence synthesis uses the methods of meta-ethnography to find out
27
28 what peoples' experiences are of both using opioids for CNMP and their attempts to
29
30 stop taking them.
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33 34 **Methods**

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37 We use Noblit and Hare's 7 stages of meta-ethnographic analysis⁷. We used the new
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39 eMERGe reporting guidelines for meta-ethnography to structure our report⁸ (*See*
40
41 *appendix 1*). The protocol is published in the international prospective register of
42
43 systematic reviews (PROSPERO) registration number: CRD42017082418.
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47 <http://www.crd.york.ac.uk/PROSPERO>

48 49 *Step 1 Getting Started.*

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51 In order to address what has been labelled an opioid epidemic⁹, we need to
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53 understand peoples' experiences of being on opioids and of coming off them. Our
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55 team was chosen because of its expertise in primary qualitative research and
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57 qualitative evidence synthesis specific to chronic pain and opioid prescription.
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3 *Step 2 Deciding what is relevant.*
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5 We undertook systematic electronic searches in June 2017 with a rerun in September
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7 2018, appraising relevant papers for quality using the Critical Appraisal Skills
8 Programme (CASP) tool for qualitative research ¹⁰. One researcher (VN) with the
9 assistance of an academic librarian (SJ) searched 7 electronic databases; Medline,
10 Embase, AMED, CINAHL, PsycInfo Web of Science and Scopus (Science citation
11 index and Social Science Citation Index) and forward citation searches. We used
12 search terms, free text and MeSH terms for all opioid drugs as well as their generic
13 names. We combined these with the MeSH term 'pain' and a wide range of MeSH
14 terms and words to describe all types of qualitative research and its analysis based
15 upon a search used by Toye, Seers and Barker in 2017 ¹¹. The search was limited to
16 those in English regarding humans with no cut-off date. Appendix 2 shows an
17 example of our search terms.
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33 Unique citations were screened independently by 2 researchers (VN ST *see*
34 *acknowledgements*) against our inclusion and exclusion criteria (see Box 1). Any
35 disagreements were arbitrated by a third researcher (KS). Papers for full text reading
36 were identified and read by two researchers. Quality was assessed using a CASP tool.
37 VN critically appraised the studies and KS independently appraised 10% for
38 consistency. The CASP scores are shown in table 1 and appendix 3. The GRADE-
39 CERQual (Confidence in Evidence from Reviews of Qualitative research) was used to
40 appraise the reviewers' confidence in the research findings ^{12, 13}.
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51 *Box 1 Inclusion/Exclusion criteria*
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54 **Included Studies**

55 Adults (18 years or older) taking or have taken opioid medication in the last five years
56 Published in English in peer review journals with no time constraint
57 Must relate to patient perspectives on using opioid medication for chronic non-malignant pain
58 Must use qualitative methodology (any analytical approach) or mixed quantitative and qualitative
59 methodology with qualitative findings reported separately
60 Where studies include participants with differing medication we will include studies where the

1
2
3 experience of those taking opioids is reported separately

4 **Excluded studies**

5 Theoretical or methodological papers

6 Purely quantitative studies or mixed methods studies where the qualitative data are not presented
7 separately

8 Studies concerning active cancer

9 Studies concerning headache

10 Studies concerning any acute, or acute postoperative, pain

11 Studies concerned only with health care professional or carer perspectives, or studies of mixed
12 carer/ patient/ professional populations where patient perspectives are not presented separately

13 Non- English language studies

14 Theses or conference abstracts which are not peer reviewed

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17 *Step 3 Reading the studies*

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19 VN read all the studies and KS and FT read half of these papers each (so all were read
20 twice) and all extracted the second order concepts independently. A second order
21 concept is a researcher's interpretation of data in a primary qualitative study¹⁴. VN,
22 KS and FT met to discuss and reach agreement, and compiled a spreadsheet of all of
23 the concepts extracted from the papers

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26 *Step 4 Determining how the studies are related?*

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28 VN sorted the concepts into categories by looking for any similarities and differences
29 across all the studies. VN, KS and FT discussed the categorisation of data on multiple
30 occasions. To enable comparison across studies, VN recorded descriptive data about
31 each study (see table 1)

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For peer review only

Table 1 Study characteristics with CASP and GRADE-CERQual relevance ratings

Studies	Country	Data collection / participants	Analytical Approach	Aims <i>Italics = verbatim quotes</i>	Comments	CASP score	Relevance
1 Arnaert et al 2006 ¹⁵ Response Phases in Methadone Treatment for Chronic Non-malignant Pain	Canada	Semi-structured interview N=11 (4M/7F)	Content analysis	<i>"...to develop an understanding and to gain knowledge about the beliefs of patients with CNMP who were taking methadone, and to explore what challenges, if any, existed that affected their beliefs when first starting methadone treatment as an activity in their personal lives."</i>	Methadone specific	17/20	P
2 Bergman et al 2013 ¹⁶ Contrasting Tensions Between Patients and PCPs in Chronic Pain Management: A Qualitative Study	USA	In-depth interviews N=26 (24m/2F)	Inductive thematic analysis	<i>"... to develop a better understanding of the respective experiences, perceptions, and challenges both patients with chronic pain and PCPs face communicating with each other about pain management in the primary care setting."</i>	USA Veteran	17/20	P
3 Blake et al 2007 ¹⁷ Experiences of patients requiring strong opioid drugs for chronic non-cancer pain: a patient initiated study	UK	One focus group N=4 (2M/2F) and interviews N=10 (3M/5F)	Interpretative Phenomenological Analysis	<i>"...to determine the attitudes and experiences of patients receiving long-term strong opioid medication for chronic non-cancer pain in primary care."</i>	Key	19/20	R
4 Brooks et al 2015 ¹⁸ Exploring the lived experience of adults using prescription opioids to manage chronic noncancer pain	Canada	In-depth interviews N=9 (4M/5F)	Interpretative Phenomenological Analysis	<i>"...to explore the lived experience of adults using prescription opioids to manage CNCP, focusing on how opioid medication affected their daily lives."</i>	Key	17/20	R

1 2 3 4 5 6 7 8 9 10 11	5 Buchbinder et al 2014 ¹⁹ “Is there any way I can get something for my pain?” Patient strategies for requesting analgesics	USA	Audio recorded clinical encounters N=74 (37M/37F)	Qualitative approach based on conversational analysis	<i>“We examined the direct and indirect means by which patients express a desire for analgesic medication.”</i>	More for acute back pain in an emergency setting. Not opioid specific although includes information about opioids	18/20	I
12 13 14 15 16 17 18 19 20	6 Chang Y-P et al 2011 ²⁰ Use of Prescription Opioid Medication among Community-Dwelling Older Adults with Noncancer Chronic Pain	USA	Face to face interview N=21 (13M/8F) ≥65yrs	Content analysis, mixed methods	<i>“... to: (1) describe older adults’ patterns of adherence to their prescription opioid medication regimens and their reasons for these medication use patterns; and (2) examine the associations between adherence of prescription opioids, pain intensity, and pain interference on daily activity.”</i>	Thematically 'thin'	16/20	P
21 22 23 24 25 26 27 28 29	7 Chang,F et al 2017 ²¹ Perceptions of Community-Dwelling Patients and Their Physicians on OxyContin® Discontinuation and the Impact on Chronic Pain Management	Canada	Pt interviews N=13 1M/ 12F	Not specified, no references given	<i>“... to explore the perceptions of patients with chronic pain and their physicians on OxyContin discontinuation and the impact that it had on chronic pain care and management.”</i>	Key	16/20	P
30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46	8 Coyne et al 2015 ²² Assessment of a Stool Symptom Screener and Understanding the Opioid-Induced Constipation Symptom Experience	USA	Cognitive interview semi structured think-aloud approach N=66 (27M/39F)	Content analysis	<i>“...to evaluate the content validity of the Stool Symptom Screener by assessing patient understanding of its items, patient ability to differentiate among response options, and patient perceptions about the use of a 2-week recall period for evaluating stool symptoms, BMs, and laxative use. - to evaluate how patients describe their</i>	PROM specific with additional questions about constipation	17/20	I

				<i>constipation experience and to understand whether this differs between patients who frequently use laxatives and those who do not.</i>			
9 Esquibel et al 2014 ²³ Doctors and patients in pain: Conflict and collaboration in opioid prescription in primary care	USA	In depth interviews with pts with CNCP receiving opioids and their physicians. N=21 pts (8M/13F)	Immersion/crystallization process to generate a thematic codebook. Mixed methods with some quant. data analysis	<i>"...to better understand the effects of COT [chronic opioid therapy] on the doctor-patient relationship."</i>	Key	20/20	R
10 Frank et al 2016 ²⁴ Patients' Perspectives on Tapering of Chronic Opioid Therapy: A Qualitative Study	USA	Semi-structured interviews N=24 (11M/13F)	Team based, mixed inductive and deductive approach guided by the Health Belief Model	<i>"... to explore patients' perspectives on opioid tapering."</i>	Key	20/20	R
11 Green et al 2017 ²⁵ Perpetuating stigma or reducing risk? Perspectives from naloxone consumers and pharmacists on pharmacy-based naloxone in 2 states	USA	8 focus groups (only 2 with patients with chronic pain) N=15 (8M/7F)	Thematic analysis. Content analysis with a collaborative codebook development process	<i>"...to explore the attitudes of various stakeholders toward pharmacy-based naloxone and opioid medication safety and to capture the range of initial experiences with pharmacy naloxone in 2 states with pharmacy naloxone policies."</i>	Naloxone specific thematically thin	18/20	P

1 2 3 4 5 6 7 8 9 10 11	12 Hooten et al 2011 ²⁶ Smoking Cessation and Chronic Pain: Patient and Pain Medicine Physician Attitudes	USA	N = 18 Interviews N= 15 and focus group N=3 10M/8F	Participatory research, mixed methods - Thematic and content analysis	<i>"...to determine the attitudes and beliefs of both patients and pain medicine physicians regarding smoking cessation interventions applied during pain therapy."</i>	Main focus smoking cessation	18/20	I
12 13 14 15 16 17 18 19 20	13 Krebs et al 2014 ²⁷ Barriers to Guideline- Concordant Opioid Management in Primary Care—A Qualitative Study	USA	Semi structured interviews N= 26 patients (14 PC physicians) 13M/13F	Immersion crystallization approach	<i>"...to better understand primary care physicians' and patients' perspectives on recommended opioid management practices and to identify potential barriers and facilitators of guideline concordant opioid management in primary care."</i>	USA specific barriers to guideline use	16/20	P
21 22 23 24 25 26 27 28 29 30	14 Matthias et al 2013 ²⁸ Communicating about opioids for chronic pain: A qualitative study of patient attributions and the influence of the patient–physician relationship	USA	Audio Recordings of primary care visits and Semi- structured interviews after clinic visit. N=30 26M/4F	Immersion/cry stallization approach	<i>"...to advance understanding about communication about opioids by directly capturing clinical communication about opioids, as well as interviewing patients to gain insight into communication patterns and their broader relationships with their physicians, and how these relationships shape communication about opioids."</i>	USA veterans medical centre.	18/20	R
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46	15 McCrorie et al 2015 ²⁹ Understanding long-term opioid prescribing for non- cancer pain in primary care: a qualitative study	UK	Semi structured interviews with patients (focus groups with GPs) N=23	Grounded approach for thematic analysis. Constant comparison	<i>"... to understand the processes which bring about and perpetuate long-term prescribing of opioids for chronic, non-cancer pain. We interviewed patients and GPs about their experiences, beliefs and expectations of analgesia prescribing, to improve understanding of how problematic long-term</i>	Key	17/20	R

		6M/17F		<i>opioid prescribing becomes established”.</i>			
16 Mueller et al 2016 ³⁰ Attitudes Toward Naloxone Prescribing in Clinical Settings: A Qualitative Study of Patients Prescribed High Dose Opioids for Chronic Non-Cancer Pain	USA	Semi-structured interview N=24 8M/16F	Ethnographic iterative methods. Inductive and deductive approaches	<i>“This study assessed the knowledge and attitudes toward naloxone prescribing among non-cancer patients prescribed opioids in primary care.”</i>	Naloxone specific	16/20	I
17 Paterson et al 2016 ³¹ Resisting Prescribed Opioids: A Qualitative Study of Decision Making in Patients Taking Opioids for Chronic Noncancer Pain	Australia	Qualitative individual interviews N=20	Constant comparison and decision making explored in depth and with a thematic analysis utilizing a published "Model of medicine-taking"	<i>“...to identify the varying influences on patients’ decisions about their use of prescribed long-term opioids. The research questions are: 1) does this conceptual Model of medicine-taking apply to people taking prescribed opioids, 2) is the concept of “resistance” to medication useful in this context, and 3) does this concept lead to new insights which may improve communication and shared decision making between”</i>	Key. Patients interested in non-medication pain management options.	18/20	P
18 Penney et al 2016 ³² Provider and patient perspectives on opioids	USA	11 Focus groups N=80 and	Thematic coding ref Ryan, Bernard	<i>“...to identify the practical issues patients and providers face when accessing alternatives to opioids, and how multiple parties view these</i>	FG and interview questions not opioid specific. No	13/20	P

and alternative treatments for managing chronic pain: a qualitative study		individual interviews N=10 27M/63F	2003	<i>issues.</i> ”	demographics		
19 Rieb et al 2016 ³³ Withdrawal-associated injury site pain (WISP): a descriptive case series of an opioid cessation phenomenon	Canada	In person semi structured interviews N=21 14M/7F	Deductive and inductive approaches. Use of survey and emergent interview themes	<i>“.... to document the existence and characteristics of this pain phenomenon that we have named withdrawal-associated injury site pain (WISP).”</i>	Thematically thin. Specific to 2 weeks post withdrawal of opioids	18/20	P
20 Simmonds et al 2015 ³⁴ A Qualitative Study of Veterans on Long-Term Opioid Analgesics: Barriers and Facilitators to Multimodality Pain Management	USA	Semi structured focus groups x 3 N=25 17M/8F	Grounded theory-informed approach. Framework provided by the theory of planned behaviour	<i>“...to examine barriers and facilitators to multimodality chronic pain care among veterans on high-dose opioid analgesics for chronic non-cancer pain.”</i>	USA veteran specific.	16/20	P
21 St Marie et al 2016 ³⁵ Primary care experiences of people who live with chronic pain and receive opioids to manage pain: A qualitative methodology	USA	Semistructured interviews. N=12 6M/6F	Thematic and interpretive analyses	<i>“...to provide a deeper understanding of the experiences, issues, and challenges that people face who live with chronic pain and received opioids to help manage their pain in primary care. The following research questions were addressed: (a) What are the experiences of individuals who live with chronic pain and receive opioid pain medications to manage</i>	9/12 had a history of substance use disorder	19/20	R

				<i>their pain in primary care? (b) What have been their healthcare experiences as they strive to manage their pain?"</i>			
22 Vallerand et al 1 2009 ³⁶ Chronic Opioid Therapy for Nonmalignant Pain: The Patient's Perspective. Part I—Life Before and After Opioid Therapy	USA	In depth serial interviews N=22 6M/16F	Phenomenologic study / Constant comparative method	<i>"...to examine the lived experience of adults receiving opioid therapy for relief of chronic non-malignant pain through the examination of data obtained through serial taper recorded interviews."</i>	Same cohort as study below.	14/20	R
23 Vallerand et al 2 2010 ³⁷ Chronic Opioid Therapy for Non-malignant Pain: The Patient's Perspective. Part II—Barriers to Chronic Opioid Therapy	USA	In depth serial narrative interviews N=22 6M/16F	Phenomenologic study / Constant comparative method	<i>"...to elucidate the essence of the lived experience of patients receiving chronic opioid therapy for chronic non-malignant pain through examining their life narratives."</i>	Same cohort as study above. Medication costs and medication may be USA specific.	13/20	R
24 Wallace et al 2014 ³⁸ Voices that may not otherwise be heard: a qualitative exploration into the perspectives of primary care patients living with chronic pain	USA	Photovoice photos, Interviews 1st N=31 2nd N=25 , and focus groups N=19	Grounded theory	<i>"...this study examined the utility of a combination of qualitative methods (Photovoice, one-on-one interviews, and focus groups) in examining the daily experiences of primary care patients living with chronic pain".</i>	All receiving opioid meds for CNCP for at least 6ms	16/20	R
25 Warms et al 2005 ³⁹ There are a few things you did not ask about my pain: writing on the margins of a survey	USA	Comments written in the margins of a questionnaire N=797	Content analysis	<i>"...to determine the characteristics of those who wrote comments [written in the margin of survey questionnaire] and to understand what was being communicated in their comments."</i>	Primarily about spinal cord injury and amputation.	16/20	P

26 Zgierska et al 2016 40 Mindfulness Meditation-Based Intervention Is Feasible, Acceptable, and Safe for Chronic Low Back Pain Requiring Long-Term Daily Opioid Therapy	USA	Qual data on treatment satisfaction and experience N= 17	Qualitative analysis methods. Grounded theory	<i>"... to determine feasibility, acceptability, and safety of an MM-based intervention in patients with CLBP requiring daily opioid therapy."</i>	Focus is on evaluating an intervention	18/20	I
27 Zheng et al 2013 41Chaos to Hope: A Narrative of Healing	Australi a	In depth qual interviews (N=20) 10M/10F	Illness narratives. Thematic analysis	<i>"...to investigate the progression of the illness and opioid journeys of people who are taking opioids for chronic non-cancer pain".</i>	Key Qualitative study nested in a RCT investigating the role of acupuncture in reducing opioid medication consumption by patients with chronic non-cancer pain	17/20	P
Rerun of search							
28 Al Achkar et al 2017 42 Exploring perceptions and experiences of patients who have chronic pain as state prescription opioid policies change: a qualitative study in Indiana	USA	N=9 3M/6F	Inductive emergent thematic analysis	<i>"...to evaluate the impact of Indiana's opioid prescription legislation on the patient experiences around pain management."</i>	USA state specific	19/20	R
29 Matthias et al 2017 43 "I'm Not Gonna Pull	USA	N=37 12M/25F	Inductive approach,	<i>"...to understand communication processes related to opioid tapering."</i>	Key	19/20	R

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the Rug out From Under You": Patient-Provider Communication About Opioid Tapering			constant comparison				
30 Matthias et al 2018 44 "I Was a Little Surprised": Qualitative Insights From Patients Enrolled in a 12-Month Trial Comparing Opioids With Nonopioid Medications for Chronic Musculoskeletal Pain	USA	N=34 28M/6F	Inductive approach, constant comparison	<i>"...to understand patients' experiences with the SPACE trial including their views and anticipated benefits of opioids, versus non - opioids, experiences with the intervention and to what extent expectations were met after completing the study."</i>	Only used data of 18 who had experience of opioid medication	18/20	R
31 Smith et al 2018 45 Seeking Chronic Pain Relief: A Hermeneutic Exploration	USA	N=15 4M/11F	Concurrent embedded mixed methods design, Heideggerian hermeneutic phenomenological approach	<i>"This research presents an interpretation of the experience of seeking pain relief for a group of people taking opioid pain medications whose pain is not adequately controlled"</i>	Key but recruited through internet Specifically uncontrolled pain	20/20	P

Legend: GRADE-CERQual Relevance component: R= Relevant, P= Partial relevance, I= Indirect relevance, U=Uncertain relevance

Step 5 Translating studies into each other

Patterns and associations between categories were explored and all researchers felt that a line of argument approach as defined by Noblit and Hare ⁷ would be the most useful method to interpret the data.

Step 6 Synthesising Translations

Agreement was reached by clearly defining the over-arching or 3rd order concepts arising from the data. A third order concept is the reviewers' interpretation of second order concepts.

Step 7 Expressing the synthesis

We developed a conceptual model to show how the themes related to each other in a line of argument. (see figure 1)

Insert figure 1 about here.

Patient and Public Involvement

We did not involve patients or the public in our work.

Findings

Two reviewers VN and ST screened 2994 titles or abstracts (after the removal of duplicates from the 5064 citations retrieved) and identified 153 full texts of interest.

Two reviewers VN and KS read these and 122 were excluded. Reasons are given in the PRISMA flowchart, see figure 2. The reviewers agreed to include 31 studies. The included studies were from US (24), Canada (4) UK (2), and Australia (2) and used a range of qualitative methods.

We report the 4 facets of GRADE-CERQual for all papers. 1) Methodological 2) Confidence 3) Relevance 4) Adequacy of data - See table 2 below.

Table 2 Confidence in review findings: GRADE-CERQual assessment

Review findings	Studies contributing	Methodological limitations	Relevance	Coherence	Adequacy of data
Reluctant users with little choice	1,3,4,5,6,7,17,18,21,22,26,27,30 (13 studies)	7 no concerns	4 Relevant 6 Partial 2 Indirect	No concerns	No concerns
Understanding opioids: the good the bad	1,3,7,9,10,11,15,16,17,23,25,27,29. (13 studies)	11 no concerns 1 minor concerns	6 Relevant 5 Partial 1 Indirect	No concerns	No concerns
A therapeutic alliance: not always on the same page	1,2,3,4,5,7,9,10,11,13,14,15,16,17,18,19,20,21,22,23,24,25,26,28,29,31(26 studies)	23 no concerns 3 minor concerns	10 Relevant 10 Partial 3 Indirect	No concerns	No concerns
Stigma: feeling scared, and secretive but needing support	1,2,3,4,7,9,10,14,16,17,18,20,21,22,23,24,27,28,31 (19 studies)	11 no concerns 3 minor concerns	8 Relevant 8 Partial 1 Indirect	No concerns	No concerns
The challenge of tapering/ withdrawal from opioids	7,10,18,19,30,31	5 no concerns 1 minor concerns	3 Relevant 3 Partial	Minor concerns	Minor concerns

Legend of GRADE-CERQual component scoring:

Methodological limitations, Coherence, Adequacy of data	No or very minor concerns Minor concerns Moderate concerns Serious concerns
Relevance:	Relevant Partial Indirect Uncertain

Synthesis of Findings

We abstracted five themes from the 2nd order concepts. Table 3 below shows how each study contributed to each theme. We have illustrated each concept with exemplary quotations.

Table 3 Themes apparent in each study

Author date	RU	U	TA	S	TW
1 Arnaert and Ciccotosto 2006	X	X	X	X	
2 Bergman, Matthias et al 2013			X	X	
3 Blake, Ruel et al 2007	X	X	X	X	

4 Brooks, Unruh et al 2015	X		X	X	
5 Buchbinder, Wilbur et al 2014	X		X		
6 Chang Y-P, Wray et al 2011	X				
7 Chang,F and Ibrahim,S 2017	X	X	X	X	X
8 Coyne, Currie et al 2015					
9 Esquibel and Borkan 2014		X	X	X	
10 Frank, Levy et al 2016		X	X	X	X
11 Green, Case et al 2017		X	X		
12 Hooten, Vickers et al 2011					
13 Krebs, Bergman et al 2014			X		
14 Matthias,Krebs et al 2013			X	X	
15 McCrorie, Closs et al 2015		X	X		
16 Mueller, Koester et al 2016		X	X	X	
17 Paterson, Ledgerwood 2016	X	X	X	X	
18 Penney, Ritenbaugh et al 2016	X		X	X	X
19 Rieb, Norman et al 2016			X		X
20 Simmonds, Finley et al 2015			X	X	
21 St Marie et al 2015	X		X	X	
22 Vallerand et al 1 2009	X		X	X	
23 Vallerand et al 2 2010		X	X	X	
24 Wallace et al 2014			X	X	
25 Warms et al 2005 o		X	X		
26 Zgierska et al 2016	X		X		
27 Zheng et al 2013	X	X		X	
Studies from search rerun	RU	U	TA	S	TW
28 Al Achkar et al 2017			X	X	X
29 Matthias et al 2017		X	X		X
30 Matthias et al 2018	X				
31 Smith et al 2018			X	X	

Legend:

RU = Reluctant users with little choice

U = Understanding about opioids: the good and the bad

TA = A therapeutic alliance: not always on the same page

S = Stigma: feeling scared, and secretive but needing support

TW = The challenges of tapering or withdrawal

X = theme present in paper

1) Reluctant users with little choice

This describes a resistance or hesitancy to take opioids mainly due to concerns about side effects or addiction, although they felt there were no other options available.

“I don’t want to become addicted, if I’m going to become addicted then as far as I’m concerned I’m a druggie, so I might as well not be here anyway, so I don’t want to become addicted...” Blake et al Pg103

1
2
3 *“I just didn’t want to go on them because I mean once you get on them that’s*
4 *it, you’re sort of stuck on them. I didn’t want to take morphine at first because*
5 *there was a girl that I went through one of the courses with and she always*
6 *seemed really dopey and drugged up so it took them a long while*
7 *to talk me to into taking the morphine because I didn’t want to be like that.*

8
9
10
11
12
13
14
15 Zheng et al pg 1832

16
17 Some spoke of underusing or were keen to reduce their medications when possible.

18
19 There was a dislike of being on long term medication and some thought that it would
20
21 not relieve their pain.

22
23
24 *“I don’t want to do that [take more morphine]. I want to stay on as little as I*
25 *possibly can because there might come a time when I need more and I don’t*
26 *want to be on high doses. I’ve always tried to keep it at a minimum amount of*
27 *tablets each day...”* Blake et al Pg 105

28
29
30
31
32
33 Even though some were reluctant there were other instances of dramatic improvement
34
35 in people’s lives. This then weighted their choice to stay on the opioids.

36
37
38 *“I mean it is just like a miracle as far as I am concerned. It is like knowing it*
39 *[the pain] is there but you have the instruments to prevent it from getting out*
40 *and [be]coming a roaring demon.”* Vallerand et al 1pg 170

41
42
43
44
45 *“But opiates, that’s my way of life. There would be no life if I didn’t have this.*
46 *And I thank God for them because without them I’d be...well I wouldn’t be. I*
47 *just couldn’t go on. I would have committed suicide a long time ago. And I say*
48 *that truthfully cause you could not live like that, with that constant, constant*
49 *pain. But, with the opiates it’s made it possible to be able to have a part of a*
50 *life, you know.”* Brooks et al pg 20

2) Understanding opioids: the good and the bad

This describes patients' knowledge or understanding about opioids which had generally been acquired ad hoc and slowly over time, from pharmacists, patient package inserts in their medication, leaflets, the internet, television programmes and from doctors, especially doctors at the pain clinic.

"When you see it in the media, when you see it on the television, you think if you're taking regular morphine you must be in a pretty bad way, you know."

Blake et al Pg103

"I always ask before I go on a medication, what are the side effects, I was told I may experience constipation; nothing else was explained to me."

Paterson et al pg 721

There was often poor knowledge about using opioids for chronic pain, and about addiction, overdose risk and side effects.

"There's not too much education about it [overdose]... When I first started taking it [the opioid medication], no one told me about OD[overdose]or anything about that. Because I was taking it not [as] prescribed...I was just like when I felt pain I would just take like five or six of them or whatever. Then at the end, I'd run out." Mueller et al pg 279

Patients often had to defend their usage and this added to their stress especially when they felt their healthcare professionals lacked an understanding of the place for opioids in the treatment of CNMP or were cautious about using them.

"The concern is that if they increase my opioid dosage, I could stop breathing.

It's ridiculous." Frank et al Pg1841

"There are still a lot of doctors out there that are against it. They think it is bad. Bad medicine. Bad practice." Vallerand et al 2 pg 129

1
2
3 In contrast, some people felt well informed which either produced more concern or
4
5 gave the patients confidence in their opioid regime.
6

7
8 *“... and from what I’ve read up, because I like to, sort of, keep on top of*
9
10 *things, that it’s an opium based drug, so you will build up some tolerance and*
11
12 *you will build up [becomes tearful] And you will potentially become sort of*
13
14 *addicted to it, if you like.” McCrorie et al pg 3*
15

16
17 *“Under Dr A [pain clinic] I’ve learnt more. And my concern has been, well it*
18
19 *was initially the possibility of addiction, but she has assured me that I’m not*
20
21 *showing no signs of addiction at all. I may have some withdrawal problems”*
22

23
24 Paterson et al Pg 721
25

26 27 28 **3) A therapeutic alliance: not always on the same page** 29

30 This describes a therapeutic alliance or the relationship between patients and their
31
32 health care providers which was considered important.
33

34 Overall there was a feeling that HCPs and patients were often ‘not on the same page’
35
36 about opioid usage.
37

38
39 *“My family doctor...does not want me to be dependent on heavy pain meds, so*
40
41 *I am intensely miserable 99% of the time.” Warms et al pg 252*
42

43
44 Some patients felt they were not listened to and were frustrated by a lack of empathy
45
46 from physicians regarding their pain experience.
47

48
49 *“I frequently have difficulty with the residents (doctors in training) explaining*
50
51 *why these drugs, this many drugs...Finally Dr. [family physician] wrote a note*
52
53 *in my file – stop harassing [participant’s name]. This is what she gets and why*
54
55 *she gets it. And they did stop but it was inconvenient. For instance, they would*
56
57 *not prescribe me three months at a time. I would be dispensed one month at a*
58
59
60

1
2
3 *time. And for someone who had been taking the same drugs for 10 years I*
4
5 *found that condescending.* ” Brooks et al pg 18
6
7

8 A reluctance to prescribe from GPs and pharmacists and the use of opioid contracts or
9
10 a restriction of medication were often considered punitive.
11

12 *“It kind of made me feel like I was doing something wrong, which I wasn’t,*
13
14 *but I signed a contract. You know, what would I be without my meds?”* Krebs
15
16 et al pg 1152
17

18
19 *“And I told my doctor that, that I wanted so I could sleep through the night.*
20
21 *And now he, well, I’ll give you 10, but it’s got to last. Like he treats me like a*
22
23 *drug addict.”* Penney et al pg 6
24
25

26 The healthcare system often worked against a therapeutic alliance with lack of
27
28 continuity or care or frequent visits which fed into mistrust. Patients complained that
29
30 provider turnover affected their ability to receive individualised care; conversations
31
32 about pain and treatment options often had to be started over again from scratch.
33
34

35 *“I don’t have the same doctor long enough to know”.* Bergman et al pg 1693
36

37 However having blood or urine tests for levels of opioids and regular checks were
38
39 seen by some as being cared for.
40
41

42 *“I would say, ‘I have this agreement and you don’t have to sign it if you don’t*
43
44 *want to, but I would like to go over it with you. These are suggestions because*
45
46 *this medication is addictive, it is dangerous, and I just want to make sure*
47
48 *you’re aware.’ I think if you really want to make it where people are not*
49
50 *hostile, say they have to have a urine test every 6 months, everybody, and that*
51
52 *it’s a policy because we care about all of you.’”* Krebs et al pg 1152
53
54

55
56 Some talked of the need for good relationships built on trust, shared decision making
57
58 and knowledgeable specialists who communicate well.
59
60

1
2
3 *“I wouldn’t say I researched it to that depth, you know, I read a little bit*
4 *about, and asked a lot of questions at my doctor, and then we decided.”*

5
6
7
8 Paterson pg 722
9

10 11 **4) Stigma: feeling scared and secretive but needing support**

12
13 This describes feelings of stigma and fear which people expressed directly in relation
14 to their opioid usage. This includes peoples’ negative attitudes from family, medical
15 professionals and work colleagues which lead to them feeling stigmatised and judged
16 for taking opioids.
17
18
19
20
21

22
23 *“So I’m constantly trying to clean up because I think people are going to*
24 *judge me. ‘Oh, because she’s on all this medication, ooh, she can’t look after*
25 *her children.’” Paterson et al pg 724*

26
27
28
29
30 *“As soon as you mention to someone that you are on pain medication it’s, ‘Oh*
31 *my god, you’ve got to get off it.’ It is viewed as weak. Somehow I am weak for*
32 *being on this medication.” Vallerand et al 2 pg 128*
33
34
35

36
37 To protect themselves some chose to keep their opioids a secret.

38
39 *“But you know, after 2 years of pain, you are physically exhausted, mentally*
40 *exhausted and depressed. So, I take my medication and I hide it at the bottom*
41 *of my drawer. It’s my secret life. It’s always a secret, and I’ve got to hide it*
42 *and not tell anyone.” Vallerand et al 1 pg 169*
43
44
45
46
47

48
49 Some people made a conscious decision about who they could tell and who they
50 couldn’t due to negative reactions. Relationships suffered when patients felt
51 unsupported.
52
53

54
55 *“My son told me I was a drug addict. He did. He really did. He was to the*
56 *point, he didn’t know what he could do for me. It really was that bad.”*
57
58

59
60 Vallerand et al 2 pg 128

1
2
3 *“I had originally told my sister and she was very concerned. Then she said,*
4 *‘As long as you don’t stay on them.’ She thought it was OK if I did it for a*
5 *while but as long as I didn’t stay on them. So I just sort of never told her. And*
6 *she never asked.”* Vallerand et al 2 pg 128
7
8
9
10
11

12 Although some seemed confident in using opioids, mostly people spoke about fears
13 such as; addiction and uncontrolled pain. Feeling supported validated their choices
14 and experiences and lessened some of their fears and concerns.
15
16
17

18
19 *“And at the end, my partner says—we sat down there and he goes ‘Stay on*
20 *them.’ ...I’ve always spoke to my partner, and if he’s been unsure— we’ve*
21 *both been unsure, we’ve both gone into the doctor together to ask questions.”*
22
23
24
25
26 Zheng et al pg 1834
27

28 *“my wife wanted me to take this medication. She was like: let’s go for it.”*
29
30
31 Arnaert et al pg 26
32
33

34 **5) The challenge of tapering/withdrawal from opioids**

35
36
37 Four papers ^{21, 24 42, 43} explore patients’ experiences of tapering or withdrawing as
38 their main content. Two further papers ^{32, 33} addressed it as a more peripheral issue
39 (see CERQual ratings in table 2). This describes the challenges and profound effects
40 of tapering or withdrawing from opioids.
41
42
43

44 Tapering and withdrawing from opioids could be challenging and provoke anxiety.
45
46

47
48 *“I have a tremendous fear in a doctor saying I want you to taper off the*
49 *methadone and get totally off the methadone with no alternative whatsoever. I*
50 *think that would be an irrational decision by a doctor, and I probably*
51 *wouldn’t take that advice.”* Frank et al pg1842
52
53
54
55

56
57 This anxiety could be alleviated by support from a trusted health care provider or
58 other person.
59
60

1
2
3 *“The best thing about it was that nobody acted like I was a bad person*
4 *because I was on these medications and was having to be going through this*
5 *really slow process of coming down off of them.” Frank et al pg1843*
6
7
8
9

10 Successful tapering was described as a collaborative agreement between HCP and
11 patient.
12
13

14 *“She put me down to 2 and a half [pills per day]. Then she said, okay, we’ll*
15 *go down to half a pill. I told her I didn’t think that just 2 a day would do it,*
16 *and she said okay, we’ll try 2 and a half, are you agreeable with that? I said*
17 *that’s fine. I mean, we can discuss stuff. It doesn’t have to be a disagreement*
18 *because we can talk about it. It’s not an argument. We’re 2 adults having a*
19 *conversation, figuring out what to do.” Matthias et al 2017 pg 1369*
20
21
22
23
24
25
26
27

28 However, not all people experienced joint decision making when tapering
29

30 *“I just don’t feel that he’s understanding. he don’t seem to care what I’m*
31 *saying, because he’s lowering it down anyway, even though I’ve told*
32 *him...that I didn’t agree with it being lowered.” Matthias et al 2017 pg 1369*
33
34
35
36

37 For those in the USA, prescribing policies, advising clinicians to monitor and
38 decrease opioid use, and the legislation to enforce these policies made those taking
39 opioids feel as if they were ‘a public health problem’. This could have a negative
40 effect on the doctor patient relationship and leave the patient feeling disempowered.
41
42
43
44
45
46

47 This was compounded when opioids had been withdrawn by legislation.^{21, 42}
48

49 *“I have to struggle, suffer, to make the next the next time that I can get my*
50 *medicine. And I don’t think that’s fair to me because if I can take my medicine*
51 *a little more regularly, I would be able to do more.....I don’t think that the*
52 *law, people, politicians, or anybody should be able to tell anybody that’s in*
53 *pain what type of medicine they can take.” Al Achkar et al pg 7*
54
55
56
57
58
59
60

1
2
3 *“That kinda got me mad, cause I thought well you know. . .they’re taking it off*
4 *the market because of people abusing it. . .It’s not fair to us, you know. . . . I*
5 *think the government was wrong to. . . pull them off the market, you know,*
6 *because of people abusing them, no like they weren’t looking at the people*
7 *that need them. . .But I think it’s really unfair that people that really do need*
8 *them can’t get them.”* Chang and Ibrahim 2017 pg 3
9
10
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12
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18 **Overarching theme: Constantly balancing**

19
20 After considering the five themes, an overarching theme emerged - ‘Constant
21 balancing’. The theme *Reluctant users with little choice* describes the need to balance
22 the pros and cons of starting opioids and the need to balance having pain with their
23 hesitancy to use opioids.
24
25
26
27
28
29

30 *“I don’t really like being on a lot of tablets, I’ve never been a tablet person,*
31 *um. . . but I mean I can’t have the pain either so it’s one evil outdoing the*
32 *other evil.* Paterson et al pg 723
33
34
35
36

37 Studies describe balancing the dose for pain management with their side effects to
38 allow them to function. Participants constantly weighed up the effects on their life;
39 dealing with an internal conflict of unresolved pain versus necessary medication,
40 being opioid free versus having uncontrolled pain and balancing other stressors
41 against opioid dose changes.
42
43
44
45
46
47

48 *“If you’re going to be able to walk, and you take one pain pill so you can walk*
49 *and live life, you’re going to do it, even though you may not like it.”* Penney et
50 al pg 6
51
52
53
54

55 The theme *Stigma feeling scared and secretive but needing support*, describes the
56 need to balance their hopes for relief with fear of side effects, and also to balance
57
58
59
60

1
2
3 whether or not to disclose their opioid use with the risk of being labelled a ‘drug
4
5 seeker’ versus having unrelieved pain.
6

7
8 *“I do it for my own protection by not telling them because I see how they react*
9
10 *by reading something in the paper...and it’s just their ignorance. And I don’t*
11
12 *have time. Well they know what’s going on but they don’t get it to this day. So*
13
14 *you have to pick your battles...” Brooks et al pg 19*
15

16
17 The theme *Understanding opioids; the good and the bad*, showed people had different
18
19 levels of understanding but weighed up their decisions and trade-offs against their
20
21 pain relief.
22

23
24 *“It’s, it’s got a good and bad side, morphine.When I take it, it works*
25
26 *really, really well but it makes you feel rather sick, umm, rather spaced out*
27
28 *and thinking wise, umm, it outcomes more on the other, do I want to be sick or*
29
30 *do I want to cry with pain? So I’d rather be sick but it is a very, very good*
31
32 *painkiller. ” Blake et al pg 105*
33

34
35 The therapeutic alliance theme showed that often it was evident that they were ‘not on
36
37 the same page’ with them balancing the advice from their doctors with what they
38
39 wanted.
40

41
42 *“[My provider] said you could die any time, and my husband and I said, well,*
43
44 *we realize that, but because of the pain, you know, we were willing to take that*
45
46 *risk that I would die from the narcotic medication.” Frank et al pg 1841*
47

48
49 It also meant that there were multiple barriers to the process of decreasing opioids due
50
51 to this constant balancing act which is described in the theme *the challenge of*
52
53 *tapering/withdrawal from opioids.*
54
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56
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1
2
3 *“I will tell her, if I do come off this medication, there are going to be*
4 *consequences. I can’t walk as often, I can’t stand as long, I just can’t do*
5 *it....” Vallerand et al 1 pg 169*
6
7
8
9

10 11 **Discussion**

12
13 Our five themes were; 1) Reluctant users with little choice; 2) Understanding opioids:
14 the good the bad; 3) A therapeutic alliance: not always on the same page; 4) Stigma:
15 feeling scared and secretive but needing support; and 5) The challenge of tapering or
16 withdrawal. An overarching theme of ‘constantly balancing’ emerged from the data.
17
18 These themes all had positive and negative aspects although the negative were more
19 prevalent by far.
20
21

22 We present a line of argument of how complex it is for the patient to balance
23 decisions at every stage of their journey. First their reluctance to start taking opioids
24 but feeling they had no option. Patients are given opioids for CNMP often as a last
25 resort when all other treatment has failed and their lives are so profoundly affected
26 that they talk of a desperation, that they would literally ‘try anything’. Patients spoke
27 about not being given any detailed information about opioids and that they had
28 learned more about them over time from different sources. This varied understanding
29 about opioids and their side effects can affect the decisions that people make. Patients
30 reported the need to keep the dosage of opioids as low as possible and often that they
31 were not at risk of addiction or overdose if they were taking them as prescribed. Even
32 those who felt they may be addicted sometimes viewed this as an acceptable trade-off
33 for short term pain relief. Our findings indicate that patient desperation combined
34 with inadequate information from healthcare professionals could trigger the
35 prescription of opioids. It may be that delivering accurate information about the
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1
2
3 potential side effects and limited efficacy of opioids for chronic pain management
4
5 would reduce the use of opioids.
6

7
8 Our findings demonstrate that the stigma surrounding how patients feel about being
9
10 on opioids can be compounded by the judgements of others. Although patients often
11
12 describe themselves in terms of ‘reluctant users’, if they experienced the benefits of
13
14 opioids through decreased pain and thus increased function they are often too scared
15
16 to reduce opioids and return to a life of potentially unmanaged pain.
17

18
19
20
21 Our findings suggest that clinicians and patients with chronic pain are not always ‘on
22
23 the same page’. The theme *Therapeutic alliance* captures the positives, but also the
24
25 tensions and mismatches of perceptions held by healthcare providers who are
26
27 attempting to limit dose escalation, and patients who may view constant dose
28
29 escalation as an acceptable trade-off for reducing relentless pain. The therapeutic
30
31 alliance is a robust theme supported by 26 of the 31 studies included. This is not
32
33 surprising as patients rely on their health care professionals to prescribe opioids. This
34
35 finding resonates with qualitative evidence syntheses (QES) exploring the experience
36
37 of patients ¹¹ and healthcare professionals ⁴⁶ It seems clear that joint decision -making
38
39 is important for appropriate healthcare; however, our findings suggests that there are
40
41 instances of mistrust on both sides. A QES exploring clinicians experience of
42
43 prescribing opioids for chronic pain demonstrate that the process of prescribing
44
45 opioids is not straightforward for clinicians who face a complex decision - ‘Should I
46
47 shouldn’t I’ prescribe opioids for chronic non-malignant pain ⁴⁶. They also
48
49 demonstrate that clinicians must walk a fine line to balance the pros and cons of
50
51 opioids whilst also maintaining patient trust. This suggests that both patients and
52
53
54
55
56
57
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60

1
2
3 HCPs find dealing with prescribing/taking opioids for CNMP is complex and involves
4
5 balancing and trade-offs.
6

7
8 Current guidance from Royal College of Anaesthetists in the UK and The Centers for
9
10 Disease Control and Prevention in the US advocate a preference for non-opioid
11
12 therapies in the treatment of CNMP⁴⁷. If a clinician feels that opioids are indicated,
13
14 then they recommend a low dose for a short duration which should be assessed for
15
16 effectiveness and regularly evaluated for benefits and harms. All but four studies in
17
18 this review are between 2005 and 2017, prior to these guidelines. Although opioid
19
20 contracts in some areas of the USA and Canada can make patients feel stigmatised
21
22 and judged, this effect can be mediated by a good therapeutic relationship. Some
23
24 physicians may view contracts as necessary to guard against uncontrolled dose
25
26 escalation, repeated demands for replacement of lost or misplaced medication,
27
28 subversion and illicit opioid intake. This finding resonates with Towe et al (2017) who
29
30 describe the moral boundary work and social guardianship that clinicians associate
31
32 with opioid prescription. Our findings suggest that this role does may not contribute to
33
34 an effective therapeutic partnership.
35
36
37
38

39 40 Limitations of this study

41
42 A majority of the studies are from the United States and the findings need to be taken
43
44 in the context of its health and social care systems. Most of the articles in this
45
46 qualitative synthesis were published or the research was conducted, before the impact
47
48 of the opioid epidemic became clear to regulators and the medical profession. Further
49
50 evidence is needed to find out if these themes are universal for developed countries or
51
52 whether there are important differences.
53

54
55 Our conceptual framework highlights patients need to constantly balance and to
56
57 consider the pros and cons of taking opioids. This can have a profound effect on
58
59
60

1
2
3 peoples' relationships with their family, friends and health care providers and their
4
5 perceived standing in the community which is reflected in their careful balancing of
6
7 disclosure. The therapeutic alliance and having a clear understanding of all the
8
9 positive and negative aspects of opioids were important factors that underpinned their
10
11 ability to maintain this fragile balance. This balance might also affect a person's
12
13 desire or ability to taper or withdraw from opioids.
14
15

16
17 The GRADE-CERQual ratings (table 2) revealed we had confidence in the findings
18
19 with only a few minor concerns and no moderate or serious concerns.
20
21

22 23 **Conclusions and recommendations for future research**

24
25 The first meta-ethnography on this topic revealed a constant balancing and a life in
26
27 flux in an effort to maintain participation in life and relationships. These are important
28
29 features of opioid use for CNMP. To maintain this delicate balance they often need
30
31 support from family or clinicians, however this balance can be upset by the feeling of
32
33 being judged by this same potential support system or peers and society at large
34
35 through the media. The therapeutic alliance with healthcare professionals, the extent
36
37 of people's understanding as well as the stigma attached to opioid use need to be
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39 navigated by people who are often reluctant to be on opioids in the first place.
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44 45 **Authors Contribution**

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47
48 VN and KS contributed to the review concept and design as part of the I-WOTCH
49
50 process evaluation team. HS, SE, MU and KS were involved in the design of the
51
52 IWOTCH study. VN, KS and FT screened search results or extracted data, conducted
53
54 the analysis and synthesis. All authors contributed to data interpretation, revised the
55
56 final manuscript critically for important intellectual content and appraised the final
57
58 manuscript. VN prepared the final manuscript and will be the corresponding author.
59
60

Funding

This project was funded by the National Institute for Health Research, Health Technology Assessment (project number 14/224/04). The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the HTA, NIHR, NHS or the Department of Health. Ethics approval was provided by Yorkshire and the Humber South Yorkshire Research Ethics committee on 13-9-16.

Declaration of competing interests

KS has undertaken other meta-ethnographies and was on the NIHR HS&DR Board until January 2018. The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

SE is grant holder on a number of NIHR studies including being Co- chief investigator of the I-WOTCH study, he has prescribed opioids as part of his pain practice.

MU was Chair of the NICE accreditation advisory committee until March 2017 for which he received a fee. He is chief investigator or co-investigator on multiple previous and current research grants from the UK National Institute for Health Research, Arthritis Research UK and is a co-investigator on grants funded by the Australian NHMRC. He is an NIHR Senior Investigator. He has received travel expenses for speaking at conferences from the professional organisations hosting the conferences. He is a director and shareholder of Clinvivo Ltd that provides electronic data collection for health services research. He is part of an academic partnership with Serco Ltd related to return to work initiatives. He is a co-investigator on a study receiving support in kind from Stryker Ltd. He has accepted honoraria for teaching

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2
3 from CARTA. He is an editor of the NIHR journal series, and a member of the NIHR
4
5 Journal Editors Group, for which he receives a fee.
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10 Data Sharing Statement: No additional data are available
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14 Acknowledgements

15
16 We would like to thank Samantha Johnson an academic librarian who helped with the
17
18 electronic searches and Dr Stephanie Tierney who helped to screen the citations.
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Figure 1 Concept model of the experiences of people taking opioid medication for chronic non-malignant pain

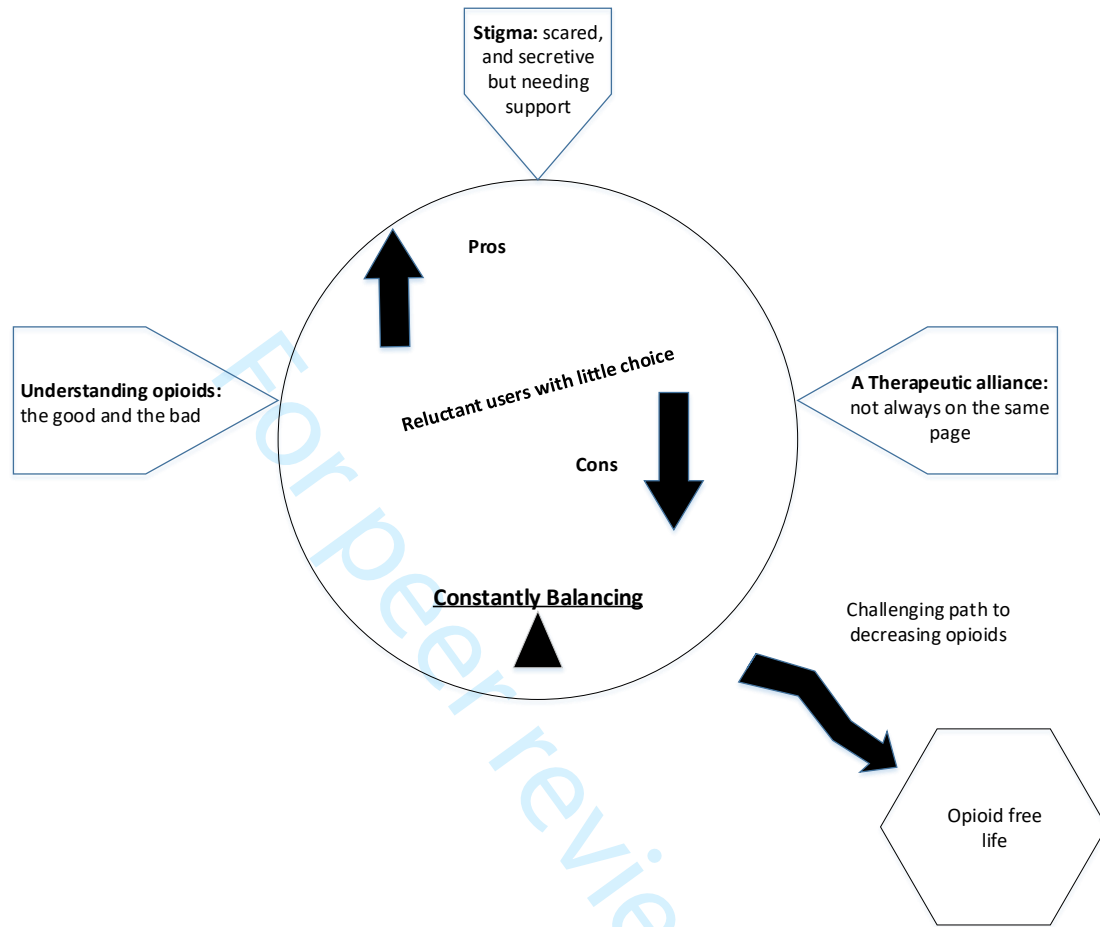
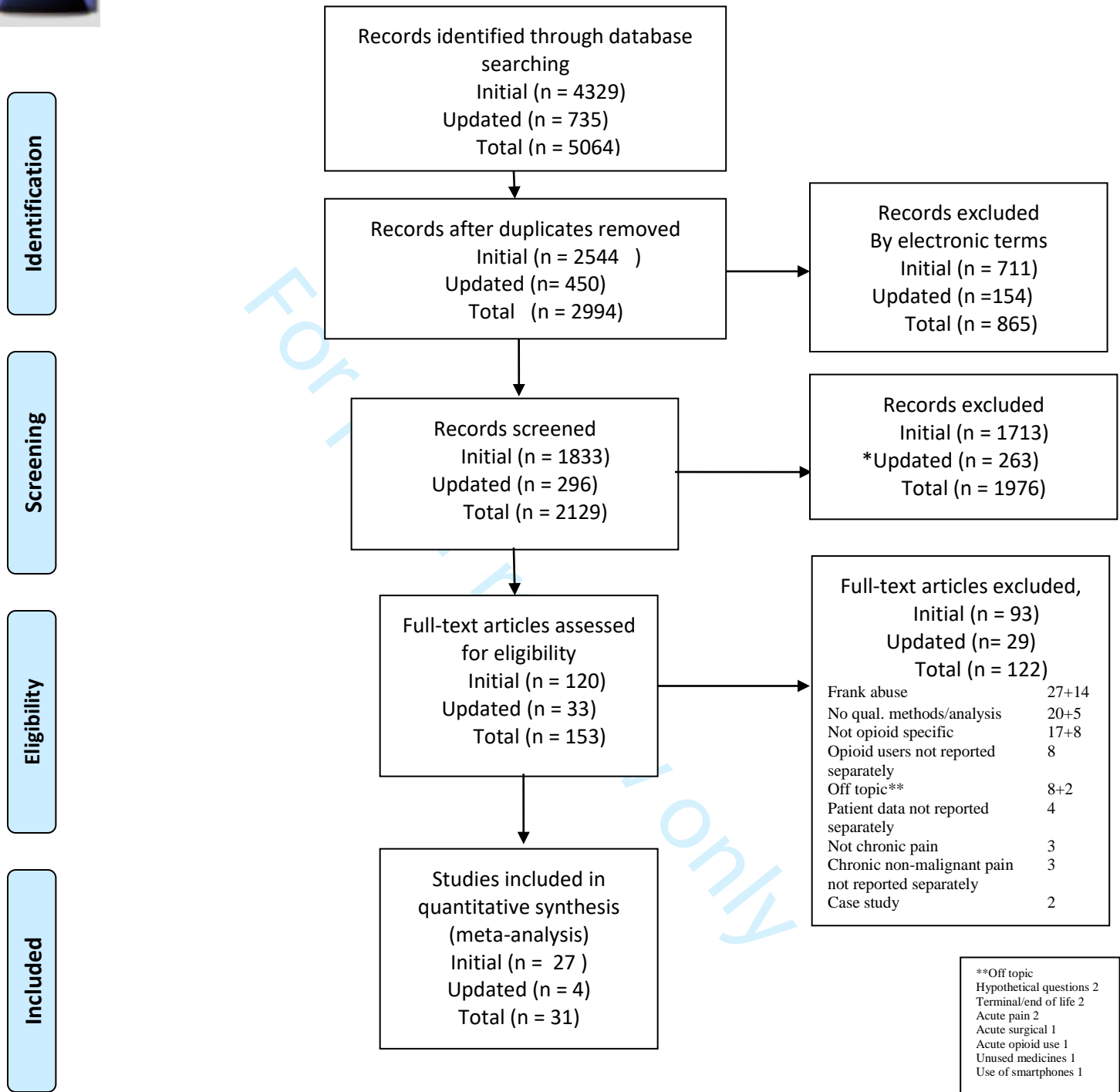




Figure 2: PRISMA Flow Diagram



Initial search June 2017 and updated search Sept 2018 reported.

The search dates for the rerun could be specified in some databases, but not all. Therefore some papers were found in both searches. These twice found duplicate papers were removed at this point*

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Appendix 1 The eMERGe meta-ethnography reporting guidance

Numbered criteria headings with explanatory reporting criteria	Page
Phase 1—Selecting meta-ethnography and getting started	
<i>Introduction</i>	
1 Rationale and context for the meta-ethnography Describe the gap in research or knowledge to be filled by the meta-ethnography, and the wider context of the meta-ethnography	4
2 Aim(s) of the meta-ethnography Describe the meta-ethnography aim(s)	4
3 Focus of the meta-ethnography Describe the meta-ethnography review question(s) (or objectives)	4
4 Rationale for using meta-ethnography Explain why meta-ethnography was considered the most appropriate qualitative synthesis methodology	4
Phase 2—Deciding what is relevant	
<i>Methods</i>	
5 Search strategy Describe the rationale for the literature search strategy	4/5
6 Search processes Describe how the literature searching was carried out and by whom	4/5
7 Selecting primary studies Describe the process of study screening and selection, and who was involved	5
<i>Findings</i>	
8 Outcome of study selection Describe the results of study searches and screening	16
Phase 3—Reading included studies	
<i>Methods</i>	
9 Reading and data extraction approach Describe the reading and data extraction method and processes	6
<i>Findings</i>	
10 Presenting characteristics of included studies Describe characteristics of the included studies	Table 1
Phase 4—Determining how studies are related	
<i>Methods</i>	
11 Process for determining how studies are related Describe the methods and processes for determining how the included studies are related: - Which aspects of studies were compared AND- How the studies were compared	6
<i>Findings</i>	
12 Outcome of relating studies Describe how studies relate to each other	17
Phase 5—Translating studies into one another	16
<i>Methods</i>	
13 Process of translating studies Describe the methods of translation: - Describe steps taken to preserve the context and meaning of the relationships between concepts within and across studies- Describe how the reciprocal and refutational translations were conducted- Describe how potential alternative interpretations or explanations were considered in the translations	16
<i>Findings</i>	
14 Outcome of translation Describe the interpretive findings of the translation.	17 to 28
Phase 6—Synthesizing translations	
<i>Methods</i>	
15 Synthesis process Describe the methods used to develop overarching concepts (“synthesised translations”)Describe how potential alternative interpretations or explanations were considered in the synthesis	16
<i>Findings</i>	
16 Outcome of synthesis process Describe the new theory, conceptual framework, model, configuration, or interpretation of data developed from the synthesis	Figure 1
Phase 7—Expressing the synthesis	

<p><i>Discussion</i></p> <p>17 Summary of findings Summarize the main interpretive findings of the translation and synthesis and compare them to existing literature</p>	28 to 30
<p>18 Strengths, limitations, and reflexivity Reflect on and describe the strengths and limitations of the synthesis: - Methodological aspects—for example, describe how the synthesis Findings were influenced by the nature of the included studies and how the meta-ethnography was conducted. - Reflexivity—for example, the impact of the research team on the synthesis findings</p>	30
<p>19 Recommendations and conclusions Describe the implications of the Synthesis</p>	31

Reference: France et al. BMC Medical Research Methodology (2019) 19:25
<https://doi.org/10.1186/s12874-018-0600-0>

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Appendix 2 – example of search terms

Scopus

((TITLE-ABS-KEY(buprenorphine or fentanyl or heroin or hydromorphone or methadone or morphine or opium or oxycodone or pentazocine or tramadol or opiate* or opioid*) OR TITLE-ABS-KEY(suboxone or bunavail or zubsolv or dipipanone or diconal or wellconal or diamorphine or duragesic or fentora or actiq or abstral or recivit or effentora or instanyl or pecfent or oxycontin or roxicodone or oramorph or papaveretum or omnopon or fortral)OR TITLE-ABS-KEY(osegon or "talwin nx" or pethidine or meperidine or demerol or tapentadol or nucynta or palexia or tapal or ultram or zytram))) and ((TITLE-ABS-KEY(qualitative w/5 (theor* or study or studies or research or analysis)) OR TITLE-ABS-KEY(ethno* or emic or etic or phenomenolog* or hermeneutic* or heidegger* or husserl* or colaizzi* or giorgi* or glaser or strauss or (van and kaam*) or (van and manen) or ricoeur or spiegelberg* or merleau) OR TITLE-ABS-KEY(constant w/3 compar*) OR TITLE-ABS-KEY(focus w/3 group*) OR TITLE-ABS-KEY(grounded w/3 (theor* or study or studies or research or analysis)) OR TITLE-ABS-KEY(narrative w/3 analysis) OR TITLE-ABS-KEY(discourse w/3 analysis) OR TITLE-ABS-KEY((lived or life) w/3 experience*) OR TITLE-ABS-KEY((theoretical or purposive) w/3 sampl*) OR TITLE-ABS-KEY("field note*" or "field record*" or fieldnote*) OR TITLE-ABS-KEY(participant* w/3 observ*) OR TITLE-ABS-KEY("action research") OR TITLE-ABS-KEY("digital adj record*" or audiorecord* or taperecord* or videorecord* or videotap*) OR TITLE-ABS-KEY(cooperative and inquir*) OR TITLE-ABS-KEY(co and operative and inquir*) OR TITLE-ABS-KEY(co-operative and inquir*) OR TITLE-ABS-KEY(("semi-structured" or semistructured or unstructured or structured) w/3 interview*) OR TITLE-ABS-KEY((Informal or in-depth or indepth or "in depth") w/3 interview*) OR TITLE-ABS-KEY(("face-to-face" or "face to face") w/3 interview*) OR TITLE-ABS-KEY("ipa" or "interpretive phenomenological analysis") OR TITLE-ABS-KEY(social and construct*) OR TITLE-ABS-KEY("appreciative inquiry") OR TITLE-ABS-KEY(poststructural* or "post structural*" or post-structural*) OR TITLE-ABS-KEY(postmodern* or "post modern*" or post-modern*) OR TITLE-ABS-KEY(feminis*) OR TITLE-ABS-KEY(humanistic or existential or experiential))) and (TITLE-ABS-KEY(pain))

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Appendix 2 Critical Appraisal Skills Programme (CASP) Quality appraisal tool scores

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Score
Arnaert 2006	Yes	Yes	Yes	Yes	?	No	Yes	Yes	Yes	Yes	17/20
Bennett 2013	Yes	Yes	Yes	Yes	Yes	No	Yes	?	Yes	Yes	17/20
Bergman 2013	Yes	Yes	Yes	Yes	Yes	No	Yes	?	Yes	Yes	17/20
Blake 2007	Yes	Yes	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	19/20
Brooks 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	?	Yes	Yes	17/20
Buchbinder 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Chang F 2017	Yes	Yes	Yes	Yes	Yes	No	?	?	Yes	Yes	16/20
Chang Y-P 2011	Yes	Yes	Yes	Yes	Yes	No	Yes	?	?	Yes	16/20
Coyne 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	?	Yes	Yes	17/20
Esquibel 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	20/20
Frank 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	20/20
Green 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Hooten 2011	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Krebs 2014	Yes	Yes	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	19/20
Lewis 2014	Yes	Yes	Yes	?	Yes	?	Yes	Yes	Yes	Yes	18/20
Matthias 2013	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
McCrorie	Yes	Yes	?	Yes	Yes	No	Yes	Yes	Yes	Yes	17/20
Mueller	Yes	Yes	Yes	Yes	?	No	Yes	Yes	?	Yes	16/20
Paterson 2016	Yes	Yes	Yes	Yes	Yes	?	?	Yes	Yes	Yes	18/20
Penney 2016	Yes	Yes	?	?	?	?	Yes	?	?	?	13/20
Rieb 2016	Yes	Yes	Yes	Yes	Yes	?	Yes	?	Yes	Yes	18/20
Simmonds 2015	Yes	Yes	?	Yes	Yes	?	Yes	Yes	?	?	16/20
St Marie 2016	Yes	Yes	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	19/20
Vallerand 1 2009	Yes	Yes	Yes	Yes	Yes	No	No	Yes	?	Yes	15/20
Vallerand 2 2010	Yes	Yes	Yes	?	Yes	No	No	Yes	?	?	13/20
Wallace 2014	Yes	Yes	Yes	Yes	Yes	No	Yes	?	?	Yes	16/20
Warms 2005	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	16/20
Zgierska 2016	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Zheng 2013	Yes	Yes	Yes	Yes	Yes	No	?	Yes	Yes	Yes	17/20
Al Achkar 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Matthias 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Matthias 2018	Yes	Yes	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	19/20
Smith 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	20/20

Legend 1 Critical Appraisal Skills Programme (CASP) questions scoring: Yes =2 ? (Can't Tell) = 1 No = 0

Q1. Was there a clear statement of the aims of the research?

Q2. Is a qualitative methodology appropriate?

Q3. Was the research design appropriate to the aims of the research?

Q4. Was the recruitment strategy appropriate to the aims of the research?

Q5. Was the data collected in a way that addressed the research issue?

Q6. Has the relationship between researcher and participants been adequately considered?

Q7. Have ethical issues been taken into consideration?

Q8. Was the data analysis sufficiently rigorous?

Q9. Is there a clear statement of findings?

Q10. How valuable is the research?

BMJ Open

A systematic review and qualitative evidence synthesis of the experiences of people taking opioid medication for chronic non-malignant pain: a meta-ethnography

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-032988.R1
Article Type:	Original research
Date Submitted by the Author:	29-Oct-2019
Complete List of Authors:	Nichols, Vivien; University of Warwick, Warwick Clinical Trials Unit, Warwick Medical School Toye, Francine; Oxford University Hospitals NHS Trust, Physiotherapy Research Unit, Nuffield Orthopaedic Centre Eldabe, Sam; The James Cook University Hospital Sandhu, Harbinder; University of Warwick, Warwick Clinical Trials Unit, Warwick Medical School Underwood, Martin; University of Warwick, Warwick Clinical Trials Unit, Warwick Medical School Seers, Kate; University of Warwick, Warwick Research in Nursing, Division of Health Sciences, Warwick Medical School
Primary Subject Heading:	Qualitative research
Secondary Subject Heading:	Patient-centred medicine
Keywords:	opioid, patients' views, QUALITATIVE RESEARCH, chronic non-malignant pain, meta-ethnography, qualitative evidence synthesis

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A systematic review and qualitative evidence synthesis of the experiences of people taking opioid medication for chronic non-malignant pain: a meta-ethnography

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Abstract

Objective To review qualitative studies of the experience of taking opioid medication for Chronic Non-Malignant Pain (CNMP) or coming off them.

Design A qualitative evidence synthesis using meta-ethnography. We used a seven step approach from the methods of meta-ethnography.

Data sources and eligibility criteria We searched selected databases for qualitative studies which gave patients' views of taking opioid medication for CNMP or of coming off them.

Data extraction and synthesis Papers were quality appraised using a Critical Appraisal Skills Programme (CASP) tool and Grading of Recommendations Assessment, Development and Evaluation working group - Confidence in Evidence from Reviews of Qualitative research) (GRADE-CERQual) guidelines were applied. We identified concepts and iteratively abstracted these concepts into a line of argument.

Results We screened 2129 unique citations, checked 153 full texts and 31 met our review criteria. We identified five themes: 1) Reluctant users with little choice; 2) Understanding opioids: the good and the bad; 3) A therapeutic alliance: not always on the same page; 4) Stigma: feeling scared and secretive but needing support; and 5) The challenge of tapering or withdrawal. A new overarching theme of 'constantly balancing' emerged from the data.

Conclusions People taking opioids are constantly balancing tensions, not always wanting to take opioids, but feeling they have no choice because of the pain. They frequently feel judged, were not always 'on the same page' as their health care professional and changes in opioid use were often challenging.

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4 **Key words:** Opioid, patients' views, qualitative research, chronic non-malignant
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7 pain, meta-ethnography, qualitative evidence synthesis.
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9 Word count 4,940
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15 **Strengths and Limitations**

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18 • To our knowledge this is the first qualitative evidence synthesis of patients'
19 experiences of taking opioid medications.
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23 • Meta-ethnography provides a thorough, systematic way of synthesising
24 qualitative findings across multiple studies and gives the reviewer's
25 interpretation of the data.
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29 • Using a GRADE-CERQual approach can assist in rating confidence in the
30 review findings.
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34 • Qualitative research that illuminates patients' perspectives can help to shape
35 future approaches to opioid management.
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40 **Introduction**

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45 Chronic non-malignant pain (CNMP) affects between an estimated 11% and 20% of
46 the population in Europe and US and can impact heavily on people's quality of life ^{1, 2}
47 . Opioid medications are strong painkillers which have a well-established role in the
48 treatment of acute and cancer pain; they have also been advocated for CNMP. Opioids
49 can have distressing side effects as dosages increase such as; constipation, sedation,
50 drowsiness, nausea, decreased concentration and memory, or mood changes ³. Most
51 people who use opioids develop tolerance to the painkilling effect of opioids, and
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3 some become dependent on them. Studies have shown that high opioid usage can also
4 put people's lives at risk⁴. Despite this, the prescription of opioid medication for
5 CNMP has risen sharply in the higher income countries. Few studies of opioids have
6 shown effectiveness beyond 12 weeks follow up. Population surveys have shown
7 long-term use to be associated with increased side effects and limited pain relief^{3 5 6}.
8 This synthesis of qualitative research was undertaken to underpin a process evaluation
9 for the Improving the Wellbeing of people with Opioid Treated CHronic pain (I-
10 WOTCH) study funded by the National Institute for Health Research. I-WOTCH is a
11 randomised controlled trial evaluating a multi-component education and patient
12 centred group intervention with a one-to-one tapering programme against a control of
13 an advice booklet with a relaxation CD. More information can be found in the main
14 study protocol⁷ and process evaluation protocol⁸.

15 This qualitative evidence synthesis uses the methods of meta-ethnography to find out
16 what peoples' experiences are of both using opioids for CNMP and their attempts to
17 stop taking them.

18 **Methods**

19 We use Noblit and Hare's 7 stages of meta-ethnographic analysis⁹. We used the new
20 eMERGe reporting guidelines for meta-ethnography to structure our report¹⁰ (*See*
21 *appendix 1*). The protocol is published in the international prospective register of
22 systematic reviews (PROSPERO) registration number: CRD42017082418.

23 <http://www.crd.york.ac.uk/PROSPERO>

24 *Step 1 Getting Started.*

25 In order to address what has been labelled an opioid epidemic¹¹, we need to
26 understand people's experiences of being on opioids and of coming off them. Our
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3 team was chosen because of its expertise in primary qualitative research and
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5 qualitative evidence synthesis specific to chronic pain and opioid prescription.
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8 *Step 2 Deciding what is relevant.*

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10 We undertook systematic electronic searches in June 2017 with a rerun in September
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12 2018, appraising relevant papers for quality using the Critical Appraisal Skills
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14 Programme (CASP) tool for qualitative research ¹². One researcher (VN) with the
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16 assistance of an academic librarian (SJ) searched seven electronic databases; Medline,
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18 Embase, AMED, CINAHL, PsycInfo Web of Science and Scopus (Science citation
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20 index and Social Science Citation Index) and forward citation searches. We used
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22 search terms, free text and MeSH terms for all opioid drugs as well as their generic
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24 names. We combined these with the MeSH term ‘pain’ and a wide range of MeSH
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26 terms and words to describe all types of qualitative research and its analysis based
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28 upon a search used by Toye, Seers and Barker in 2017 ¹³. The search was limited to
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30 those in English regarding humans with no cut-off date. Appendix 2 shows an
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32 example of our search terms.
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37 Unique citations were screened independently by 2 researchers (VN ST *see*
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39 *acknowledgements*) against our inclusion and exclusion criteria (see Box 1). Any
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41 disagreements were arbitrated by a third researcher (KS). Papers for full text reading
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43 were identified and read by two researchers. Quality was assessed using a CASP tool.
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45 VN critically appraised the studies and KS independently appraised 10% for
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47 consistency. The CASP scores are shown in table 1 and appendix 3. The GRADE-
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49 CERQual was used to appraise the reviewers’ confidence in the research findings ¹⁴.
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Box 1 Inclusion/Exclusion criteria

Included Studies

Adults (18 years or older) taking or have taken opioid medication in the last five years

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Published in English in peer review journals with no time constraint
Must relate to patient perspectives on using opioid medication for chronic non-malignant pain
Must use qualitative methodology (any analytical approach) or mixed quantitative and qualitative methodology with qualitative findings reported separately
Where studies include participants with differing medication we will include studies where the experience of those taking opioids is reported separately

Excluded studies

Theoretical or methodological papers
Purely quantitative studies or mixed methods studies where the qualitative data are not presented separately
Studies concerning active cancer
Studies concerning headache
Studies concerning any acute, or acute postoperative, pain
Studies concerned only with health care professional or carer perspectives, or studies of mixed carer/ patient/ professional populations where patient perspectives are not presented separately
Non- English language studies
Theses or conference abstracts which are not peer reviewed

Step 3 Reading the studies

VN read all the studies and KS and FT read half of these papers each (so all were read twice) and all extracted the second order concepts independently. A second order concept is a researcher's interpretation of data in a primary qualitative study¹⁶. VN, KS and FT met to discuss and reach agreement, and compiled a spreadsheet of all of the concepts extracted from the papers

Step 4 Determining how the studies are related?

VN sorted the concepts into categories by looking for any similarities and differences across all the studies. VN, KS and FT discussed the categorisation of data on multiple occasions. To enable comparison across studies, VN recorded descriptive data about each study (see table 1)

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For peer review only

Table 1 Study characteristics with CASP and GRADE-CERQual relevance ratings

Studies	Country	Data collection / participants	Analytical Approach	Aims <i>Italics = verbatim quotes</i>	Morphine Equivalent Daily Dose mg/day (MED)	CASP score	Relevance
1 Arnaert et al 2006 ¹⁷ Response Phases in Methadone Treatment for Chronic Non-malignant Pain	Canada	Semi-structured interview N=11 (4M/7F)	Content analysis	<i>"...to develop an understanding and to gain knowledge about the beliefs of patients with CNMP who were taking methadone, and to explore what challenges, if any, existed that affected their beliefs when first starting methadone treatment as an activity in their personal lives."</i>	None reported	17/20	P
2 Bergman et al 2013 ¹⁸ Contrasting Tensions Between Patients and PCPs in Chronic Pain Management: A Qualitative Study	USA	In-depth interviews N=26 (24m/2F)	Inductive thematic analysis	<i>"... to develop a better understanding of the respective experiences, perceptions, and challenges both patients with chronic pain and PCPs face communicating with each other about pain management in the primary care setting."</i>	None reported	17/20	P
3 Blake et al 2007 ¹⁹ Experiences of patients requiring strong opioid drugs for chronic non-cancer pain: a patient initiated study	UK	One focus group N=4 (2M/2F) and interviews N=10 (3M/5F)	Interpretative Phenomenological Analysis	<i>"...to determine the attitudes and experiences of patients receiving long-term strong opioid medication for chronic non-cancer pain in primary care."</i>	Individual opioid dosages	19/20	R
4 Brooks et al 2015 ²⁰ Exploring the lived experience of adults using prescription opioids to manage chronic noncancer pain	Canada	In-depth interviews N=9 (4M/5F)	Interpretative Phenomenological Analysis	<i>"...to explore the lived experience of adults using prescription opioids to manage CNCP, focusing on how opioid medication affected their daily lives."</i>	None reported	17/20	R

1 2 3 4 5 6 7 8 9 10	5 Buchbinder et al 2014 ²¹ “Is there any way I can get something for my pain?” Patient strategies for requesting analgesics	USA	Audio recorded clinical encounters N=74 (37M/37F)	Qualitative approach based on conversational analysis	<i>“We examined the direct and indirect means by which patients express a desire for analgesic medication.”</i>	None reported	18/20	I
11 12 13 14 15 16 17 18 19	6 Chang Y-P et al 2011 ²² Use of Prescription Opioid Medication among Community-Dwelling Older Adults with Noncancer Chronic Pain	USA	Face to face interview N=21 (13M/8F) ≥65yrs	Content analysis, mixed methods	<i>“... to: (1) describe older adults’ patterns of adherence to their prescription opioid medication regimens and their reasons for these medication use patterns; and (2) examine the associations between adherence of prescription opioids, pain intensity, and pain interference on daily activity.”</i>	None reported	16/20	P
20 21 22 23 24 25 26 27 28	7 Chang,F et al 2017 ²³ Perceptions of Community-Dwelling Patients and Their Physicians on OxyContin® Discontinuation and the Impact on Chronic Pain Management	Canada	Pt interviews N=13 1M/ 12F	Not specified, no references given	<i>“... to explore the perceptions of patients with chronic pain and their physicians on OxyContin discontinuation and the impact that it had on chronic pain care and management.”</i>	None reported	16/20	P
29 30 31 32 33 34 35 36 37 38	8 Coyne et al 2015 ²⁴ Assessment of a Stool Symptom Screener and Understanding the Opioid-Induced Constipation Symptom Experience	USA	Cognitive interview semi structured think-aloud approach N=66 (27M/39F)	Content analysis	<i>“...to evaluate the content validity of the Stool Symptom Screener by assessing patient understanding of its items, patient ability to differentiate among response options, and patient perceptions about the use of a 2-week recall period for evaluating stool symptoms, BMs, and laxative use. - to evaluate how patients describe their constipation experience and to understand</i>	None reported	17/20	I

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				<i>whether this differs between patients who frequently use laxatives and those who do not.</i>			
9 Esquibel et al 2014 ²⁵ Doctors and patients in pain: Conflict and collaboration in opioid prescription in primary care	USA	In depth interviews with pts with CNCP receiving opioids and their physicians. N=21 pts (8M/13F)	Immersion/ crystallization process to generate a thematic codebook. Mixed methods with some quant. data analysis	<i>"...to better understand the effects of COT [chronic opioid therapy] on the doctor-patient relationship."</i>	None reported	20/20	R
10 Frank et al 2016 ²⁶ Patients' Perspectives on Tapering of Chronic Opioid Therapy: A Qualitative Study	USA	Semi-structured interviews N=24 (11M/13F)	Team based, mixed inductive and deductive approach guided by the Health Belief Model	<i>"... to explore patients' perspectives on opioid tapering."</i>	MED: Used algorithm Median (IQR) 70 (30-165) Range 15-1845	20/20	R
11 Green et al 2017 ²⁷ Perpetuating stigma or reducing risk? Perspectives from naloxone consumers and pharmacists on pharmacy-based naloxone in 2 states	USA	8 focus groups (only 2 with patients with chronic pain) N=15 (8M/7F)	Thematic analysis. Content analysis with a collaborative codebook development process	<i>"...to explore the attitudes of various stakeholders toward pharmacy-based naloxone and opioid medication safety and to capture the range of initial experiences with pharmacy naloxone in 2 states with pharmacy naloxone policies."</i>	None reported	18/20	P

1 2 3 4 5 6 7 8 9 10 11	12 Hooten et al 2011 ²⁸ Smoking Cessation and Chronic Pain: Patient and Pain Medicine Physician Attitudes	USA	N = 18 Interviews N= 15 and focus group N=3 10M/8F	Participatory research, mixed methods - Thematic and content analysis	<i>"...to determine the attitudes and beliefs of both patients and pain medicine physicians regarding smoking cessation interventions applied during pain therapy."</i>	MED - used equianalgesic conversion software programme Mean ± SD 227 ± 356	18/20	I
12 13 14 15 16 17 18 19 20	13 Krebs et al 2014 ²⁹ Barriers to Guideline- Concordant Opioid Management in Primary Care—A Qualitative Study	USA	Semi structured interviews N= 26 patients (14 PC physicians) 13M/13F	Immersion crystallization approach	<i>"...to better understand primary care physicians' and patients' perspectives on recommended opioid management practices and to identify potential barriers and facilitators of guideline concordant opioid management in primary care."</i>	None reported	16/20	P
21 22 23 24 25 26 27 28 29 30	14 Matthias et al 2014 ³⁰ Communicating about opioids for chronic pain: A qualitative study of patient attributions and the influence of the patient–physician relationship	USA	Audio Recordings of primary care visits and Semi- structured interviews after clinic visit. N=30 26M/4F	Immersion/cry stallization approach	<i>"...to advance understanding about communication about opioids by directly capturing clinical communication about opioids, as well as interviewing patients to gain insight into communication patterns and their broader relationships with their physicians, and how these relationships shape communication about opioids."</i>	None reported	18/20	R
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46	15 McCrorie et al 2015 ³¹ Understanding long-term opioid prescribing for non- cancer pain in primary care: a qualitative study	UK	Semi structured interviews with patients (focus groups with	Grounded approach for thematic analysis. Constant comparison	<i>"... to understand the processes which bring about and perpetuate long-term prescribing of opioids for chronic, non-cancer pain. We interviewed patients and GPs about their experiences, beliefs and expectations of analgesia prescribing, to improve understanding of how</i>	None reported	17/20	R

		GPs) N=23 6M/17F		<i>problematic long-term opioid prescribing becomes established</i> ".			
16 Mueller et al 2016 ³² Attitudes Toward Naloxone Prescribing in Clinical Settings: A Qualitative Study of Patients Prescribed High Dose Opioids for Chronic Non-Cancer Pain	USA	Semi-structured interview N=24 8M/16F	Ethnographic iterative methods. Inductive and deductive approaches	<i>"This study assessed the knowledge and attitudes toward naloxone prescribing among non-cancer patients prescribed opioids in primary care."</i>	Inclusion criteria ≥ 100 mg MED	16/20	I
17 Paterson et al 2016 ³³ Resisting Prescribed Opioids: A Qualitative Study of Decision Making in Patients Taking Opioids for Chronic Noncancer Pain	Australia	Qualitative individual interviews N=20	Constant comparison and decision making explored in depth and with a thematic analysis utilizing a published "Model of medicine-taking"	<i>"...to identify the varying influences on patients' decisions about their use of prescribed long-term opioids. The research questions are: 1) does this conceptual Model of medicine-taking apply to people taking prescribed opioids, 2) is the concept of "resistance" to medication useful in this context, and 3) does this concept lead to new insights which may improve communication and shared decision making between"</i>	None reported	18/20	P
18 Penney et al 2016 ³⁴ Provider and patient perspectives on opioids	USA	11 Focus groups N=80 and	Thematic coding ref	<i>"...to identify the practical issues patients and providers face when accessing alternatives to</i>	None reported	13/20	P

and alternative treatments for managing chronic pain: a qualitative study		individual interviews N=10 27M/63F	Ryan, Bernard 2003	<i>opioids, and how multiple parties view these issues."</i>			
19 Rieb et al 2016 ³⁵ Withdrawal-associated injury site pain (WISP): a descriptive case series of an opioid cessation phenomenon	Canada	In person semi structured interviews N=21 14M/7F	Deductive and inductive approaches. Use of survey and emergent interview themes	<i>".... to document the existence and characteristics of this pain phenomenon that we have named withdrawal-associated injury site pain (WISP)."</i>	Recalled dose before WISP	18/20	P
20 Simmonds et al 2015 ³⁶ A Qualitative Study of Veterans on Long-Term Opioid Analgesics: Barriers and Facilitators to Multimodality Pain Management	USA	Semi structured focus groups x 3 N=25 17M/8F	Grounded theory-informed approach. Framework provided by the theory of planned behaviour	<i>"...to examine barriers and facilitators to multimodality chronic pain care among veterans on high-dose opioid analgesics for chronic non-cancer pain."</i>	Inclusion criteria at least 50 mg MED	16/20	P
21 St Marie et al 2016 ³⁷ Primary care experiences of people who live with chronic pain and receive opioids to manage pain: A qualitative methodology	USA	Semistructured interviews. N=12 6M/6F	Thematic and interpretive analyses	<i>"...to provide a deeper understanding of the experiences, issues, and challenges that people face who live with chronic pain and received opioids to help manage their pain in primary care. The following research questions were addressed: (a) What are the experiences of individuals who live with chronic pain and receive opioid pain medications to manage their pain in</i>	None reported	19/20	R

				<i>primary care? (b) What have been their healthcare experiences as they strive to manage their pain?"</i>			
22 Vallerand et al 1 2009 ³⁸ Chronic Opioid Therapy for Nonmalignant Pain: The Patient's Perspective. Part I— Life Before and After Opioid Therapy	USA	In depth serial interviews N=22 6M/16F	Phenomenologic study / Constant comparative method	<i>"...to examine the lived experience of adults receiving opioid therapy for relief of chronic non-malignant pain through the examination of data obtained through serial taper recorded interviews."</i>	Range 22.5 to 3,200	14/20	R
23 Vallerand et al 2 2010 ³⁹ Chronic Opioid Therapy for Non-malignant Pain: The Patient's Perspective. Part II— Barriers to Chronic Opioid Therapy	USA	In depth serial narrative interviews N=22 6M/16F	Phenomenologic study / Constant comparative method	<i>"...to elucidate the essence of the lived experience of patients receiving chronic opioid therapy for chronic non-malignant pain through examining their life narratives."</i>	None reported	13/20	R
24 Wallace et al 2014 ⁴⁰ Voices that may not otherwise be heard: a qualitative exploration into the perspectives of primary care patients living with chronic pain	USA	Photovoice photos, Interviews 1st N=31 2nd N=25 , and focus groups N=19	Grounded theory	<i>"...this study examined the utility of a combination of qualitative methods (Photovoice, one-on-one interviews, and focus groups) in examining the daily experiences of primary care patients living with chronic pain".</i>	None reported	16/20	R
25 Warms et al 2005 ⁴¹ There are a few things you did not ask about my pain: writing on the margins of a survey	USA	Comments written in the margins of a questionnaire N=797	Content analysis	<i>"...to determine the characteristics of those who wrote comments [written in the margin of survey questionnaire] and to understand what was being communicated in their comments."</i>	None reported	16/20	P

1 2 3 4 5 6 7 8 9 10 11 12 13	26 Zgierska et al 2016 ⁴² Mindfulness Meditation-Based Intervention Is Feasible, Acceptable, and Safe for Chronic Low Back Pain Requiring Long-Term Daily Opioid Therapy	USA	Qual data on treatment satisfaction and experience N= 17	Qualitative analysis methods. Grounded theory	<i>"... to determine feasibility, acceptability, and safety of an MM-based intervention in patients with CLBP requiring daily opioid therapy."</i>	Inclusion criteria ≥ 30 mg MED Mean \pm SD 166.9 \pm 153.7	18/20	I
14 15 16 17 18 19 20 21 22	27 Zheng et al 2013 ⁴³ Chaos to Hope: A Narrative of Healing	Australia	In depth qual interviews (N=20) 10M/10F	Illness narratives. Thematic analysis	<i>"...to investigate the progression of the illness and opioid journeys of people who are taking opioids for chronic non-cancer pain".</i>	None reported	17/20	P
23	Rerun of search							
24 25 26 27 28 29 30 31 32 33	28 Al Achkar et al 2017 ⁴⁴ Exploring perceptions and experiences of patients who have chronic pain as state prescription opioid policies change: a qualitative study in Indiana	USA	N=9 3M/6F	Inductive emergent thematic analysis	<i>"...to evaluate the impact of Indiana's opioid prescription legislation on the patient experiences around pain management."</i>	None reported	18/20	R
34 35 36 37 38 39 40 41 42 43 44 45 46	29 Matthias et al 2017 ⁴⁵ "I'm Not Gonna Pull the Rug out From Under You": Patient-Provider	USA	N=37 12M/25F	Inductive approach, constant comparison	<i>"...to understand communication processes related to opioid tapering."</i>	None reported	18/20	R

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Communication About Opioid Tapering							
30 Matthias et al 2018 ⁴⁶ "I Was a Little Surprised": Qualitative Insights From Patients Enrolled in a 12-Month Trial Comparing Opioids With Nonopioid Medications for Chronic Musculoskeletal Pain	USA	N=34 28M/6F	Inductive approach, constant comparison	<i>"...to understand patients' experiences with the SPACE trial including their views and anticipated benefits of opioids, versus non -opioids, experiences with the intervention and to what extent expectations were met after completing the study."</i>	None reported	19/20	R
31 Smith et al 2018 ⁴⁷ Seeking Chronic Pain Relief: A Hermeneutic Exploration	USA	N=15 4M/11F	Concurrent embedded mixed methods design, Heideggerian hermeneutic phenomenological approach	<i>"This research presents an interpretation of the experience of seeking pain relief for a group of people taking opioid pain medications whose pain is not adequately controlled"</i>	None reported	20/20	P

Legend: GRADE-CERQual Relevance component: R= Relevant, P= Partial relevance, I= Indirect relevance, U=Uncertain relevance

IQR = Interquartile Range, SD = Standard Deviation

Step 5 Translating studies into each other

Patterns and associations between categories were explored and all researchers felt that a line of argument approach as defined by Noblit and Hare⁹ would be the most useful method to interpret the data.

Step 6 Synthesising Translations

Agreement was reached by clearly defining the over-arching or 3rd order concepts arising from the data. A third order concept is the reviewers' interpretation of second order concepts.

Step 7 Expressing the synthesis

We developed a conceptual model to show how the themes related to each other in a line of argument. (see figure 1)

Insert figure 1 about here.

Patient and Public Involvement

We did not involve patients or the public in our work.

Results

Two reviewers VN and ST screened 2994 titles or abstracts (after the removal of duplicates from the 5064 citations retrieved) and identified 153 full texts of interest.

Two reviewers VN and KS read these and 122 were excluded. Reasons are given in the PRISMA flowchart, see figure 2. The reviewers agreed to include 31 studies. The included studies were from US (23), Canada (4) UK (2), and Australia (2) and used a range of qualitative methods.

We report the 4 facets of GRADE-CERQual for all papers. 1) Methodological 2) Confidence 3) Relevance 4) Adequacy of data - See table 2 below.

Table 2 Confidence in review findings: GRADE-CERQual assessment

Review findings	Studies contributing (see table 1 column 1 for study number)	Methodological limitations (study number)	Relevance (See table 1 end column)	Coherence	Adequacy of data
Reluctant users with little choice	1,3,4,5,6,7,17,18,21,22,26,27,30 (13 studies)	11 no concerns 2 minor concerns (18,22)	5 Relevant 6 Partial 2 Indirect	No concerns	No concerns
Understanding opioids: the good the bad	1,3,7,9,10,11,15,16,17,23,25,27,29 (13 studies)	12 no concerns 1 minor concerns (23)	6 Relevant 6 Partial 1 Indirect	No concerns	No concerns
A therapeutic alliance: not always on the same page	1,2,3,4,5,7,9,10,11,13,14,15,16,17,18,19,20,21,22,23,24,25,26,28,29,31 (26 studies)	23 no concerns 3 minor concerns (18,22,23)	12 Relevant 11 Partial 3 Indirect	No concerns	No concerns
Stigma: feeling scared, and secretive but needing support	1,2,3,4,7,9,10,14,16,17,18,20,21,22,23,24,27,28,31 (19 studies)	16 no concerns 3 minor concerns (18,22,23)	10 Relevant 8 Partial 1 Indirect	No concerns	No concerns
The challenge of tapering/ withdrawal from opioids	7,10,18,19,30,31 (6 studies)	5 no concerns 1 minor concerns (18)	2 Relevant 4 Partial	Minor concerns	Minor concerns

Legend of GRADE-CERQual component scoring:

Methodological limitations, Coherence, Adequacy of data	No or very minor concerns Minor concerns Moderate concerns Serious concerns
Relevance:	Relevant Partial Indirect Uncertain

Synthesis of Findings

We abstracted five themes from the 2nd order concepts. Table 3 below shows how each study contributed to each theme. We have illustrated each concept with exemplary quotations.

Table 3 Themes apparent in each study

Author date	RU	U	TA	S	TW
1 Arnaert and Ciccotosto 2006	X	X	X	X	

2 Bergman, Matthias et al 2013			X	X	
3 Blake, Ruel et al 2007	X	X	X	X	
4 Brooks, Unruh et al 2015	X		X	X	
5 Buchbinder, Wilbur et al 2014	X		X		
6 Chang Y-P, Wray et al 2011	X				
7 Chang,F and Ibrahim,S 2017	X	X	X	X	X
8 Coyne, Currie et al 2015					
9 Esquibel and Borkan 2014		X	X	X	
10 Frank, Levy et al 2016		X	X	X	X
11 Green, Case et al 2017		X	X		
12 Hooten, Vickers et al 2011					
13 Krebs, Bergman et al 2014			X		
14 Matthias,Krebs et al 2013			X	X	
15 McCrorie, Closs et al 2015		X	X		
16 Mueller, Koester et al 2016		X	X	X	
17 Paterson, Ledgerwood 2016	X	X	X	X	
18 Penney, Ritenbaugh et al 2016	X		X	X	X
19 Rieb, Norman et al 2016			X		X
20 Simmonds, Finley et al 2015			X	X	
21 St Marie et al 2015	X		X	X	
22 Vallerand et al 1 2009	X		X	X	
23 Vallerand et al 2 2010		X	X	X	
24 Wallace et al 2014			X	X	
25 Warms et al 2005 o		X	X		
26 Zgierska et al 2016	X		X		
27 Zheng et al 2013	X	X		X	
Studies from search rerun	RU	U	TA	S	TW
28 Al Achkar et al 2017			X	X	X
29 Matthias et al 2017		X	X		X
30 Matthias et al 2018	X				
31 Smith et al 2018			X	X	

Legend:

RU = Reluctant users with little choice

U = Understanding about opioids: the good and the bad

TA = A therapeutic alliance: not always on the same page

S = Stigma: feeling scared, and secretive but needing support

TW = The challenges of tapering or withdrawal

X = theme present in paper

1) Reluctant users with little choice

This describes a resistance or hesitancy to take opioids mainly due to concerns about side effects or addiction, although they felt there were no other options available.

“I don’t want to become addicted, if I’m going to become addicted then as far as I’m concerned I’m a druggie, so I might as well not be here anyway, so I don’t want to become addicted...” Blake et al Pg103

1
2
3 *"I just didn't want to go on them because I mean once you get on them that's*
4 *it, you're sort of stuck on them. I didn't want to take morphine at first because*
5 *there was a girl that I went through one of the courses with and she always*
6 *seemed really dopey and drugged up so it took them a long while*
7 *to talk me to into taking the morphine because I didn't want to be like that.*

8
9
10
11
12
13
14
15 Zheng et al pg 1832

16
17 Some spoke of underusing or were keen to reduce their medications when possible.

18
19 There was a dislike of being on long term medication and some thought that it would
20
21 not relieve their pain.

22
23 *"I don't want to do that [take more morphine]. I want to stay on as little as I*
24 *possibly can because there might come a time when I need more and I don't*
25 *want to be on high doses. I've always tried to keep it at a minimum amount of*
26 *tablets each day..."* Blake et al Pg 105
27
28
29
30
31

32
33 Even though some were reluctant there were other instances of dramatic improvement
34
35 in people's lives. This then weighted their choice to stay on the opioids.

36
37 *"I mean it is just like a miracle as far as I am concerned. It is like knowing it*
38 *[the pain] is there but you have the instruments to prevent it from getting out*
39 *and [be]coming a roaring demon."* Vallerand et al 1pg 170
40
41
42
43

44 *"But opiates, that's my way of life. There would be no life if I didn't have this.*
45 *And I thank God for them because without them I'd be...well I wouldn't be. I*
46 *just couldn't go on. I would have committed suicide a long time ago. And I say*
47 *that truthfully cause you could not live like that, with that constant, constant*
48 *pain. But, with the opiates it's made it possible to be able to have a part of a*
49 *life, you know."* Brooks et al pg 20
50
51
52
53
54
55
56
57
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59
60

2) Understanding opioids: the good and the bad

This describes patients' knowledge or understanding about opioids which had generally been acquired ad hoc and slowly over time, from pharmacists, patient package inserts in their medication, leaflets, the internet, television programmes and from doctors, especially doctors at the pain clinic.

"When you see it in the media, when you see it on the television, you think if you're taking regular morphine you must be in a pretty bad way, you know."

Blake et al Pg103

"I always ask before I go on a medication, what are the side effects, I was told I may experience constipation; nothing else was explained to me."

Paterson et al pg 721

There was often poor knowledge about using opioids for chronic pain, and about addiction, overdose risk and side effects.

"There's not too much education about it [overdose]... When I first started taking it [the opioid medication], no one told me about OD[overdose]or anything about that. Because I was taking it not [as] prescribed...I was just like when I felt pain I would just take like five or six of them or whatever. Then at the end, I'd run out." Mueller et al pg 279

Patients often had to defend their usage and this added to their stress especially when they felt their healthcare professionals lacked an understanding of the place for opioids in the treatment of CNMP or were cautious about using them.

"The concern is that if they increase my opioid dosage, I could stop breathing.

It's ridiculous." Frank et al Pg1841

"There are still a lot of doctors out there that are against it. They think it is bad. Bad medicine. Bad practice." Vallerand et al 2 pg 129

1
2
3 In contrast, some people felt well informed which either produced more concern or
4
5 gave the patients confidence in their opioid regime.
6

7
8 *“... and from what I’ve read up, because I like to, sort of, keep on top of*
9
10 *things, that it’s an opium based drug, so you will build up some tolerance and*
11
12 *you will build up [becomes tearful] And you will potentially become sort of*
13
14 *addicted to it, if you like.” McCrorie et al pg 3*
15

16
17 *“Under Dr A [pain clinic] I’ve learnt more. And my concern has been, well it*
18
19 *was initially the possibility of addiction, but she has assured me that I’m not*
20
21 *showing no signs of addiction at all. I may have some withdrawal problems”*
22

23
24 Paterson et al Pg 721
25

26 27 **3) A therapeutic alliance: not always on the same page** 28

29
30 This describes a therapeutic alliance or the relationship between patients and their
31
32 health care providers which was considered important.
33

34
35 Overall there was a feeling that HCPs and patients were often ‘not on the same page’
36
37 about opioid usage.
38

39
40 *“My family doctor...does not want me to be dependent on heavy pain meds, so*
41
42 *I am intensely miserable 99% of the time.” Warms et al pg 252*
43

44
45 Some patients felt they were not listened to and were frustrated by a lack of empathy
46
47 from physicians regarding their pain experience.

48
49 *“I frequently have difficulty with the residents (doctors in training) explaining*
50
51 *why these drugs, this many drugs...Finally Dr. [family physician] wrote a note*
52
53 *in my file – stop harassing [participant’s name]. This is what she gets and why*
54
55 *she gets it. And they did stop but it was inconvenient. For instance, they would*
56
57 *not prescribe me three months at a time. I would be dispensed one month at a*
58
59
60

1
2
3 *time. And for someone who had been taking the same drugs for 10 years I*
4
5 *found that condescending.* ” Brooks et al pg 18
6
7

8 A reluctance to prescribe from GPs and pharmacists and the use of opioid contracts or
9
10 a restriction of medication were often considered punitive.
11

12 *“It kind of made me feel like I was doing something wrong, which I wasn’t,*
13
14 *but I signed a contract. You know, what would I be without my meds?”* Krebs
15
16 et al pg 1152
17

18
19 *“And I told my doctor that, that I wanted so I could sleep through the night.*
20
21 *And now he, well, I’ll give you 10, but it’s got to last. Like he treats me like a*
22
23 *drug addict.”* Penney et al pg 6
24
25

26 The healthcare system often worked against a therapeutic alliance with lack of
27
28 continuity or care or frequent visits which fed into mistrust. Patients complained that
29
30 provider turnover affected their ability to receive individualised care; conversations
31
32 about pain and treatment options often had to be started over again from scratch.
33
34

35 *“I don’t have the same doctor long enough to know”.* Bergman et al pg 1693
36

37 However having blood or urine tests for levels of opioids and regular checks were
38
39 seen by some as being cared for.
40
41

42 *“I would say, ‘I have this agreement and you don’t have to sign it if you don’t*
43
44 *want to, but I would like to go over it with you. These are suggestions because*
45
46 *this medication is addictive, it is dangerous, and I just want to make sure*
47
48 *you’re aware.’ I think if you really want to make it where people are not*
49
50 *hostile, say they have to have a urine test every 6 months, everybody, and that*
51
52 *it’s a policy because we care about all of you.’”* Krebs et al pg 1152
53
54
55

56 Some talked of the need for good relationships built on trust, shared decision making
57
58 and knowledgeable specialists who communicate well.
59
60

1
2
3 *“I wouldn’t say I researched it to that depth, you know, I read a little bit*
4 *about, and asked a lot of questions at my doctor, and then we decided.”*

5
6
7
8 Paterson pg 722
9

10 11 **4) Stigma: feeling scared and secretive but needing support**

12
13 This describes feelings of stigma and fear which people expressed directly in relation
14 to their opioid usage. This includes peoples’ negative attitudes from family, medical
15 professionals and work colleagues which lead to them feeling stigmatised and judged
16 for taking opioids. This includes peoples’ negative attitudes from family, medical
17 professionals and work colleagues which lead to them feeling stigmatised and judged
18 for taking opioids.
19
20
21

22
23 *“So I’m constantly trying to clean up because I think people are going to*
24 *judge me. ‘Oh, because she’s on all this medication, ooh, she can’t look after*
25 *her children.’” Paterson et al pg 724*

26
27
28
29
30 *“As soon as you mention to someone that you are on pain medication it’s, ‘Oh*
31 *my god, you’ve got to get off it.’ It is viewed as weak. Somehow I am weak for*
32 *being on this medication.” Vallerand et al 2 pg 128*
33
34
35

36
37 To protect themselves some chose to keep their opioids a secret.

38
39 *“But you know, after 2 years of pain, you are physically exhausted, mentally*
40 *exhausted and depressed. So, I take my medication and I hide it at the bottom*
41 *of my drawer. It’s my secret life. It’s always a secret, and I’ve got to hide it*
42 *and not tell anyone.” Vallerand et al 1 pg 169*
43
44
45
46
47

48
49 Some people made a conscious decision about who they could tell and who they
50 couldn’t due to negative reactions. Relationships suffered when patients felt
51 unsupported.
52
53

54
55 *“My son told me I was a drug addict. He did. He really did. He was to the*
56 *point, he didn’t know what he could do for me. It really was that bad.”*
57
58

59
60 Vallerand et al 2 pg 128

1
2
3 *“I had originally told my sister and she was very concerned. Then she said,*
4 *‘As long as you don’t stay on them.’ She thought it was OK if I did it for a*
5 *while but as long as I didn’t stay on them. So I just sort of never told her. And*
6 *she never asked.”* Vallerand et al 2 pg 128
7
8
9
10
11

12 Although some seemed confident in using opioids, mostly people spoke about fears
13 such as; addiction and uncontrolled pain. Feeling supported validated their choices
14 and experiences and lessened some of their fears and concerns.
15
16
17

18
19 *“And at the end, my partner says—we sat down there and he goes ‘Stay on*
20 *them.’ ...I’ve always spoke to my partner, and if he’s been unsure— we’ve*
21 *both been unsure, we’ve both gone into the doctor together to ask questions.”*
22
23
24
25
26 Zheng et al pg 1834
27

28 *“my wife wanted me to take this medication. She was like: let’s go for it.”*
29
30
31 Arnaert et al pg 26
32
33

34 **5) The challenge of tapering/withdrawal from opioids**

35
36
37 Four papers^{23, 26 44, 45} explore patients’ experiences of tapering or withdrawing as
38 their main content. Two further papers^{34, 35} addressed it as a more peripheral issue
39 (see CERQual ratings in table 2). This describes the challenges and profound effects
40 of tapering or withdrawing from opioids.
41
42
43

44 Tapering and withdrawing from opioids could be challenging and provoke anxiety.
45
46

47
48 *“I have a tremendous fear in a doctor saying I want you to taper off the*
49 *methadone and get totally off the methadone with no alternative whatsoever. I*
50 *think that would be an irrational decision by a doctor, and I probably*
51 *wouldn’t take that advice.”* Frank et al pg1842
52
53
54
55

56
57 This anxiety could be alleviated by support from a trusted health care provider or
58 other person.
59
60

1
2
3 *“The best thing about it was that nobody acted like I was a bad person*
4 *because I was on these medications and was having to be going through this*
5 *really slow process of coming down off of them.” Frank et al pg1843*
6
7
8
9

10 Successful tapering was described as a collaborative agreement between HCP and
11 patient.
12
13

14 *“She put me down to 2 and a half [pills per day]. Then she said, okay, we’ll*
15 *go down to half a pill. I told her I didn’t think that just 2 a day would do it,*
16 *and she said okay, we’ll try 2 and a half, are you agreeable with that? I said*
17 *that’s fine. I mean, we can discuss stuff. It doesn’t have to be a disagreement*
18 *because we can talk about it. It’s not an argument. We’re 2 adults having a*
19 *conversation, figuring out what to do.” Matthias et al 2017 pg 1369*
20
21
22
23
24
25
26
27

28 However, not all people experienced joint decision making when tapering
29

30 *“I just don’t feel that he’s understanding. he don’t seem to care what I’m*
31 *saying, because he’s lowering it down anyway, even though I’ve told*
32 *him...that I didn’t agree with it being lowered.” Matthias et al 2017 pg 1369*
33
34
35
36

37 For those in the USA, prescribing policies, advising clinicians to monitor and
38 decrease opioid use, and the legislation to enforce these policies made those taking
39 opioids feel as if they were ‘a public health problem’. This could have a negative
40 effect on the doctor patient relationship and leave the patient feeling disempowered.
41
42
43
44
45
46

47 This was compounded when opioids had been withdrawn by legislation.^{23, 44}
48

49 *“I have to struggle, suffer, to make the next the next time that I can get my*
50 *medicine. And I don’t think that’s fair to me because if I can take my medicine*
51 *a little more regularly, I would be able to do more.....I don’t think that the*
52 *law, people, politicians, or anybody should be able to tell anybody that’s in*
53 *pain what type of medicine they can take.” Al Achkar et al pg 7*
54
55
56
57
58
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60

1
2
3 “That kinda got me mad, cause I thought well you know. . .they’re taking it off
4 the market because of people abusing it. . .It’s not fair to us, you know. . . . I
5 think the government was wrong to. . . pull them off the market, you know,
6 because of people abusing them, no like they weren’t looking at the people
7 that need them. . .But I think it’s really unfair that people that really do need
8 them can’t get them.” Chang and Ibrahim 2017 pg 3
9
10
11
12
13
14
15
16
17

18 **Overarching theme: Constantly balancing**

19
20 After considering the five themes, an overarching theme emerged - ‘Constant
21 balancing’. The theme *Reluctant users with little choice* describes the need to balance
22 the pros and cons of starting opioids and the need to balance having pain with their
23 hesitancy to use opioids.
24
25
26
27
28
29

30 “I don’t really like being on a lot of tablets, I’ve never been a tablet person,
31 um. . . but I mean I can’t have the pain either so it’s one evil outdoing the
32 other evil. Paterson et al pg 723
33
34
35
36

37 Studies describe balancing the dose for pain management with their side effects to
38 allow them to function. Participants constantly weighed up the effects on their life;
39 dealing with an internal conflict of unresolved pain versus necessary medication,
40 being opioid free versus having uncontrolled pain and balancing other stressors
41 against opioid dose changes.
42
43
44
45
46
47

48 “If you’re going to be able to walk, and you take one pain pill so you can walk
49 and live life, you’re going to do it, even though you may not like it.” Penney et
50 al pg 6
51
52
53
54

55 The theme *Stigma feeling scared and secretive but needing support*, describes the
56 need to balance their hopes for relief with fear of side effects, and also to balance
57
58
59
60

1
2
3 whether or not to disclose their opioid use with the risk of being labelled a ‘drug
4
5 seeker’ versus having unrelieved pain.
6

7
8 *“I do it for my own protection by not telling them because I see how they react*
9
10 *by reading something in the paper...and it’s just their ignorance. And I don’t*
11
12 *have time. Well they know what’s going on but they don’t get it to this day. So*
13
14 *you have to pick your battles...” Brooks et al pg 19*
15

16
17 The theme *Understanding opioids; the good and the bad*, showed people had different
18
19 levels of understanding but weighed up their decisions and trade-offs against their
20
21 pain relief.
22

23
24 *“It’s, it’s got a good and bad side, morphine.When I take it, it works*
25
26 *really, really well but it makes you feel rather sick, umm, rather spaced out*
27
28 *and thinking wise, umm, it outcomes more on the other, do I want to be sick or*
29
30 *do I want to cry with pain? So I’d rather be sick but it is a very, very good*
31
32 *painkiller. ” Blake et al pg 105*
33

34
35 The therapeutic alliance theme showed that often it was evident that they were ‘not on
36
37 the same page’ with them balancing the advice from their doctors with what they
38
39 wanted.
40

41
42 *“[My provider] said you could die any time, and my husband and I said, well,*
43
44 *we realize that, but because of the pain, you know, we were willing to take that*
45
46 *risk that I would die from the narcotic medication.” Frank et al pg 1841*
47

48
49 It also meant that there were multiple barriers to the process of decreasing opioids due
50
51 to this constant balancing act which is described in the theme *the challenge of*
52
53 *tapering/withdrawal from opioids.*
54
55
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57
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1
2
3 *“I will tell her, if I do come off this medication, there are going to be*
4 *consequences. I can’t walk as often, I can’t stand as long, I just can’t do it....”*

5
6
7
8 *Vallerand et al 1 pg 169*
9

10 11 **Discussion**

12
13 Our five themes were; 1) Reluctant users with little choice; 2) Understanding opioids:
14 the good the bad; 3) A therapeutic alliance: not always on the same page; 4) Stigma:
15 feeling scared and secretive but needing support; and 5) The challenge of tapering or
16 withdrawal. An overarching theme of ‘constantly balancing’ emerged from the data.
17
18 These themes all had positive and negative aspects although the negative were more
19 prevalent by far.
20
21

22 We present a line of argument of how complex it is for the patient to balance
23 decisions at every stage of their journey. First their reluctance to start taking opioids
24 but feeling they had no option. Patients are given opioids for CNMP often as a last
25 resort when all other treatment has failed and their lives are so profoundly affected
26 that they talk of a desperation, that they would literally ‘try anything’. Patients spoke
27 about not being given any detailed information about opioids and that they had
28 learned more about them over time from different sources. This varied understanding
29 about opioids and their side effects can affect the decisions that people make. Patients
30 reported the need to keep the dosage of opioids as low as possible and often that they
31 were not at risk of addiction or overdose if they were taking them as prescribed. Even
32 those who felt they may be addicted sometimes viewed this as an acceptable trade-off
33 for pain relief. Our findings indicate that patient desperation combined with
34 inadequate information from healthcare professionals could trigger the prescription of
35 opioids. It may be that delivering accurate information about the potential side effects
36
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1
2
3 and limited efficacy of opioids for chronic pain management would reduce the use of
4
5
6 opioids.

7
8 Our findings demonstrate that the stigma surrounding how patients feel about being
9
10 on opioids can be compounded by the judgements of others. Although patients often
11
12 describe themselves in terms of 'reluctant users', if they experienced the benefits of
13
14 opioids through decreased pain and thus increased function they are often too scared
15
16 to reduce opioids and return to a life of potentially unmanaged pain.

17
18
19
20
21 Our findings suggest that clinicians and patients with chronic pain are not always 'on
22
23 the same page'. The theme *Therapeutic alliance* captures the positives, but also the
24
25 tensions and mismatches of perceptions held by healthcare providers who are
26
27 attempting to limit dose escalation, and patients who may view constant dose
28
29 escalation as an acceptable trade-off for reducing relentless pain. The therapeutic
30
31 alliance is a robust theme supported by 26 of the 31 studies included. This is not
32
33 surprising as patients rely on their health care professionals to prescribe opioids. This
34
35 finding resonates with qualitative evidence syntheses (QES) exploring the experience
36
37 of patients¹³ and healthcare professionals⁴⁸ It seems clear that joint decision -making
38
39 is important for appropriate healthcare; however, our findings suggests that there are
40
41 instances of mistrust on both sides. A QES exploring clinicians experience of
42
43 prescribing opioids for chronic pain demonstrate that the process of prescribing
44
45 opioids is not straightforward for clinicians who face a complex decision - 'Should I
46
47 shouldn't I' prescribe opioids for chronic non-malignant pain⁴⁸. They also
48
49 demonstrate that clinicians must walk a fine line to balance the pros and cons of
50
51 opioids whilst also maintaining patient trust. This suggests that both patients and
52
53
54
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1
2
3 HCPs find dealing with prescribing/taking opioids for CNMP is complex and involves
4
5 balancing and trade-offs.
6

7
8 Current guidance from Royal College of Anaesthetists in the UK and The Centers for
9
10 Disease Control and Prevention in the US advocate a preference for non-opioid
11
12 therapies in the treatment of CNMP⁴⁹. If a clinician feels that opioids are indicated,
13
14 then they recommend a low dose for a short duration which should be assessed for
15
16 effectiveness and regularly evaluated for benefits and harms. All but four studies in
17
18 this review are between 2005 and 2017, prior to these guidelines. Opioid contracts in
19
20 some areas of the USA and Canada can make patients feel stigmatised and judged,
21
22 this effect can be moderated by a good therapeutic relationship, and reframing these
23
24 as agreements rather than contracts⁵⁰. Some physicians may view
25
26 contracts/agreements as necessary to guard against uncontrolled dose escalation,
27
28 repeated demands for replacement of lost or misplaced medication, subversion and
29
30 illicit opioid intake. This finding resonates with Toye et al (2017) who describe the
31
32 moral boundary work and social guardianship that clinicians associate with opioid
33
34 prescription. Our findings suggest that this role does may not contribute to an
35
36 effective therapeutic partnership.
37
38
39
40
41

42 Limitations of this study

43
44 A majority of the studies are from the United States and the findings need to be taken
45
46 in the context of its health and social care systems. Most of the articles in this
47
48 qualitative synthesis were published or the research was conducted, before the impact
49
50 of the opioid epidemic became clear to regulators and the medical profession. Some
51
52 papers discuss using opioids as a last resort, although the opioid epidemic, especially
53
54 in the US suggests they are not always given as a last resort. We acknowledge that
55
56 our interpretation of the data might have been influenced by the current, much more
57
58
59
60

1
2
3 critical perception of opioid use for chronic non-malignant pain. Further evidence is
4
5 needed to find out if these themes are universal for developed countries or whether
6
7 there are important differences.
8
9

10 Our conceptual framework highlights patients need to constantly balance and to
11
12 consider the pros and cons of taking opioids. This can have a profound effect on
13
14 peoples' relationships with their family, friends and health care providers and their
15
16 perceived standing in the community which is reflected in their careful balancing of
17
18 disclosure. The therapeutic alliance and having a clear understanding of all the
19
20 positive and negative aspects of opioids were important factors that underpinned their
21
22 ability to maintain this fragile balance. This balance might also affect a person's
23
24 desire or ability to taper or withdraw from opioids.
25
26
27

28 The GRADE-CERQual ratings (table 2) revealed we had confidence in the findings
29
30 with only a few minor concerns and no moderate or serious concerns.
31
32
33

34 **Conclusions and recommendations for future research**

35
36 The first meta-ethnography on this topic revealed a constant balancing and a life in
37
38 flux in an effort to maintain participation in life and relationships. These are important
39
40 features of opioid use for CNMP. To maintain this delicate balance they often need
41
42 support from family or clinicians, however this balance can be upset by the feeling of
43
44 being judged by this same potential support system or peers and society at large
45
46 through the media. The therapeutic alliance with healthcare professionals, the extent
47
48 of people's understanding as well as the stigma attached to opioid use need to be
49
50 navigated by people who are often reluctant to be on opioids in the first place.
51
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Authors Contribution

VN and KS contributed to the review concept and design as part of the I-WOTCH process evaluation team. HS, SE, MU and KS were involved in the design of the IWOTCH study. VN, KS and FT screened search results or extracted data, conducted the analysis and synthesis. All authors contributed to data interpretation, revised the final manuscript critically for important intellectual content and appraised the final manuscript. VN prepared the final manuscript and will be the corresponding author.

Funding

This project was funded by the National Institute for Health Research, Health Technology Assessment (project number 14/224/04). The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the HTA, NIHR, NHS or the Department of Health. Ethics approval was provided by Yorkshire and the Humber South Yorkshire Research Ethics committee on 13-9-16.

Declaration of competing interests

KS has undertaken other meta-ethnographies and was on the NIHR HS&DR Board until January 2018.

SE is investigator on a number of NIHR and industry sponsored studies. He received travel expenses for speaking at conferences from the professional organisations. SE consults for Medtronic, Abbott, Boston Scientific and Mainstay Medical, none in relation to opioids. SE is chair of the BPS Science and Research Committee. SE is deputy Chair of the NIHR CRN Anaesthesia Pain and Perioperative Medicine National Specialty Group. SE's department has received fellowship funding from Medtronic as well as nurse funding from Abbott.

1
2
3 HS is director of Health Psychology Services Ltd, providing psychological services
4
5 for a range of health related conditions.
6

7
8 MU was Chair of the NICE accreditation advisory committee until March 2017 for
9
10 which he received a fee. He is chief investigator or co-investigator on multiple
11
12 previous and current research grants from the UK National Institute for Health
13
14 Research, Arthritis Research UK and is a co-investigator on grants funded by the
15
16 Australian NHMRC. He is an NIHR Senior Investigator. He has received travel
17
18 expenses for speaking at conferences from the professional organisations hosting the
19
20 conferences. He is a director and shareholder of Clinvivo Ltd that provides electronic
21
22 data collection for health services research. He is part of an academic partnership with
23
24 Serco Ltd related to return to work initiatives. He is a co-investigator on a study
25
26 receiving support in kind from Stryker Ltd. He has accepted honoraria for teaching
27
28 from CARTA. He is an editor of the NIHR journal series, and a member of the NIHR
29
30 Journal Editors Group, for which he receives a fee.
31
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38 Data Availability Statement: Data is available on reasonable request.
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41 Acknowledgements

42
43 We would like to thank Samantha Johnson an academic librarian who helped with the
44
45 electronic searches and Dr Stephanie Tierney who helped to screen the citations.
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Figure 1 Concept model of the experiences of people taking opioid medication for chronic non-malignant pain

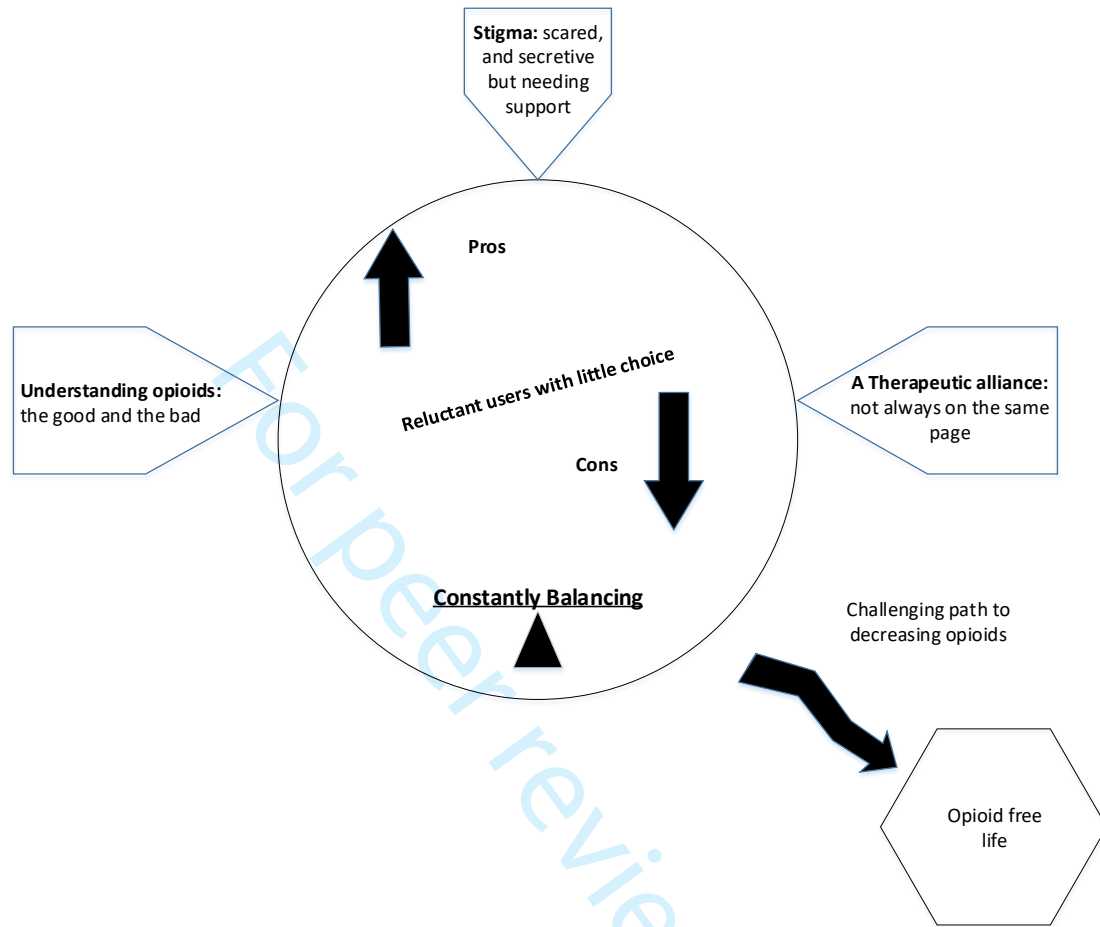
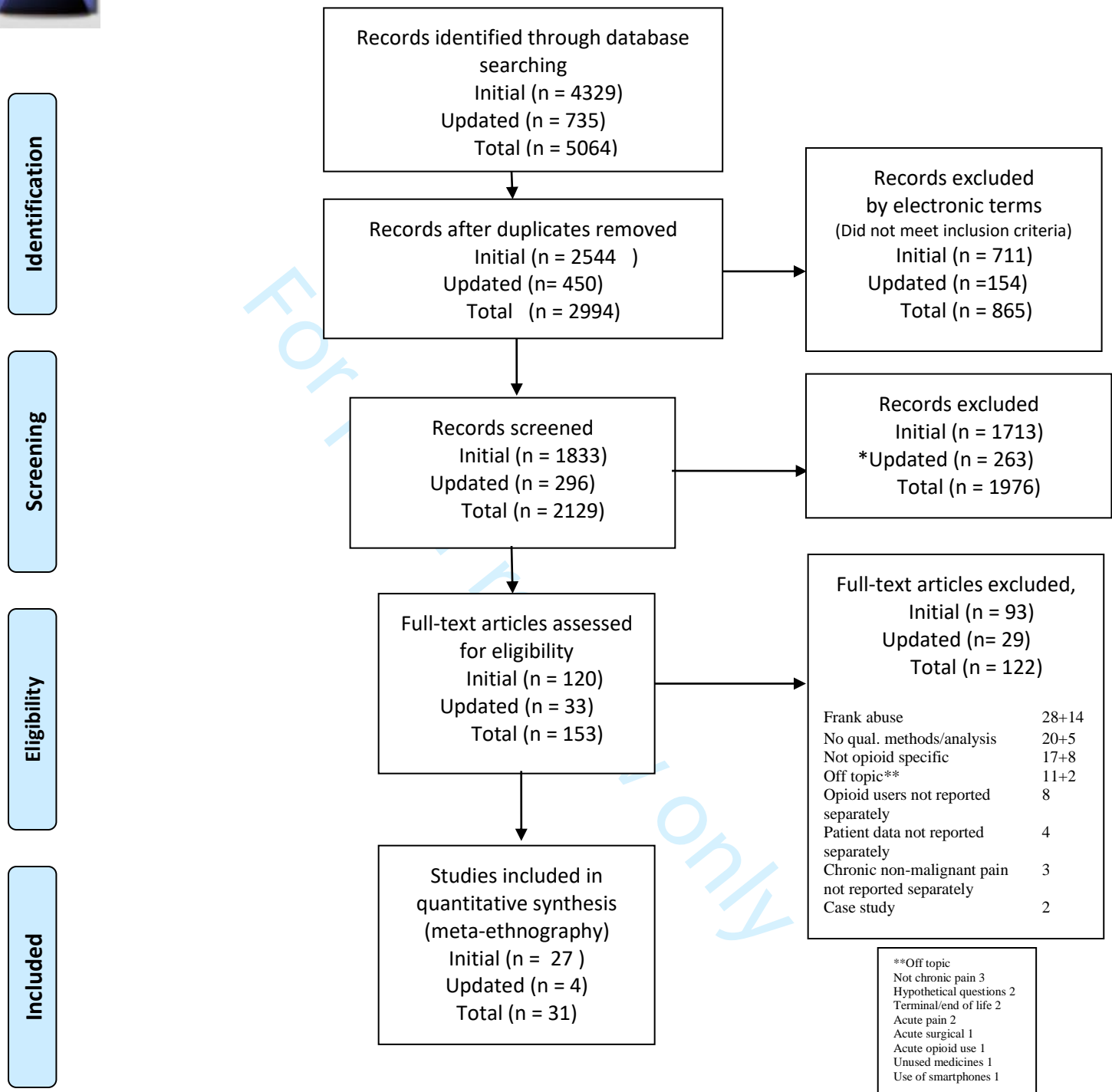




Figure 2: PRISMA Flow Diagram



Initial search June 2017 and updated search Sept 2018 reported.

The search dates for the rerun could be specified in some databases, but not all. Therefore some papers were found in both searches. These twice found duplicate papers were removed at this point*

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Appendix 1 The eMERGe meta-ethnography reporting guidance

Numbered criteria headings with explanatory reporting criteria	Page
Phase 1—Selecting meta-ethnography and getting started	
<i>Introduction</i>	
1 Rationale and context for the meta-ethnography Describe the gap in research or knowledge to be filled by the meta-ethnography, and the wider context of the meta-ethnography	4
2 Aim(s) of the meta-ethnography Describe the meta-ethnography aim(s)	4
3 Focus of the meta-ethnography Describe the meta-ethnography review question(s) (or objectives)	4
4 Rationale for using meta-ethnography Explain why meta-ethnography was considered the most appropriate qualitative synthesis methodology	4
Phase 2—Deciding what is relevant	
<i>Methods</i>	
5 Search strategy Describe the rationale for the literature search strategy	4/5
6 Search processes Describe how the literature searching was carried out and by whom	4/5
7 Selecting primary studies Describe the process of study screening and selection, and who was involved	5
<i>Findings</i>	
8 Outcome of study selection Describe the results of study searches and screening	16
Phase 3—Reading included studies	
<i>Methods</i>	
9 Reading and data extraction approach Describe the reading and data extraction method and processes	6
<i>Findings</i>	
10 Presenting characteristics of included studies Describe characteristics of the included studies	Table 1
Phase 4—Determining how studies are related	
<i>Methods</i>	
11 Process for determining how studies are related Describe the methods and processes for determining how the included studies are related: - Which aspects of studies were compared AND- How the studies were compared	6
<i>Findings</i>	
12 Outcome of relating studies Describe how studies relate to each other	17
Phase 5—Translating studies into one another	16
<i>Methods</i>	
13 Process of translating studies Describe the methods of translation: - Describe steps taken to preserve the context and meaning of the relationships between concepts within and across studies- Describe how the reciprocal and refutational translations were conducted- Describe how potential alternative interpretations or explanations were considered in the translations	16
<i>Findings</i>	
14 Outcome of translation Describe the interpretive findings of the translation.	17 to 28
Phase 6—Synthesizing translations	
<i>Methods</i>	
15 Synthesis process Describe the methods used to develop overarching concepts (“synthesised translations”)Describe how potential alternative interpretations or explanations were considered in the synthesis	16
<i>Findings</i>	
16 Outcome of synthesis process Describe the new theory, conceptual framework, model, configuration, or interpretation of data developed from the synthesis	Figure 1
Phase 7—Expressing the synthesis	

<p><i>Discussion</i></p> <p>17 Summary of findings Summarize the main interpretive findings of the translation and synthesis and compare them to existing literature</p>	<p>28 to 30</p>
<p>18 Strengths, limitations, and reflexivity Reflect on and describe the strengths and limitations of the synthesis: - Methodological aspects—for example, describe how the synthesis Findings were influenced by the nature of the included studies and how the meta-ethnography was conducted. - Reflexivity—for example, the impact of the research team on the synthesis findings</p>	<p>30</p>
<p>19 Recommendations and conclusions Describe the implications of the Synthesis</p>	<p>31</p>

Reference: France et al. BMC Medical Research Methodology (2019) 19:25
<https://doi.org/10.1186/s12874-018-0600-0>

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Appendix 2 – example of search terms

Scopus

((TITLE-ABS-KEY(buprenorphine or fentanyl or heroin or hydromorphone or methadone or morphine or opium or oxycodone or pentazocine or tramadol or opiate* or opioid*) OR TITLE-ABS-KEY(suboxone or bunavail or zubsolv or dipipanone or diconal or wellconal or diamorphine or duragesic or fentora or actiq or abstral or recivit or effentora or instanyl or pecfent or oxycontin or roxicodone or oramorph or papaveretum or omnopon or fortral)OR TITLE-ABS-KEY(osegon or "talwin nx" or pethidine or meperidine or demerol or tapentadol or nucynta or palexia or tapal or ultram or zytram))) and ((TITLE-ABS-KEY(qualitative w/5 (theor* or study or studies or research or analysis)) OR TITLE-ABS-KEY(ethno* or emic or etic or phenomenolog* or hermeneutic* or heidegger* or husserl* or colaizzi* or giorgi* or glaser or strauss or (van and kaam*) or (van and manen) or ricoeur or spiegelberg* or merleau) OR TITLE-ABS-KEY(constant w/3 compar*) OR TITLE-ABS-KEY(focus w/3 group*) OR TITLE-ABS-KEY(grounded w/3 (theor* or study or studies or research or analysis)) OR TITLE-ABS-KEY(narrative w/3 analysis) OR TITLE-ABS-KEY(discourse w/3 analysis) OR TITLE-ABS-KEY((lived or life) w/3 experience*) OR TITLE-ABS-KEY((theoretical or purposive) w/3 sampl*) OR TITLE-ABS-KEY("field note*" or "field record*" or fieldnote*) OR TITLE-ABS-KEY(participant* w/3 observ*) OR TITLE-ABS-KEY("action research") OR TITLE-ABS-KEY("digital adj record*" or audiorecord* or taperecord* or videorecord* or videotap*) OR TITLE-ABS-KEY(cooperative and inquir*) OR TITLE-ABS-KEY(co and operative and inquir*) OR TITLE-ABS-KEY(co-operative and inquir*) OR TITLE-ABS-KEY(("semi-structured" or semistructured or unstructured or structured) w/3 interview*) OR TITLE-ABS-KEY((Informal or in-depth or indepth or "in depth") w/3 interview*) OR TITLE-ABS-KEY(("face-to-face" or "face to face") w/3 interview*) OR TITLE-ABS-KEY("ipa" or "interpretive phenomenological analysis") OR TITLE-ABS-KEY(social and construct*) OR TITLE-ABS-KEY("appreciative inquiry") OR TITLE-ABS-KEY(poststructural* or "post structural*" or post-structural*) OR TITLE-ABS-KEY(postmodern* or "post modern*" or post-modern*) OR TITLE-ABS-KEY(feminis*) OR TITLE-ABS-KEY(humanistic or existential or experiential))) and (TITLE-ABS-KEY(pain))

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Appendix 3 Critical Appraisal Skills Programme (CASP) Quality appraisal tool scores

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Score
Arnaert 2006	Yes	Yes	Yes	Yes	?	No	Yes	Yes	Yes	Yes	17/20
Bergman 2013	Yes	Yes	Yes	Yes	Yes	No	Yes	?	Yes	Yes	17/20
Blake 2007	Yes	Yes	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	19/20
Brooks 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	?	Yes	Yes	17/20
Buchbinder 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Chang F 2017	Yes	Yes	Yes	Yes	Yes	No	?	?	Yes	Yes	16/20
Chang Y-P 2011	Yes	Yes	Yes	Yes	Yes	No	Yes	?	?	Yes	16/20
Coyne 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	?	Yes	Yes	17/20
Esquibel 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	20/20
Frank 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	20/20
Green 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Hooten 2011	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Krebs 2014	Yes	Yes	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	19/20
Matthias 2014	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
McCrorie 2015	Yes	Yes	?	Yes	Yes	No	Yes	Yes	Yes	Yes	17/20
Mueller 2017	Yes	Yes	Yes	Yes	?	No	Yes	Yes	?	Yes	16/20
Paterson 2016	Yes	Yes	Yes	Yes	Yes	?	?	Yes	Yes	Yes	18/20
Penney 2017	Yes	Yes	?	?	?	?	Yes	?	?	?	13/20
Rieb 2016	Yes	Yes	Yes	Yes	Yes	?	Yes	?	Yes	Yes	18/20
Simmonds 2015	Yes	Yes	?	Yes	Yes	?	Yes	Yes	?	?	16/20
St Marie 2016	Yes	Yes	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	19/20
Vallerand 1 2009	Yes	Yes	Yes	Yes	Yes	No	No	Yes	?	Yes	15/20
Vallerand 2 2010	Yes	Yes	Yes	?	Yes	No	No	Yes	?	?	13/20
Wallace 2014	Yes	Yes	Yes	Yes	Yes	No	Yes	?	?	Yes	16/20
Warms 2005	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	16/20
Zgierska 2016	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Zheng 2013	Yes	Yes	Yes	Yes	Yes	No	?	Yes	Yes	Yes	17/20
Al Achkar 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Matthias 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Matthias 2018	Yes	Yes	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	19/20
Smith 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	20/20

Legend 1 Critical Appraisal Skills Programme (CASP) questions scoring: Yes =2 ? (Can't Tell) = 1 No = 0

Q1. Was there a clear statement of the aims of the research?

Q2. Is a qualitative methodology appropriate?

Q3. Was the research design appropriate to the aims of the research?

Q4. Was the recruitment strategy appropriate to the aims of the research?

Q5. Was the data collected in a way that addressed the research issue?

Q6. Has the relationship between researcher and participants been adequately considered?

Q7. Have ethical issues been taken into consideration?

Q8. Was the data analysis sufficiently rigorous?

Q9. Is there a clear statement of findings?

Q10. How valuable is the research?

BMJ Open

A systematic review and qualitative evidence synthesis of the experiences of people taking opioid medication for chronic non-malignant pain: a meta-ethnography

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-032988.R2
Article Type:	Original research
Date Submitted by the Author:	13-Dec-2019
Complete List of Authors:	Nichols, Vivien; University of Warwick, Warwick Clinical Trials Unit, Warwick Medical School Toye, Francine; Oxford University Hospitals NHS Trust, Physiotherapy Research Unit, Nuffield Orthopaedic Centre Eldabe, Sam; The James Cook University Hospital Sandhu, Harbinder; University of Warwick, Warwick Clinical Trials Unit, Warwick Medical School Underwood, Martin; University of Warwick, Warwick Clinical Trials Unit, Warwick Medical School Seers, Kate; University of Warwick, Warwick Research in Nursing, Division of Health Sciences, Warwick Medical School
Primary Subject Heading:	Qualitative research
Secondary Subject Heading:	Patient-centred medicine
Keywords:	opioid, patients' views, QUALITATIVE RESEARCH, chronic non-malignant pain, meta-ethnography, qualitative evidence synthesis

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A systematic review and qualitative evidence synthesis of the experiences of people taking opioid medication for chronic non-malignant pain: a meta-ethnography

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Abstract

Objective To review qualitative studies of the experience of taking opioid medication for Chronic Non-Malignant Pain (CNMP) or coming off them.

Design A qualitative evidence synthesis using meta-ethnography. We used a seven step approach from the methods of meta-ethnography.

Data sources and eligibility criteria We searched selected databases: Medline, Embase, AMED, CINAHL, PsycInfo, Web of Science and Scopus (Science citation index and Social Science Citation Index) for qualitative studies which gave patients' views of taking opioid medication for CNMP or of coming off them (June 2017, updated September 2018).

Data extraction and synthesis Papers were quality appraised using a Critical Appraisal Skills Programme (CASP) tool and Grading of Recommendations Assessment, Development and Evaluation working group - Confidence in Evidence from Reviews of Qualitative research (GRADE-CERQual) guidelines were applied. We identified concepts and iteratively abstracted these concepts into a line of argument.

Results We screened 2129 unique citations, checked 153 full texts and 31 met our review criteria. We identified five themes: 1) Reluctant users with little choice; 2) Understanding opioids: the good and the bad; 3) A therapeutic alliance: not always on the same page; 4) Stigma: feeling scared and secretive but needing support; and 5) The challenge of tapering or withdrawal. A new overarching theme of 'constantly balancing' emerged from the data.

Conclusions People taking opioids were constantly balancing tensions, not always wanting to take opioids, weighing the pros and cons of opioids but feeling they had no choice because of the pain. They frequently felt stigmatised, were not always 'on the

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3 same page' as their health care professional and changes in opioid use were often
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5 challenging.
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10 **Key words:** Opioid, patients' views, qualitative research, chronic non-malignant
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12 pain, meta-ethnography, qualitative evidence synthesis.
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16 Word count 4,971
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22 **Strengths and Limitations**

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25 • To our knowledge this is the first qualitative evidence synthesis of patients'
26 experiences of taking opioid medications.
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29 • Meta-ethnography provides a thorough, systematic way of synthesising
30 qualitative findings across multiple studies.
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33 • Meta-ethnography provides the reviewer's interpretation of second order
34 concepts.
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37 • Using a GRADE-CERQual approach can assist in rating confidence in the
38 review findings.
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41 • Qualitative research that illuminates patients' perspectives can help to shape
42 future approaches to opioid management.
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50 **Introduction**

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53 Chronic non-malignant pain (CNMP) affects between an estimated 11% and 20% of
54 the population in Europe and US and can impact heavily on people's quality of life ^{1, 2}
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56 . Opioid medications are strong painkillers which have a well-established role in the
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3 treatment of acute and cancer pain; they have also been advocated for CNMP. Opioids
4
5 can have distressing side effects as dosages increase such as; constipation, sedation,
6
7 drowsiness, nausea, decreased concentration and memory, or mood changes ³. Most
8
9 people who use opioids develop tolerance to the painkilling effect of opioids, and
10
11 some become dependent on them. Studies have shown that high opioid usage can also
12
13 put people's lives at risk ⁴. Despite this, the prescription of opioid medication for
14
15 CNMP has risen sharply in the higher income countries. Few studies of opioids have
16
17 shown effectiveness beyond 12 weeks follow up. Population surveys have shown
18
19 long-term use to be associated with increased side effects and limited pain relief ^{3 5 6}.
20
21 This synthesis of qualitative research was undertaken to underpin a process evaluation
22
23 for the Improving the Wellbeing of people with Opioid Treated CHronic pain (I-
24
25 WOTCH) study funded by the National Institute for Health Research. I-WOTCH is a
26
27 randomised controlled trial evaluating a multi-component education and patient
28
29 centred group intervention with a one-to-one tapering programme against a control of
30
31 an advice booklet with a relaxation CD. More information can be found in the main
32
33 study protocol ⁷ and process evaluation protocol ⁸.
34
35 This qualitative evidence synthesis uses the methods of meta-ethnography to find out
36
37 what peoples' experiences are of both using opioids for CNMP and their attempts to
38
39 stop taking them.
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48 **Methods**

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51 We use Noblit and Hare's 7 stages of meta-ethnographic analysis ⁹. We used the new
52
53 eMERGe reporting guidelines for meta-ethnography to structure our report ¹⁰ (*See*
54
55 *appendix 1*). The protocol is published in the international prospective register of
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3 systematic reviews (PROSPERO) registration number: CRD42017082418.

4
5 <http://www.crd.york.ac.uk/PROSPERO>

6
7
8 *Step 1 Getting Started.*

9
10 In order to address what has been labelled an opioid epidemic¹¹, we need to
11 understand people's experiences of being on opioids and of coming off them. Our
12 team was chosen because of its expertise in primary qualitative research and
13 qualitative evidence synthesis specific to chronic pain and opioid prescription.

14
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17
18
19 *Step 2 Deciding what is relevant.*

20 We undertook systematic electronic searches in June 2017 with a rerun in September
21 2018, appraising relevant papers for quality using the Critical Appraisal Skills
22 Programme (CASP) tool for qualitative research¹². One researcher (VN) with the
23 assistance of an academic librarian (SJ) searched seven electronic databases; Medline,
24 Embase, AMED, CINAHL, PsycInfo Web of Science and Scopus (Science citation
25 index and Social Science Citation Index) and forward citation searches. We used
26 search terms, free text and MeSH terms for all opioid drugs as well as their generic
27 names. We combined these with the MeSH term 'pain' and a wide range of MeSH
28 terms and words to describe all types of qualitative research and its analysis based
29 upon a search used by Toye, Seers and Barker in 2017¹³. The search was limited to
30 those in English regarding humans with no cut-off date. Appendix 2 shows an
31 example of our search terms.

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49 Unique citations were screened independently by 2 researchers (VN ST *see*
50 *acknowledgements*) against our inclusion and exclusion criteria (see Box 1). Any
51 disagreements were arbitrated by a third researcher (KS). Papers for full text reading
52 were identified and read by two researchers. Quality was assessed using a CASP tool.
53
54
55
56
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58
59
60 VN critically appraised the studies and KS independently appraised 10% for

consistency. The CASP scores are shown in table 1 and appendix 3. The GRADE-CERQual was used to appraise the reviewers' confidence in the research findings ¹⁴,
15.

Box 1 Inclusion/Exclusion criteria

Included Studies

Adults (18 years or older) taking or have taken opioid medication in the last five years
Published in English in peer review journals with no time constraint
Must relate to patient perspectives on using opioid medication for chronic non-malignant pain
Must use qualitative methodology (any analytical approach) or mixed quantitative and qualitative methodology with qualitative findings reported separately
Where studies include participants with differing medication we will include studies where the experience of those taking opioids is reported separately

Excluded studies

Paediatric studies (age less than 18 years)
Theoretical or methodological papers
Purely quantitative studies or mixed methods studies where the qualitative data are not presented separately
Studies concerning active cancer
Studies concerning headache
Studies concerning any acute, or acute postoperative, pain
Studies concerned only with health care professional or carer perspectives, or studies of mixed carer/ patient/ professional populations where patient perspectives are not presented separately
Non- English language studies
Theses or conference abstracts which are not peer reviewed

Step 3 Reading the studies

VN read all the studies and KS and FT read half of these papers each (so all were read twice) and all extracted the second order concepts independently. A second order concept is a researcher's interpretation of data in a primary qualitative study ¹⁶. VN, KS and FT met to discuss and reach agreement, and compiled a spreadsheet of all of the concepts extracted from the papers

Step 4 Determining how the studies are related?

VN sorted the concepts into categories by looking for any similarities and differences across all the studies. VN, KS and FT discussed the categorisation of data on multiple occasions. To enable comparison across studies, VN recorded descriptive data about each study (see table 1)

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For peer review only

Table 1 Study characteristics with CASP and GRADE-CERQual relevance ratings

Studies	Country	Data collection / participants	Analytical Approach	Aims <i>Italics = verbatim quotes</i>	Morphine Equivalent Daily Dose mg/day (MED)	CASP score	Relevance
1 Arnaert et al 2006¹⁷ Response Phases in Methadone Treatment for Chronic Non-malignant Pain	Canada	Semi-structured interview N=11 (4M/7F)	Content analysis	<i>“...to develop an understanding and to gain knowledge about the beliefs of patients with CNMP who were taking methadone, and to explore what challenges, if any, existed that affected their beliefs when first starting methadone treatment as an activity in their personal lives.”</i>	None reported	17/20	P
2 Bergman et al 2013¹⁸ Contrasting Tensions Between Patients and PCPs in Chronic Pain Management: A Qualitative Study	USA	In-depth interviews N=26 (24m/2F)	Inductive thematic analysis	<i>“... to develop a better understanding of the respective experiences, perceptions, and challenges both patients with chronic pain and PCPs face communicating with each other about pain management in the primary care setting.”</i>	None reported	17/20	P
3 Blake et al 2007¹⁹ Experiences of patients requiring strong opioid drugs for chronic non-cancer pain: a patient initiated study	UK	One focus group N=4 (2M/2F) and interviews N=10 (3M/5F)	Interpretative Phenomenological Analysis	<i>“...to determine the attitudes and experiences of patients receiving long-term strong opioid medication for chronic non-cancer pain in primary care.”</i>	Individual opioid dosages	19/20	R
4 Brooks et al 2015²⁰ Exploring the lived experience of adults using prescription opioids to manage chronic noncancer pain	Canada	In-depth interviews N=9 (4M/5F)	Interpretative Phenomenological Analysis	<i>“...to explore the lived experience of adults using prescription opioids to manage CNCP, focusing on how opioid medication affected their daily lives.”</i>	None reported	17/20	R

1 2 3 4 5 6 7 8 9 10	5 Buchbinder et al 2014 ²¹ “Is there any way I can get something for my pain?” Patient strategies for requesting analgesics	USA	Audio recorded clinical encounters N=74 (37M/37F)	Qualitative approach based on conversational analysis	<i>“We examined the direct and indirect means by which patients express a desire for analgesic medication.”</i>	None reported	18/20	I
11 12 13 14 15 16 17 18 19	6 Chang Y-P et al 2011 ²² Use of Prescription Opioid Medication among Community-Dwelling Older Adults with Noncancer Chronic Pain	USA	Face to face interview N=21 (13M/8F) ≥65yrs	Content analysis, mixed methods	<i>“... to: (1) describe older adults’ patterns of adherence to their prescription opioid medication regimens and their reasons for these medication use patterns; and (2) examine the associations between adherence of prescription opioids, pain intensity, and pain interference on daily activity.”</i>	None reported	16/20	P
20 21 22 23 24 25 26 27 28	7 Chang, F et al 2017 ²³ Perceptions of Community-Dwelling Patients and Their Physicians on OxyContin® Discontinuation and the Impact on Chronic Pain Management	Canada	Pt interviews N=13 1M/ 12F	Not specified, no references given	<i>“... to explore the perceptions of patients with chronic pain and their physicians on OxyContin discontinuation and the impact that it had on chronic pain care and management.”</i>	None reported	16/20	P
29 30 31 32 33 34 35 36 37 38	8 Coyne et al 2015 ²⁴ Assessment of a Stool Symptom Screener and Understanding the Opioid-Induced Constipation Symptom Experience	USA	Cognitive interview semi structured think-aloud approach N=66 (27M/39F)	Content analysis	<i>“...to evaluate the content validity of the Stool Symptom Screener by assessing patient understanding of its items, patient ability to differentiate among response options, and patient perceptions about the use of a 2-week recall period for evaluating stool symptoms, BMs, and laxative use. - to evaluate how patients describe their constipation experience and to understand</i>	None reported	17/20	I

				<i>whether this differs between patients who frequently use laxatives and those who do not.</i>			
9 Esquibel et al 2014 ²⁵ Doctors and patients in pain: Conflict and collaboration in opioid prescription in primary care	USA	In depth interviews with pts with CNCP receiving opioids and their physicians. N=21 pts (8M/13F)	Immersion/crystallization process to generate a thematic codebook. Mixed methods with some quant. data analysis	<i>"...to better understand the effects of COT [chronic opioid therapy] on the doctor-patient relationship."</i>	None reported	20/20	R
10 Frank et al 2016 ²⁶ Patients' Perspectives on Tapering of Chronic Opioid Therapy: A Qualitative Study	USA	Semi-structured interviews N=24 (11M/13F)	Team based, mixed inductive and deductive approach guided by the Health Belief Model	<i>"... to explore patients' perspectives on opioid tapering."</i>	MED: Used algorithm Median (IQR) 70 (30-165) Range 15-1845	20/20	R
11 Green et al 2017 ²⁷ Perpetuating stigma or reducing risk? Perspectives from naloxone consumers and pharmacists on pharmacy-based naloxone in 2 states	USA	8 focus groups (only 2 with patients with chronic pain) N=15 (8M/7F)	Thematic analysis. Content analysis with a collaborative codebook development process	<i>"...to explore the attitudes of various stakeholders toward pharmacy-based naloxone and opioid medication safety and to capture the range of initial experiences with pharmacy naloxone in 2 states with pharmacy naloxone policies."</i>	None reported	18/20	P

1 2 3 4 5 6 7 8 9 10 11	12 Hooten et al 2011 ²⁸ Smoking Cessation and Chronic Pain: Patient and Pain Medicine Physician Attitudes	USA	N = 18 Interviews N= 15 and focus group N=3 10M/8F	Participatory research, mixed methods - Thematic and content analysis	<i>"...to determine the attitudes and beliefs of both patients and pain medicine physicians regarding smoking cessation interventions applied during pain therapy."</i>	MED - used equianalgesic conversion software programme Mean ± SD 227 ± 356	18/20	I
12 13 14 15 16 17 18 19 20	13 Krebs et al 2014 ²⁹ Barriers to Guideline- Concordant Opioid Management in Primary Care—A Qualitative Study	USA	Semi structured interviews N= 26 patients (14 PC physicians) 13M/13F	Immersion crystallization approach	<i>"...to better understand primary care physicians' and patients' perspectives on recommended opioid management practices and to identify potential barriers and facilitators of guideline concordant opioid management in primary care."</i>	None reported	16/20	P
21 22 23 24 25 26 27 28 29 30	14 Matthias et al 2014 ³⁰ Communicating about opioids for chronic pain: A qualitative study of patient attributions and the influence of the patient–physician relationship	USA	Audio Recordings of primary care visits and Semi- structured interviews after clinic visit. N=30 26M/4F	Immersion/cry stallization approach	<i>"...to advance understanding about communication about opioids by directly capturing clinical communication about opioids, as well as interviewing patients to gain insight into communication patterns and their broader relationships with their physicians, and how these relationships shape communication about opioids."</i>	None reported	18/20	R
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46	15 McCrorie et al 2015 ³¹ Understanding long-term opioid prescribing for non- cancer pain in primary care: a qualitative study	UK	Semi structured interviews with patients (focus groups with	Grounded approach for thematic analysis. Constant comparison	<i>"... to understand the processes which bring about and perpetuate long-term prescribing of opioids for chronic, non-cancer pain. We interviewed patients and GPs about their experiences, beliefs and expectations of analgesia prescribing, to improve understanding of how</i>	None reported	17/20	R

		GPs) N=23 6M/17F		<i>problematic long-term opioid prescribing becomes established</i> ".			
16 Mueller et al 2016 ³² Attitudes Toward Naloxone Prescribing in Clinical Settings: A Qualitative Study of Patients Prescribed High Dose Opioids for Chronic Non-Cancer Pain	USA	Semi-structured interview N=24 8M/16F	Ethnographic iterative methods. Inductive and deductive approaches	<i>"This study assessed the knowledge and attitudes toward naloxone prescribing among non-cancer patients prescribed opioids in primary care."</i>	Inclusion criteria ≥ 100 mg MED	16/20	I
17 Paterson et al 2016 ³³ Resisting Prescribed Opioids: A Qualitative Study of Decision Making in Patients Taking Opioids for Chronic Noncancer Pain	Australia	Qualitative individual interviews N=20	Constant comparison and decision making explored in depth and with a thematic analysis utilizing a published "Model of medicine-taking"	<i>"...to identify the varying influences on patients' decisions about their use of prescribed long-term opioids. The research questions are: 1) does this conceptual Model of medicine-taking apply to people taking prescribed opioids, 2) is the concept of "resistance" to medication useful in this context, and 3) does this concept lead to new insights which may improve communication and shared decision making between"</i>	None reported	18/20	P
18 Penney et al 2016 ³⁴ Provider and patient perspectives on opioids	USA	11 Focus groups N=80 and	Thematic coding ref	<i>"...to identify the practical issues patients and providers face when accessing alternatives to</i>	None reported	13/20	P

and alternative treatments for managing chronic pain: a qualitative study		individual interviews N=10 27M/63F	Ryan, Bernard 2003	<i>opioids, and how multiple parties view these issues."</i>			
19 Rieb et al 2016 ³⁵ Withdrawal-associated injury site pain (WISP): a descriptive case series of an opioid cessation phenomenon	Canada	In person semi structured interviews N=21 14M/7F	Deductive and inductive approaches. Use of survey and emergent interview themes	<i>".... to document the existence and characteristics of this pain phenomenon that we have named withdrawal-associated injury site pain (WISP)."</i>	Recalled dose before WISP	18/20	P
20 Simmonds et al 2015 ³⁶ A Qualitative Study of Veterans on Long-Term Opioid Analgesics: Barriers and Facilitators to Multimodality Pain Management	USA	Semi structured focus groups x 3 N=25 17M/8F	Grounded theory-informed approach. Framework provided by the theory of planned behaviour	<i>"...to examine barriers and facilitators to multimodality chronic pain care among veterans on high-dose opioid analgesics for chronic non-cancer pain."</i>	Inclusion criteria at least 50 mg MED	16/20	P
21 St Marie et al 2016 ³⁷ Primary care experiences of people who live with chronic pain and receive opioids to manage pain: A qualitative methodology	USA	Semistructured interviews. N=12 6M/6F	Thematic and interpretive analyses	<i>"...to provide a deeper understanding of the experiences, issues, and challenges that people face who live with chronic pain and received opioids to help manage their pain in primary care. The following research questions were addressed: (a) What are the experiences of individuals who live with chronic pain and receive opioid pain medications to manage their pain in</i>	None reported	19/20	R

				<i>primary care? (b) What have been their healthcare experiences as they strive to manage their pain?"</i>			
22 Vallerand et al 1 2009 ³⁸ Chronic Opioid Therapy for Nonmalignant Pain: The Patient’s Perspective. Part I— Life Before and After Opioid Therapy	USA	In depth serial interviews N=22 6M/16F	Phenomenologic study / Constant comparative method	<i>“...to examine the lived experience of adults receiving opioid therapy for relief of chronic non-malignant pain through the examination of data obtained through serial taper recorded interviews.”</i>	Range 22.5 to 3,200	14/20	R
23 Vallerand et al 2 2010 ³⁹ Chronic Opioid Therapy for Non-malignant Pain: The Patient’s Perspective. Part II— Barriers to Chronic Opioid Therapy	USA	In depth serial narrative interviews N=22 6M/16F	Phenomenologic study / Constant comparative method	<i>“...to elucidate the essence of the lived experience of patients receiving chronic opioid therapy for chronic non-malignant pain through examining their life narratives.”</i>	None reported	13/20	R
24 Wallace et al 2014 ⁴⁰ Voices that may not otherwise be heard: a qualitative exploration into the perspectives of primary care patients living with chronic pain	USA	Photovoice photos, Interviews 1st N=31 2nd N=25 , and focus groups N=19	Grounded theory	<i>“...this study examined the utility of a combination of qualitative methods (Photovoice, one-on-one interviews, and focus groups) in examining the daily experiences of primary care patients living with chronic pain”.</i>	None reported	16/20	R
25 Warms et al 2005 ⁴¹ There are a few things you did not ask about my pain: writing on the margins of a survey	USA	Comments written in the margins of a questionnaire N=797	Content analysis	<i>“...to determine the characteristics of those who wrote comments [written in the margin of survey questionnaire] and to understand what was being communicated in their comments.”</i>	None reported	16/20	P

				*that comments were written in the margin is a potential limitation.			
26 Zgierska et al 2016 ⁴² Mindfulness Meditation-Based Intervention Is Feasible, Acceptable, and Safe for Chronic Low Back Pain Requiring Long-Term Daily Opioid Therapy	USA	Qual data on treatment satisfaction and experience N= 17	Qualitative analysis methods. Grounded theory	<i>"... to determine feasibility, acceptability, and safety of an MM-based intervention in patients with CLBP requiring daily opioid therapy."</i>	Inclusion criteria ≥ 30 mg MED Mean \pm SD 166.9 \pm 153.7	18/20	I
27 Zheng et al 2013 ⁴³ Chaos to Hope: A Narrative of Healing	Australia	In depth qual interviews (N=20) 10M/10F	Illness narratives. Thematic analysis	<i>"...to investigate the progression of the illness and opioid journeys of people who are taking opioids for chronic non-cancer pain".</i>	None reported	17/20	P
Rerun of search							
28 Al Achkar et al 2017 ⁴⁴ Exploring perceptions and experiences of patients who have chronic pain as state prescription opioid policies change: a qualitative study in Indiana	USA	N=9 3M/6F	Inductive emergent thematic analysis	<i>"...to evaluate the impact of Indiana's opioid prescription legislation on the patient experiences around pain management."</i>	None reported	18/20	R

<p>29 Matthias et al 2017 ⁴⁵ "I'm Not Gonna Pull the Rug out From Under You": Patient-Provider Communication About Opioid Tapering</p>	USA	N=37 12M/25F	Inductive approach, constant comparison	<p><i>"...to understand communication processes related to opioid tapering."</i></p>	None reported	18/20	R
<p>30 Matthias et al 2018 ⁴⁶ "I Was a Little Surprised": Qualitative Insights From Patients Enrolled in a 12-Month Trial Comparing Opioids With Nonopioid Medications for Chronic Musculoskeletal Pain</p>	USA	N=34 28M/6F	Inductive approach, constant comparison	<p><i>"...to understand patients' experiences with the SPACE trial including their views and anticipated benefits of opioids, versus non -opioids, experiences with the intervention and to what extent expectations were met after completing the study."</i></p>	None reported	19/20	R
<p>31 Smith et al 2018 ⁴⁷ Seeking Chronic Pain Relief: A Hermeneutic Exploration</p>	USA	N=15 4M/11F	Concurrent embedded mixed methods design, Heideggerian hermeneutic phenomenological approach	<p><i>"This research presents an interpretation of the experience of seeking pain relief for a group of people taking opioid pain medications whose pain is not adequately controlled"</i></p>	None reported	20/20	P

Legend: GRADE-CERQual Relevance component: R= Relevant, P= Partial relevance, I= Indirect relevance, U=Uncertain relevance

IQR = Interquartile Range, SD = Standard Deviation

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4 *Step 5 Translating studies into each other*
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7 Patterns and associations between categories were explored and all researchers felt
8
9 that a line of argument approach as defined by Noblit and Hare ⁹ would be the most
10
11 useful method to interpret the data.
12

13 *Step 6 Synthesising Translations*
14

15 Agreement was reached by clearly defining the over-arching or 3rd order concepts
16
17 arising from the data. A third order concept is the reviewers' interpretation of second
18
19 order concepts.
20
21

22 *Step 7 Expressing the synthesis*
23

24 We developed a conceptual model to show how the themes related to each other in a
25
26 line of argument. (see figure 1)
27
28

29 *Insert figure 1 about here.*
30

31 *Patient and Public Involvement*
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35 We did not involve patients or the public in our work.
36
37

38 *Results*
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40 Two reviewers VN and ST screened 2994 titles or abstracts (after the removal of
41
42 duplicates from the 5064 citations retrieved) and identified 153 full texts of interest.
43
44

45 Two reviewers VN and KS read these and 122 were excluded. Reasons are given in
46
47 the PRISMA flowchart, see figure 2. The reviewers agreed to include 31 studies. The
48
49 included studies were from US (23), Canada (4) UK (2), and Australia (2) and used a
50
51 range of qualitative methods.
52
53

54 We report the 4 facets of GRADE-CERQual for all papers. 1) Methodological 2)
55
56 Confidence 3) Relevance 4) Adequacy of data - See table 2 and 3 below.
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Table 2 Confidence in review findings: GRADE-CERQual assessment

Review findings	Studies contributing (see table 1 column 1 for study number)	Methodological limitations (study number)	Relevance (See table 1 end column)	Coherence	Adequacy of data
Reluctant users with little choice	1,3,4,5,6,7,17,18,21,22,26,27,30 (13 studies)	11 no concerns 2 minor concerns (18,22)	5 Relevant 6 Partial 2 Indirect	No concerns	No concerns
Understanding opioids: the good the bad	1,3,7,9,10,11,15,16,17,23,25,27,29 (13 studies)	12 no concerns 1 minor concerns (23)	6 Relevant 6 Partial 1 Indirect	No concerns	No concerns
A therapeutic alliance: not always on the same page	1,2,3,4,5,7,9,10,11,13,14,15,16,17,18,19,20,21,22,23,24,25,26,28,29,31 (26 studies)	23 no concerns 3 minor concerns (18,22,23)	12 Relevant 11 Partial 3 Indirect	No concerns	No concerns
Stigma: feeling scared, and secretive but needing support	1,2,3,4,7,9,10,14,16,17,18,20,21,22,23,24,27,28,31 (19 studies)	16 no concerns 3 minor concerns (18,22,23)	10 Relevant 8 Partial 1 Indirect	No concerns	No concerns
The challenge of tapering/ withdrawal from opioids	7,10,18,19,30,31 (6 studies)	5 no concerns 1 minor concerns (18)	2 Relevant 4 Partial	Minor concerns	Minor concerns

Table 3 GRADE-CERQual component scoring

Methodological limitations	No or very minor concerns
Coherence	Minor concerns
Adequacy of data	Moderate concerns
	Serious concerns
Relevance	Relevant
	Partial
	Indirect
	Uncertain

Synthesis of Findings

We abstracted five themes from the 2nd order concepts. Table 4 below shows how each study contributed to each theme. We have illustrated each concept with exemplary quotations.

Table 4 Themes apparent in each study

Author date	RU	U	TA	S	TW
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1	1 Arnaert and Ciccotosto 2006	X	X	X	X	
2	2 Bergman, Matthias et al 2013			X	X	
3	3 Blake, Ruel et al 2007	X	X	X	X	
4	4 Brooks, Unruh et al 2015	X		X	X	
5	5 Buchbinder, Wilbur et al 2014	X		X		
6	6 Chang Y-P, Wray et al 2011	X				
7	7 Chang,F and Ibrahim,S 2017	X	X	X	X	X
8	8 Coyne, Currie et al 2015					
9	9 Esquibel and Borkan 2014		X	X	X	
10	10 Frank, Levy et al 2016		X	X	X	X
11	11 Green, Case et al 2017		X	X		
12	12 Hooten, Vickers et al 2011					
13	13 Krebs, Bergman et al 2014			X		
14	14 Matthias,Krebs et al 2013			X	X	
15	15 McCrorie, Closs et al 2015		X	X		
16	16 Mueller, Koester et al 2016		X	X	X	
17	17 Paterson, Ledgerwood 2016	X	X	X	X	
18	18 Penney, Ritenbaugh et al 2016	X		X	X	X
19	19 Rieb, Norman et al 2016			X		X
20	20 Simmonds, Finley et al 2015			X	X	
21	21 St Marie et al 2015	X		X	X	
22	22 Vallerand et al 1 2009	X		X	X	
23	23 Vallerand et al 2 2010		X	X	X	
24	24 Wallace et al 2014			X	X	
25	25 Warms et al 2005 o		X	X		
26	26 Zgierska et al 2016	X		X		
27	27 Zheng et al 2013	X	X		X	
28	Studies from search rerun	RU	U	TA	S	TW
29	28 Al Achkar et al 2017			X	X	X
30	29 Matthias et al 2017		X	X		X
31	30 Matthias et al 2018	X				
32	31 Smith et al 2018			X	X	

Legend:

RU = Reluctant users with little choice

U = Understanding about opioids: the good and the bad

TA = A therapeutic alliance: not always on the same page

S = Stigma: feeling scared, and secretive but needing support

TW = The challenges of tapering or withdrawal

X = theme present in paper

1) Reluctant users with little choice

This describes a resistance or hesitancy to take opioids mainly due to concerns about side effects or addiction, although they felt there were no other options available.

1
2
3 *“I don’t want to become addicted, if I’m going to become addicted then as far*
4 *as I’m concerned I’m a druggie, so I might as well not be here anyway, so I*
5 *don’t want to become addicted...” Blake et al Pg103*

6
7
8
9
10 *“I just didn’t want to go on them because I mean once you get on them that’s*
11 *it, you’re sort of stuck on them. I didn’t want to take morphine at first because*
12 *there was a girl that I went through one of the courses with and she always*
13 *seemed really dopey and drugged up so it took them a long while*
14 *to talk me to into taking the morphine because I didn’t want to be like that.*
15
16
17
18
19
20
21 Zheng et al pg 1832

22
23
24 Some spoke of underusing or were keen to reduce their medications when possible.

25
26 There was a dislike of being on long term medication and some thought that it would
27
28 not relieve their pain.

29
30 *“I don’t want to do that [take more morphine]. I want to stay on as little as I*
31 *possibly can because there might come a time when I need more and I don’t*
32 *want to be on high doses. I’ve always tried to keep it at a minimum amount of*
33 *tablets each day...” Blake et al Pg 105*

34
35
36
37
38
39
40 Even though some were reluctant there were other instances of dramatic improvement
41
42 in people’s lives. This then weighted their choice to stay on the opioids.

43
44 *“I mean it is just like a miracle as far as I am concerned. It is like knowing it*
45 *[the pain] is there but you have the instruments to prevent it from getting out*
46 *and [be]coming a roaring demon.” Vallerand et al 1pg 170*

47
48
49
50
51 *“But opiates, that’s my way of life. There would be no life if I didn’t have this.*
52 *And I thank God for them because without them I’d be...well I wouldn’t be. I*
53 *just couldn’t go on. I would have committed suicide a long time ago. And I say*
54 *that truthfully cause you could not live like that, with that constant, constant*
55
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1
2
3 *pain. But, with the opiates it's made it possible to be able to have a part of a*
4
5 *life, you know."* Brooks et al pg 20
6
7
8
9

10 **2) Understanding opioids: the good and the bad**

11
12
13 This describes patients' knowledge or understanding about opioids which had
14
15 generally been acquired ad hoc and slowly over time, from pharmacists, patient
16
17 package inserts in their medication, leaflets, the internet, television programmes and
18
19 from doctors, especially doctors at the pain clinic.
20
21

22
23 *"When you see it in the media, when you see it on the television, you think if*
24
25 *you're taking regular morphine you must be in a pretty bad way, you know."*
26

27
28 Blake et al Pg103

29
30 *"I always ask before I go on a medication, what are the side effects, I was*
31
32 *told I may experience constipation; nothing else was explained to me."*
33

34
35 Paterson et al pg 721

36
37 There was often poor knowledge about using opioids for chronic pain, and about
38
39 addiction, overdose risk and side effects.
40

41
42 *"There's not too much education about it [overdose]... When I first started*
43
44 *taking it [the opioid medication], no one told me about OD[overdose]or*
45
46 *anything about that. Because I was taking it not [as] prescribed...I was just*
47
48 *like when I felt pain I would just take like five or six of them or whatever. Then*
49
50 *at the end, I'd run out."* Mueller et al pg 279
51

52
53 Patients often had to defend their usage and this added to their stress especially when
54
55 they felt their healthcare professionals lacked an understanding of the place for
56
57 opioids in the treatment of CNMP or were cautious about using them.
58
59
60

1
2
3 *“The concern is that if they increase my opioid dosage, I could stop breathing.*

4
5 *It’s ridiculous.”* Frank et al Pg1841

6
7 *“There are still a lot of doctors out there that are against it. They think it is*
8
9 *bad. Bad medicine. Bad practice.”* Vallerand et al 2 pg 129

10
11
12 In contrast, some people felt well informed which either produced more concern or
13
14 gave the patients confidence in their opioid regime.

15
16
17 *“... and from what I’ve read up, because I like to, sort of, keep on top of*
18
19 *things, that it’s an opium based drug, so you will build up some tolerance and*
20
21 *you will build up [becomes tearful] And you will potentially become sort of*
22
23 *addicted to it, if you like.”* McCrorie et al pg 3

24
25
26 *“Under Dr A [pain clinic] I’ve learnt more. And my concern has been, well it*
27
28 *was initially the possibility of addiction, but she has assured me that I’m not*
29
30 *showing no signs of addiction at all. I may have some withdrawal problems”*
31
32
33 Paterson et al Pg 721

36 37 **3) A therapeutic alliance: not always on the same page**

38
39 This describes a therapeutic alliance or the relationship between patients and their
40
41 health care providers which was considered important.

42
43 Overall there was a feeling that HCPs and patients were often ‘not on the same page’
44
45 about opioid usage.

46
47
48 *“My family doctor...does not want me to be dependent on heavy pain meds, so*
49
50 *I am intensely miserable 99% of the time.”* Warms et al pg 252

51
52
53 Some patients felt they were not listened to and were frustrated by a lack of empathy
54
55 from physicians regarding their pain experience.

56
57
58 *“I frequently have difficulty with the residents (doctors in training) explaining*
59
60 *why these drugs, this many drugs...Finally Dr. [family physician] wrote a note*

1
2
3 *in my file – stop harassing [participant’s name]. This is what she gets and why*
4 *she gets it. And they did stop but it was inconvenient. For instance, they would*
5 *not prescribe me three months at a time. I would be dispensed one month at a*
6 *time. And for someone who had been taking the same drugs for 10 years I*
7 *found that condescending. ” Brooks et al pg 18*

14 A reluctance to prescribe from GPs and pharmacists and the use of opioid contracts or
15 a restriction of medication were often considered punitive.

19 *“It kind of made me feel like I was doing something wrong, which I wasn’t,*
20 *but I signed a contract. You know, what would I be without my meds?” Krebs*
21 *et al pg 1152*

26 *“And I told my doctor that, that I wanted so I could sleep through the night.*
27 *And now he, well, I’ll give you 10, but it’s got to last. Like he treats me like a*
28 *drug addict.” Penney et al pg 6*

33 The healthcare system often worked against a therapeutic alliance with lack of
34 continuity or care or frequent visits which fed into mistrust. Patients complained that
35 provider turnover affected their ability to receive individualised care; conversations
36 about pain and treatment options often had to be started over again from scratch.

42 *“I don’t have the same doctor long enough to know”. Bergman et al pg 1693*

44 However having blood or urine tests for levels of opioids and regular checks were
45 seen by some as being cared for.

49 *“I would say, ‘I have this agreement and you don’t have to sign it if you don’t*
50 *want to, but I would like to go over it with you. These are suggestions because*
51 *this medication is addictive, it is dangerous, and I just want to make sure*
52 *you’re aware.’ I think if you really want to make it where people are not*

1
2
3 *hostile, say they have to have a urine test every 6 months, everybody, and that*
4
5 *'it's a policy because we care about all of you.'*" Krebs et al pg 1152
6
7

8 Some talked of the need for good relationships built on trust, shared decision making
9
10 and knowledgeable specialists who communicate well.
11

12 *"I wouldn't say I researched it to that depth, you know, I read a little bit*
13 *about, and asked a lot of questions at my doctor, and then we decided."*
14

15
16
17 Paterson pg 722
18

20 21 **4) Stigma: feeling scared and secretive but needing support** 22

23 This describes feelings of stigma and fear which people expressed directly in relation
24 to their opioid usage. This includes peoples' negative attitudes from family, medical
25 professionals and work colleagues which lead to them feeling stigmatised and judged
26 for taking opioids.
27
28
29
30
31

32 *"So I'm constantly trying to clean up because I think people are going to*
33 *judge me. 'Oh, because she's on all this medication, ooh, she can't look after*
34 *her children.'"* Paterson et al pg 724
35
36
37

38
39 *"As soon as you mention to someone that you are on pain medication it's, 'Oh*
40 *my god, you've got to get off it.' It is viewed as weak. Somehow I am weak for*
41 *being on this medication."* Vallerand et al 2 pg 128
42
43
44
45

46 To protect themselves some chose to keep their opioids a secret.
47

48 *"But you know, after 2 years of pain, you are physically exhausted, mentally*
49 *exhausted and depressed. So, I take my medication and I hide it at the bottom*
50 *of my drawer. It's my secret life. It's always a secret, and I've got to hide it*
51 *and not tell anyone."* Vallerand et al 1 pg 169
52
53
54
55
56
57
58
59
60

1
2
3 Some people made a conscious decision about who they could tell and who they
4
5 couldn't due to negative reactions. Relationships suffered when patients felt
6
7 unsupported.
8
9

10 *"My son told me I was a drug addict. He did. He really did. He was to the*
11 *point, he didn't know what he could do for me. It really was that bad."*

12
13
14 Vallerand et al 2 pg 128

15
16
17 *"I had originally told my sister and she was very concerned. Then she said,*
18 *'As long as you don't stay on them.' She thought it was OK if I did it for a*
19 *while but as long as I didn't stay on them. So I just sort of never told her. And*
20 *she never asked."* Vallerand et al 2 pg 128
21
22
23
24
25

26 Although some seemed confident in using opioids, mostly people spoke about fears
27
28 such as; addiction and uncontrolled pain. Feeling supported validated their choices
29
30 and experiences and lessened some of their fears and concerns.
31
32

33 *"And at the end, my partner says—we sat down there and he goes 'Stay on*
34 *them.' ...I've always spoke to my partner, and if he's been unsure— we've*
35 *both been unsure, we've both gone into the doctor together to ask questions."*

36
37
38
39
40 Zheng et al pg 1834

41
42 *"my wife wanted me to take this medication. She was like: let's go for it."*

43
44
45 Arnaert et al pg 26
46
47

48 **5) The challenge of tapering/withdrawal from opioids**

49

50 Four papers ^{23, 26 44, 45} explore patients' experiences of tapering or withdrawing as
51
52 their main content. Two further papers ^{34, 35} addressed it as a more peripheral issue
53
54 (see CERQual ratings in table 2). This describes the challenges and profound effects
55
56 of tapering or withdrawing from opioids.
57
58

59 Tapering and withdrawing from opioids could be challenging and provoke anxiety.
60

1
2
3 *“I have a tremendous fear in a doctor saying I want you to taper off the*
4 *methadone and get totally off the methadone with no alternative whatsoever. I*
5 *think that would be an irrational decision by a doctor, and I probably*
6 *wouldn't take that advice.”* Frank et al pg1842
7
8
9
10

11
12 This anxiety could be alleviated by support from a trusted health care provider or
13
14 other person.
15

16
17 *“The best thing about it was that nobody acted like I was a bad person*
18 *because I was on these medications and was having to be going through this*
19 *really slow process of coming down off of them.”* Frank et al pg1843
20
21
22

23
24 Successful tapering was described as a collaborative agreement between HCP and
25
26 patient.
27

28
29 *“She put me down to 2 and a half [pills per day]. Then she said, okay, we'll*
30 *go down to half a pill. I told her I didn't think that just 2 a day would do it,*
31 *and she said okay, we'll try 2 and a half, are you agreeable with that? I said*
32 *that's fine. I mean, we can discuss stuff. It doesn't have to be a disagreement*
33 *because we can talk about it. It's not an argument. We're 2 adults having a*
34 *conversation, figuring out what to do.”* Matthias et al 2017 pg 1369
35
36
37
38
39
40

41
42 However, not all people experienced joint decision making when tapering
43

44
45 *“I just don't feel that he's understanding. he don't seem to care what I'm*
46 *saying, because he's lowering it down anyway, even though I've told*
47 *him...that I didn't agree with it being lowered.”* Matthias et al 2017 pg 1369
48
49
50

51
52 For those in the USA, prescribing policies, advising clinicians to monitor and
53
54 decrease opioid use, and the legislation to enforce these policies made those taking
55
56 opioids feel as if they were ‘a public health problem’. This could have a negative
57
58
59
60

1
2
3 effect on the doctor patient relationship and leave the patient feeling disempowered.

4
5 This was compounded when opioids had been withdrawn by legislation.^{23, 44}

6
7
8 *“I have to struggle, suffer, to make the next the next time that I can get my*
9
10 *medicine. And I don’t think that’s fair to me because if I can take my medicine*
11 *a little more regularly , I would be able to do more.....I don’t think that the*
12 *law, people, politicians, or anybody should be able to tell anybody that’s in*
13 *pain what type of medicine they can take.” Al Achkar et al pg 7*

14
15
16
17
18
19 *“That kinda got me mad, cause I thought well you know. . .they’re taking it off*
20 *the market because of people abusing it. . .It’s not fair to us, you know. . . . I*
21 *think the government was wrong to. . . pull them off the market, you know,*
22 *because of people abusing them, no like they weren’t looking at the people*
23 *that need them. . .But I think it’s really unfair that people that really do need*
24 *them can’t get them.” Chang and Ibrahim 2017 pg 3*

34 **Overarching theme: Constantly balancing**

35
36
37 After considering the five themes, an overarching theme emerged - ‘Constant
38
39 balancing’. The theme *Reluctant users with little choice* describes the need to balance
40
41 the pros and cons of starting opioids and the need to balance having pain with their
42
43 hesitancy to use opioids.

44
45
46 *“I don’t really like being on a lot of tablets, I’ve never been a tablet person,*
47
48 *um. . . but I mean I can’t have the pain either so it’s one evil outdoing the*
49
50 *other evil.* Paterson et al pg 723

51
52
53 Studies describe balancing the dose for pain management with their side effects to
54
55 allow them to function. Participants constantly weighed up the effects on their life;
56
57 dealing with an internal conflict of unresolved pain versus necessary medication,
58
59
60

1
2
3 being opioid free versus having uncontrolled pain and balancing other stressors
4
5 against opioid dose changes.
6

7
8 *“If you’re going to be able to walk, and you take one pain pill so you can walk*
9
10 *and live life, you’re going to do it, even though you may not like it.”* Penney et
11
12 al pg 6

13
14 The theme *Stigma feeling scared and secretive but needing support*, describes the
15
16 need to balance their hopes for relief with fear of side effects, and also to balance
17
18 whether or not to disclose their opioid use with the risk of being labelled a ‘drug
19
20 seeker’ versus having unrelieved pain.
21
22

23
24 *“I do it for my own protection by not telling them because I see how they react*
25
26 *by reading something in the paper...and it’s just their ignorance. And I don’t*
27
28 *have time. Well they know what’s going on but they don’t get it to this day. So*
29
30 *you have to pick your battles...”* Brooks et al pg 19

31
32
33 The theme *Understanding opioids; the good and the bad*, showed people had different
34
35 levels of understanding but weighed up their decisions and trade-offs against their
36
37 pain relief.
38
39

40
41 *“It’s, it’s got a good and bad side, morphine.When I take it, it works*
42
43 *really, really well but it makes you feel rather sick, umm, rather spaced out*
44
45 *and thinking wise, umm, it outcomes more on the other, do I want to be sick or*
46
47 *do I want to cry with pain? So I’d rather be sick but it is a very, very good*
48
49 *painkiller.”* Blake et al pg 105

50
51 The therapeutic alliance theme showed that often it was evident that they were ‘not on
52
53 the same page’ with them balancing the advice from their doctors with what they
54
55 wanted.
56
57
58
59
60

1
2
3 “[My provider] said you could die any time, and my husband and I said, well,
4
5 we realize that, but because of the pain, you know, we were willing to take that
6
7 risk that I would die from the narcotic medication.” Frank et al pg 1841
8
9

10 It also meant that there were multiple barriers to the process of decreasing opioids due
11
12 to this constant balancing act which is described in the theme *the challenge of*
13
14 *tapering/withdrawal from opioids*.
15

16
17 “I will tell her, if I do come off this medication, there are going to be
18
19 consequences. I can’t walk as often, I can’t stand as long, I just can’t do it....”
20
21 Vallerand et al 1 pg 169
22
23

24 25 Discussion

26
27 Our five themes were; 1) Reluctant users with little choice; 2) Understanding opioids:
28
29 the good the bad; 3) A therapeutic alliance: not always on the same page; 4) Stigma:
30
31 feeling scared and secretive but needing support; and 5) The challenge of tapering or
32
33 withdrawal. An overarching theme of ‘constantly balancing’ emerged from the data.
34
35 These themes all had positive and negative aspects although the negative were more
36
37 prevalent by far.
38
39

40 We present a line of argument of how complex it is for the patient to balance
41
42 decisions at every stage of their journey. First their reluctance to start taking opioids
43
44 but feeling they had no option. Patients are given opioids for CNMP often as a last
45
46 resort when all other treatment has failed and their lives are so profoundly affected
47
48 that they talk of a desperation, that they would literally ‘try anything’. Patients spoke
49
50 about not being given any detailed information about opioids and that they had
51
52 learned more about them over time from different sources. This varied understanding
53
54 about opioids and their side effects can affect the decisions that people make. Patients
55
56 reported the need to keep the dosage of opioids as low as possible and often that they
57
58
59
60

1
2
3 were not at risk of addiction or overdose if they were taking them as prescribed. Even
4
5 those who felt they may be addicted sometimes viewed this as an acceptable trade-off
6
7 for pain relief. Our findings indicate that patient desperation combined with
8
9 inadequate information from healthcare professionals could trigger the prescription of
10
11 opioids. It may be that delivering accurate information about the potential side effects
12
13 and limited efficacy of opioids for chronic pain management would reduce the use of
14
15
16
17 opioids.

18
19 Our findings demonstrate that the stigma surrounding how patients feel about being
20
21 on opioids can be compounded by the judgements of others. Although patients often
22
23 describe themselves in terms of 'reluctant users', if they experienced the benefits of
24
25 opioids through decreased pain and thus increased function they are often too scared
26
27 to reduce opioids and return to a life of potentially unmanaged pain.
28
29
30
31

32
33 Our findings suggest that clinicians and patients with chronic pain are not always 'on
34
35 the same page'. The theme *a therapeutic alliance* captures the positives, but also the
36
37 tensions and mismatches of perceptions held by healthcare providers who are
38
39 attempting to limit dose escalation, and patients who may view constant dose
40
41 escalation as an acceptable trade-off for reducing relentless pain. The therapeutic
42
43 alliance is a robust theme supported by 26 of the 31 studies included. This is not
44
45 surprising as patients rely on their health care professionals to prescribe opioids. This
46
47 finding resonates with qualitative evidence syntheses (QES) exploring the experience
48
49 of patients¹³ and healthcare professionals⁴⁸ It seems clear that joint decision -making
50
51 is important for appropriate healthcare; however, our findings suggests that there are
52
53 instances of mistrust on both sides. A QES exploring clinicians experience of
54
55 prescribing opioids for chronic pain demonstrate that the process of prescribing
56
57
58
59
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1
2
3 opioids is not straightforward for clinicians who face a complex decision - 'Should I
4 shouldn't I' prescribe opioids for chronic non-malignant pain⁴⁸. They also
5 demonstrate that clinicians must walk a fine line to balance the pros and cons of
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opioids whilst also maintaining patient trust. This suggests that both patients and HCPs find dealing with prescribing/taking opioids for CNMP is complex and involves balancing and trade-offs.

Current guidance from Royal College of Anaesthetists in the UK and The Centers for Disease Control and Prevention in the US advocate a preference for non-opioid therapies in the treatment of CNMP⁴⁹. If a clinician feels that opioids are indicated, then they recommend a low dose for a short duration which should be assessed for effectiveness and regularly evaluated for benefits and harms. All but four studies in this review are between 2005 and 2017, prior to these guidelines. Opioid contracts in some areas of the USA and Canada can make patients feel stigmatised and judged, this effect can be moderated by a good therapeutic relationship, and reframing these as agreements rather than contracts⁵⁰. Some physicians may view contracts/agreements as necessary to guard against uncontrolled dose escalation, repeated demands for replacement of lost or misplaced medication, subversion and illicit opioid intake. This finding resonates with Toye et al (2017) who describe the moral boundary work and social guardianship that clinicians associate with opioid prescription. Our findings suggest that this role does may not contribute to an effective therapeutic partnership.

Limitations of this study

A majority of the studies are from the United States and the findings need to be taken in the context of its health and social care systems. Most of the articles in this qualitative synthesis were published or the research was conducted, before the impact

1
2
3 of the opioid epidemic became clear to regulators and the medical profession. Some
4
5 papers discuss using opioids as a last resort, although the opioid epidemic, especially
6
7 in the US indicates that the threshold for prescribing opioids was low until recent
8
9 initiatives to discourage prescribing long-term opioids for chronic pain⁵¹. Not all
10
11 studies gave morphine equivalent data so we cannot determine what proportion were
12
13 taking high, medium or low doses. We acknowledge that our interpretation of the
14
15 data might have been influenced by the current, much more critical perception of
16
17 opioid use for chronic non-malignant pain. Further evidence is needed to find out if
18
19 these themes are universal for developed countries or whether there are important
20
21 differences.
22
23
24

25
26 Our conceptual framework highlights patients need to constantly balance and to
27
28 consider the pros and cons of taking opioids. This can have a profound effect on
29
30 peoples' relationships with their family, friends and health care providers and their
31
32 perceived standing in the community which is reflected in their careful balancing of
33
34 disclosure. The therapeutic alliance and having a clear understanding of all the
35
36 positive and negative aspects of opioids were important factors that underpinned their
37
38 ability to maintain this fragile balance. This balance might also affect a person's
39
40 desire or ability to taper or withdraw from opioids.
41
42
43

44
45 The GRADE-CERQual ratings (table 2) revealed we had confidence in the findings
46
47 with only a few minor concerns and no moderate or serious concerns.
48
49

50 **Conclusions and recommendations for future research**

51
52 The first meta-ethnography on this topic revealed a constant balancing and a life in
53
54 flux in an effort to maintain participation in life and relationships. These are important
55
56 features of opioid use for CNMP. To maintain this delicate balance they often need
57
58 support from family or clinicians, however this balance can be upset by the feeling of
59
60

1
2
3 being judged by this same potential support system or peers and society at large
4
5 through the media. The therapeutic alliance with healthcare professionals, the extent
6
7 of people's understanding as well as the stigma attached to opioid use need to be
8
9 navigated by people who are often reluctant to be on opioids in the first place.
10
11
12

13 **Authors Contribution**

14
15
16
17 VN and KS contributed to the review concept and design as part of the I-WOTCH
18
19 process evaluation team. HS, SE, MU and KS were involved in the design of the
20
21 IWOTCH study. VN, KS and FT screened search results or extracted data, conducted
22
23 the analysis and synthesis. All authors contributed to data interpretation, revised the
24
25 final manuscript critically for important intellectual content and appraised the final
26
27 manuscript. VN prepared the final manuscript and will be the corresponding author.
28
29
30
31
32

33 **Funding**

34
35 This project was funded by the National Institute for Health Research, Health
36
37 Technology Assessment (project number 14/224/04). The views and opinions
38
39 expressed therein are those of the authors and do not necessarily reflect those of the
40
41 HTA, NIHR, NHS or the Department of Health. Ethics approval was provided by
42
43 Yorkshire and the Humber South Yorkshire Research Ethics committee on 13-9-16.
44
45
46
47

48 **Declaration of competing interests**

49
50 KS has undertaken other meta-ethnographies and was on the NIHR HS&DR Board
51
52 until January 2018.

53
54 SE is investigator on a number of NIHR and industry sponsored studies. He received
55
56 travel expenses for speaking at conferences from the professional organisations. SE
57
58 consults for Medtronic, Abbott, Boston Scientific and Mainstay Medical, none in
59
60

1
2
3 relation to opioids. SE is chair of the BPS Science and Research Committee. SE is
4
5 deputy Chair of the NIHR CRN Anaesthesia Pain and Perioperative Medicine
6
7 National Specialty Group. SE's department has received fellowship funding from
8
9 Medtronic as well as nurse funding from Abbott.

10
11
12 HS is director of Health Psychology Services Ltd, providing psychological services
13
14 for a range of health related conditions.

15
16
17 MU was Chair of the NICE accreditation advisory committee until March 2017 for
18
19 which he received a fee. He is chief investigator or co-investigator on multiple
20
21 previous and current research grants from the UK National Institute for Health
22
23 Research, Arthritis Research UK and is a co-investigator on grants funded by the
24
25 Australian NHMRC. He is an NIHR Senior Investigator. He has received travel
26
27 expenses for speaking at conferences from the professional organisations hosting the
28
29 conferences. He is a director and shareholder of Clinvivo Ltd that provides electronic
30
31 data collection for health services research. He is part of an academic partnership with
32
33 Serco Ltd related to return to work initiatives. He is a co-investigator on a study
34
35 receiving support in kind from Stryker Ltd. He has accepted honoraria for teaching
36
37 from CARTA. He is an editor of the NIHR journal series, and a member of the NIHR
38
39 Journal Editors Group, for which he receives a fee.
40
41
42
43
44
45
46

47 Data Availability Statement: Data is available on reasonable request.

48 49 50 **Acknowledgements**

51
52 We would like to thank Samantha Johnson an academic librarian who helped with the
53
54 electronic searches and Dr Stephanie Tierney who helped to screen the citations.
55
56

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Figure 1 Concept model

Figure 2 PRISMA flow diagram

Figure 1 Concept model of the experiences of people taking opioid medication for chronic non-malignant pain

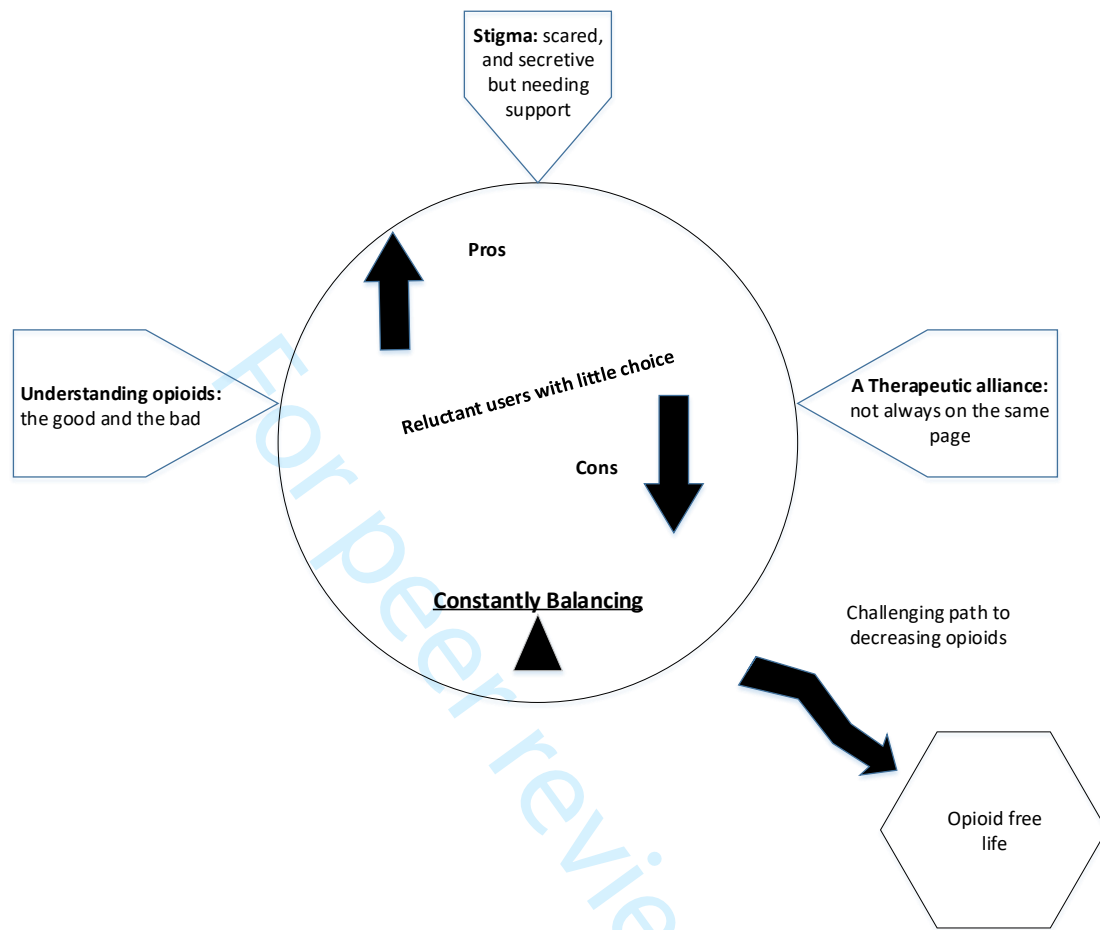
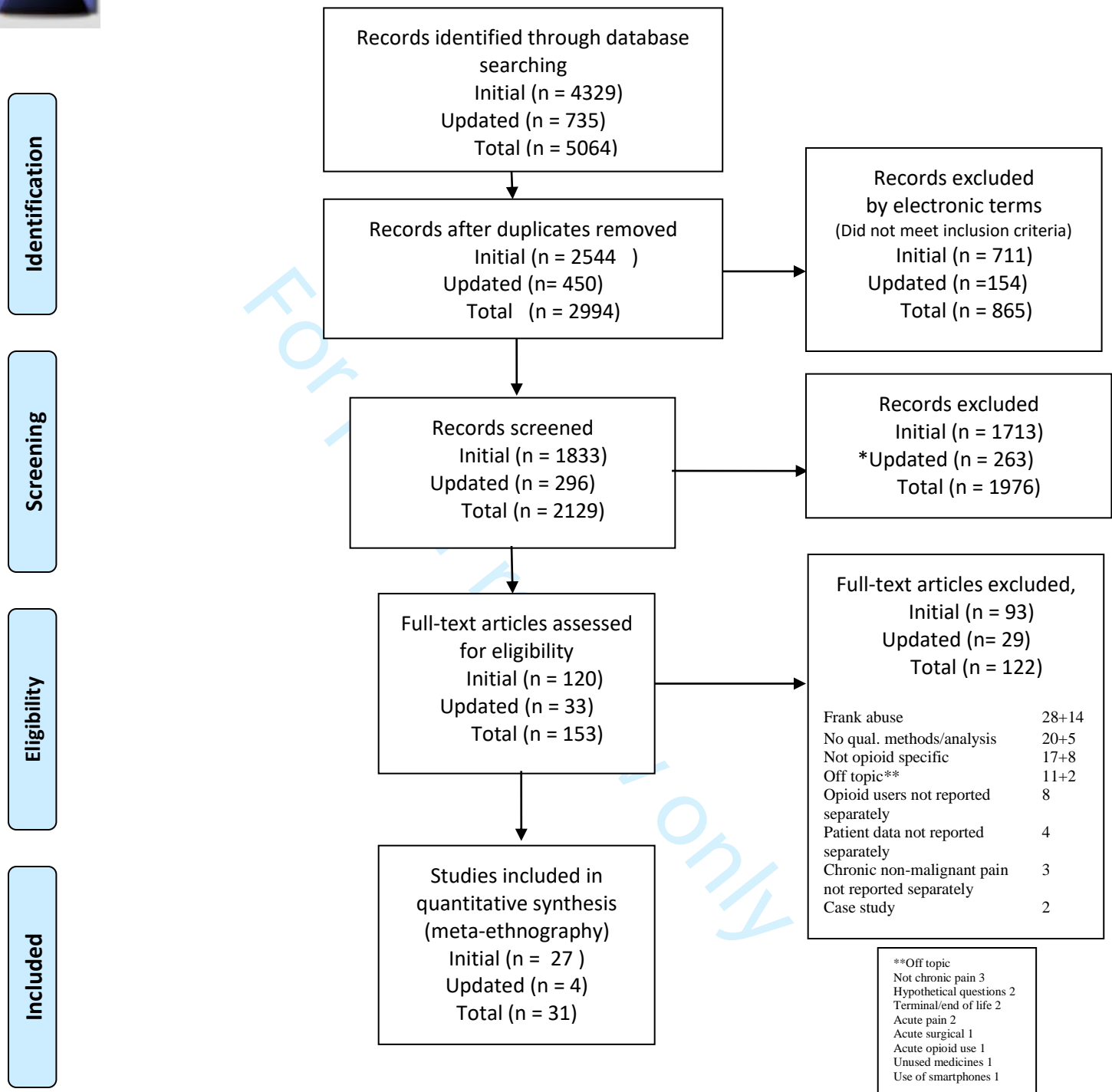




Figure 2: PRISMA Flow Diagram



Initial search June 2017 and updated search Sept 2018 reported.

The search dates for the rerun could be specified in some databases, but not all. Therefore some papers were found in both searches. These twice found duplicate papers were removed at this point*

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Appendix 1 The eMERGe meta-ethnography reporting guidance

Numbered criteria headings with explanatory reporting criteria	Page
Phase 1—Selecting meta-ethnography and getting started	
<i>Introduction</i>	
1 Rationale and context for the meta-ethnography Describe the gap in research or knowledge to be filled by the meta-ethnography, and the wider context of the meta-ethnography	4
2 Aim(s) of the meta-ethnography Describe the meta-ethnography aim(s)	4
3 Focus of the meta-ethnography Describe the meta-ethnography review question(s) (or objectives)	4
4 Rationale for using meta-ethnography Explain why meta-ethnography was considered the most appropriate qualitative synthesis methodology	4
Phase 2—Deciding what is relevant	
<i>Methods</i>	
5 Search strategy Describe the rationale for the literature search strategy	4/5
6 Search processes Describe how the literature searching was carried out and by whom	4/5
7 Selecting primary studies Describe the process of study screening and selection, and who was involved	5
<i>Findings</i>	
8 Outcome of study selection Describe the results of study searches and screening	16
Phase 3—Reading included studies	
<i>Methods</i>	
9 Reading and data extraction approach Describe the reading and data extraction method and processes	6
<i>Findings</i>	
10 Presenting characteristics of included studies Describe characteristics of the included studies	Table1
Phase 4—Determining how studies are related	
<i>Methods</i>	
11 Process for determining how studies are related Describe the methods and processes for determining how the included studies are related: - Which aspects of studies were compared AND- How the studies were compared	6
<i>Findings</i>	
12 Outcome of relating studies Describe how studies relate to each other	17
Phase 5—Translating studies into one another	16
<i>Methods</i>	
13 Process of translating studies Describe the methods of translation: - Describe steps taken to preserve the context and meaning of the relationships between concepts within and across studies- Describe how the reciprocal and refutational translations were conducted- Describe how potential alternative interpretations or explanations were considered in the translations	16
<i>Findings</i>	
14 Outcome of translation Describe the interpretive findings of the translation.	17 to 28
Phase 6—Synthesizing translations	
<i>Methods</i>	
15 Synthesis process Describe the methods used to develop overarching concepts (“synthesised translations”)Describe how potential alternative interpretations or explanations were considered in the synthesis	16
<i>Findings</i>	
16 Outcome of synthesis process Describe the new theory, conceptual framework, model, configuration, or interpretation of data developed from the synthesis	Figure 1
Phase 7—Expressing the synthesis	

<p><i>Discussion</i></p> <p>17 Summary of findings Summarize the main interpretive findings of the translation and synthesis and compare them to existing literature</p>	28 to 30
<p>18 Strengths, limitations, and reflexivity Reflect on and describe the strengths and limitations of the synthesis: - Methodological aspects—for example, describe how the synthesis Findings were influenced by the nature of the included studies and how the meta-ethnography was conducted. - Reflexivity—for example, the impact of the research team on the synthesis findings</p>	30
<p>19 Recommendations and conclusions Describe the implications of the Synthesis</p>	31

Reference: France et al. BMC Medical Research Methodology (2019) 19:25
<https://doi.org/10.1186/s12874-018-0600-0>

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Appendix 2 – example of search terms

Scopus

((TITLE-ABS-KEY(buprenorphine or fentanyl or heroin or hydromorphone or methadone or morphine or opium or oxycodone or pentazocine or tramadol or opiate* or opioid*) OR TITLE-ABS-KEY(suboxone or bunavail or zubsolv or dipipanone or diconal or wellconal or diamorphine or duragesic or fentora or actiq or abstral or recivit or effentora or instanyl or pecfent or oxycontin or roxicodone or oramorph or papaveretum or omnopon or fortral)OR TITLE-ABS-KEY(osegon or "talwin nx" or pethidine or meperidine or demerol or tapentadol or nucynta or palexia or tapal or ultram or zytram))) and ((TITLE-ABS-KEY(qualitative w/5 (theor* or study or studies or research or analysis)) OR TITLE-ABS-KEY(ethno* or emic or etic or phenomenolog* or hermeneutic* or heidegger* or husserl* or colaizzi* or giorgi* or glaser or strauss or (van and kaam*) or (van and manen) or ricoeur or spiegelberg* or merleau) OR TITLE-ABS-KEY(constant w/3 compar*) OR TITLE-ABS-KEY(focus w/3 group*) OR TITLE-ABS-KEY(grounded w/3 (theor* or study or studies or research or analysis)) OR TITLE-ABS-KEY(narrative w/3 analysis) OR TITLE-ABS-KEY(discourse w/3 analysis) OR TITLE-ABS-KEY((lived or life) w/3 experience*) OR TITLE-ABS-KEY((theoretical or purposive) w/3 sampl*) OR TITLE-ABS-KEY("field note*" or "field record*" or fieldnote*) OR TITLE-ABS-KEY(participant* w/3 observ*) OR TITLE-ABS-KEY("action research") OR TITLE-ABS-KEY("digital adj record*" or audiorecord* or taperecord* or videorecord* or videotap*) OR TITLE-ABS-KEY(cooperative and inquir*) OR TITLE-ABS-KEY(co and operative and inquir*) OR TITLE-ABS-KEY(co-operative and inquir*) OR TITLE-ABS-KEY(("semi-structured" or semistructured or unstructured or structured) w/3 interview*) OR TITLE-ABS-KEY((Informal or in-depth or indepth or "in depth") w/3 interview*) OR TITLE-ABS-KEY(("face-to-face" or "face to face") w/3 interview*) OR TITLE-ABS-KEY("ipa" or "interpretive phenomenological analysis") OR TITLE-ABS-KEY(social and construct*) OR TITLE-ABS-KEY("appreciative inquiry") OR TITLE-ABS-KEY(poststructural* or "post structural*" or post-structural*) OR TITLE-ABS-KEY(postmodern* or "post modern*" or post-modern*) OR TITLE-ABS-KEY(feminis*) OR TITLE-ABS-KEY(humanistic or existential or experiential))) and (TITLE-ABS-KEY(pain))

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Appendix 3 Critical Appraisal Skills Programme (CASP) Quality appraisal tool scores

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Score
Arnaert 2006	Yes	Yes	Yes	Yes	?	No	Yes	Yes	Yes	Yes	17/20
Bergman 2013	Yes	Yes	Yes	Yes	Yes	No	Yes	?	Yes	Yes	17/20
Blake 2007	Yes	Yes	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	19/20
Brooks 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	?	Yes	Yes	17/20
Buchbinder 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Chang F 2017	Yes	Yes	Yes	Yes	Yes	No	?	?	Yes	Yes	16/20
Chang Y-P 2011	Yes	Yes	Yes	Yes	Yes	No	Yes	?	?	Yes	16/20
Coyne 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	?	Yes	Yes	17/20
Esquibel 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	20/20
Frank 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	20/20
Green 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Hooten 2011	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Krebs 2014	Yes	Yes	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	19/20
Matthias 2014	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
McCrorie 2015	Yes	Yes	?	Yes	Yes	No	Yes	Yes	Yes	Yes	17/20
Mueller 2017	Yes	Yes	Yes	Yes	?	No	Yes	Yes	?	Yes	16/20
Paterson 2016	Yes	Yes	Yes	Yes	Yes	?	?	Yes	Yes	Yes	18/20
Penney 2017	Yes	Yes	?	?	?	?	Yes	?	?	?	13/20
Rieb 2016	Yes	Yes	Yes	Yes	Yes	?	Yes	?	Yes	Yes	18/20
Simmonds 2015	Yes	Yes	?	Yes	Yes	?	Yes	Yes	?	?	16/20
St Marie 2016	Yes	Yes	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	19/20
Vallerand 1 2009	Yes	Yes	Yes	Yes	Yes	No	No	Yes	?	Yes	15/20
Vallerand 2 2010	Yes	Yes	Yes	?	Yes	No	No	Yes	?	?	13/20
Wallace 2014	Yes	Yes	Yes	Yes	Yes	No	Yes	?	?	Yes	16/20
Warms 2005	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	16/20
Zgierska 2016	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Zheng 2013	Yes	Yes	Yes	Yes	Yes	No	?	Yes	Yes	Yes	17/20
Al Achkar 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Matthias 2017	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	18/20
Matthias 2018	Yes	Yes	Yes	Yes	Yes	?	Yes	Yes	Yes	Yes	19/20
Smith 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	20/20

Legend 1 Critical Appraisal Skills Programme (CASP) questions scoring: Yes =2 ? (Can't Tell) = 1 No = 0

Q1. Was there a clear statement of the aims of the research?

Q2. Is a qualitative methodology appropriate?

Q3. Was the research design appropriate to the aims of the research?

Q4. Was the recruitment strategy appropriate to the aims of the research?

Q5. Was the data collected in a way that addressed the research issue?

Q6. Has the relationship between researcher and participants been adequately considered?

Q7. Have ethical issues been taken into consideration?

Q8. Was the data analysis sufficiently rigorous?

Q9. Is there a clear statement of findings?

Q10. How valuable is the research?